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Evaluation of the Role of Gum Arabic Extract on Renal Damage Induced by Oral Bisphenol A Administration in White Rats

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Abstract:

In the current review, we explored the impact of Gum arabic (GA) against Bisphenol A (BPA)- prompted nephrotoxicity in male albino rats. Thirty-five adult male albino rats were divided into five groups: group (1) served as a control, group (2) rats received 8 mg/ kg of GA extract, group (3) received BPA 50 mg / kg b.wt. by oral gavage, group (4) consists of rats received first GA extract + BPA, and finally group (5) consists of rats received first BPA + GA extract. Urea, Creatinine, Superoxide dismutase (SOD) glutathione (GSH), and malondialdehyde (MDA) were assayed, in addition to histological study. The results of this study showed that there was a significant increase in the levels of all urea, Creatinine, and MDA, and a significant decrease in the levels of both GSH and SOD in the third group exposed to BPS, while there was a significant decrease in all of urea, Creatinine, and MDA, and a significant increase in the level of antioxidants GSH, SOD in the fourth and fifth groups Which was dosed with GA extract and BPS. Histopathological changes of kidney were observed in third group (treated with BPA) and fourth group (BPA + GA treated) as compared to control group. This study demonstrated the antioxidant effect of GA and against BPS -induced renal injury.

Keywords: Bisphenol A; Gum arabic ; kidney; SOD ; Albino Rats.

تأثير الصمغ العربي على كبد وكلى ذكور الجرذ الابيض المعاملة بمركب بيسفينول *A* ، دراسة نسيجية وفسيولوجية.

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الخلاصة

في دراستنا الحالية، وضحنا تأثير الصمغ العربي (GA) ضد السمية الكلوية الناجمة عن مادة بيسفينول أ (BPA) في ذكور الفئران البيضاء. خمسة وثلاثين من ذكور الفئران البيضاء البالغة تم تقسيمهم عشوائيا إلى خمس مجموعات: المجموعة (1) عملت كمجموعة سيطرة، المجموعة (2) جرعت الجرذان 8 مجم / كجم من مستخلص الصمغ العربي، المجموعة (3) جرعت فمويا بـ 50 مجم / كجم من وزن الجسم من مادة بيسفينول أ ، المجموعة (4) جرعت أولا مستخلص صمغ عربي + مادة بيسفينول أ، وأخيرًا المجموعة (5) جرعت اولا مادة بيسفينول أ + مستخلص الصمغ العربي . تم تحليل اليوريا والكرياتينين وفائق أكسيد ديسميوتاز والجلوتاثيون والمالونداييهايد ، بالإضافة إلى الدراسة النسيجية .أظهرت نتائج هذه الدراسة وجود زيادة معنوية في مستويات كل من اليوريا والكرياتينين والمالونداييهايد وانخفاض معنوي في مستويات كل من الجلوتاثيون وفائق أكسيد ديسميوتاز في المجموعة الثالثة المعرضة للبيسفينول أ، بينما كان هناك انخفاض معنوي في كل من اليوريا والكرياتينين والمالونداييهايد وارتفاع معنوي في مستوى مضادات الأكسدة الجلوتاثيون وفائق أكسيد ديسميوتاز في المجموعتين الرابعة والخامسة التي تم معاملتها بمستخلص الصمغ العربي وبيسفينول أ، كما لوحظت تغيرات نسيجية مرضية في الكلى في المجموعة الثالثة (المعالجة ببيسفينول أ) والمجموعة الرابعة (المعالجة ببيسفينول أ + الصمغ العربي) مقارنة بمجموعة السيطرة. وقد أظهرت هذه الدراسة التأثير المضاد للأكسدة للصمغ العربي ضد إصابة الكلى الناتجة عن البيسفينول أ.

1. Introduction

Bisphenol A (BPA) is widely used worldwide. It is mainly used in the production of polycarbonate plastic and epoxy resin. It is used as an intermediate in the manufacture of various products due to its light weight, hardness, and resistance to temperature [1].
The increased use of BPA has led to the occurrence of some health problems, and these problems include the impact on the growth and neurological development of children and fetuses, and the increased risk of autism, hyperactivity disorder, and learning disorders[2]. It may also affect the cardiovascular and respiratory systems, as it increases the risk of heart disease, high blood pressure, and asthma, chronic bronchitis and abnormalities in liver enzymes and kidney function[3].

Exposure to high concentrations of BPA causes abnormalities in the cardiovascular system through the presence of adverse effects of BPA in the brain and leads to the formation of multinucleated giant cells[4]. It also causes rupture of hepatic cell membranes, the release of their enzymes, and the occurrence of toxic stress in liver tissue, and the kidneys, brain and other organs by forming reactive oxygen species (ROS)[5].

The discovery of pure and effective compounds of plants in the nineteenth century led to a major development in the field of treatment with natural extracts to take up a large part of the molecular sciences that helped to identify and extract many natural and pure compounds with effective biological activity, which are among the most important chemical compounds found in the gum arabic plant[6].

Gum Arabic (GA) is considered a widely used antioxidant and is a natural resinous substance secreted from the stems and branches of trees belonging to the Acacia senegal genus[7]. It is an important commercial substance consisting of polysaccharides and contains calcium, magnesium, and potassium salts[8]. It is used in the manufacture of foodstuffs such as soft drinks and gelatin desserts[9].

As GA treatment reduces lipid peroxidation and enhances the activities of antioxidant enzymes and their mRNA expression in hepatocytes of diabetic mice[7], also oral administration of GA offers numerous health benefits for various organs and diseases[10]. GA has potent antioxidant effects in patients with sickle cell iron deficiency through its capacity to increment total antioxidant capacity (TAC)[11]. The current study aimed to evaluate the effectiveness of gum arabic against nephrotoxicity induced by bisphenol A.

2. Material and Methods

2.1 Animals used in the Study

We used 35 male Swiss white rats (Sprague Dawely), whose weight was between 165 and 210 grams with an age of not less than one month and not more than three months. This study was conducted in the animal house of the Department of biology / College of Education for Pure Sciences / University of Anbar, inside plastic cages with metal covers prepared for this purpose. Water ad libitum was provided under 12-hour light and 12-hour dark schedule at room temperature 25^{o}C.

2.2 Bisphenol A (BPA)

(2,2 Bis-4-hydroxyl phenyl propane) was obtained from Sigma Chemical Company and mixed with olive oil [12].

2.3 Preparation of Gum Arabic Extract

Gum Arabic is purchased in local markets in Ramadi city from apothecaries in the form of solid blocks or solid knots. It was ground finely and prepared at a concentration of 15% by

weighing 15 g of GA. It was dissolved in an amount of distilled water and the volume was completed to 100 ml and stirred well to completely dissolve, and the rats were dosed with the glue with water instead of drinking water and placed in opaque glass bottles to prevent its oxidation by light[13]

2.4 The Experiment Design

The animals were divided into (5) groups and distributed randomly, and each group contains (7) animals:

The first group: Control: was given 0.5 ml of olive oil per rat. The second group received aqueous extract of GA 8 g / kg of rat weight. The third group: received BPA 50 mg/kg of rat weight (dissolved in olive oil).The fourth group: Preventive group: first dose received aqueous extract of GA, and after two hours dose received BPA Same concentration as above and Fifth group - Therapeutic group: received only BPA for six weeks, then left for three days, after received aqueous extract of GA. The dosing period for all of the above groups is between one day and another for a period of 90 days.

2.5 Biochemical analysis

Rats were anesthetized through inhalation of diethyl ether to immediately confirm the biomarkers of Renal function include , Serum creatinine and Serum urea were measured by a modified kinetic method determined using assay kits (Linear Research facilities, Aspania) according to the manufacturer's instructions. ,malondialdehyde (MDA) were measured using colorimetric assay[14], The concentration of SOD in serum was estimated following the working method[15], Finally, the procedure to estimate the glutathione (GSH) level followed the technique described by Griffith[16].

Blood samples were collected and processed at −20°C. For the purpose of histopathological examination, a portion of each rat's kidney was preserved in 10% neutral formalin.

2.6 Histological Examination

Kidney samples were fixed in 10% formalin solution. Some kidney sections were fixed in 10% formalin, hydrated in graded alcohol, embedded in paraffin wax, sliced (5 μm) thick and stained with hematoxylin and eosin (HandE). for light microscopic examination [17].

2.7 Statistical analysis

The results obtained from the experiments were represented as mean ± SEM (P value $P \leq 0.05$). Data were analyzed using SPSS software using the one-way analysis of variance (ANOVA) method.

3. Results

3.1 The effect of gum arabic on urea and creatinine concentration

In the results of our current study, it was found that in the third group receiving bisphenol A, there was a significant increase ($P \leq 0.05$) in the concentration of urea and creatinine, while in the second group that was given gum arabic extract, no significant differences appeared when compared with the first group (control), while the results noted a significant reducing ($P \leq 0.05$) in the concentration of urea and creatinine. In the fourth and fifth groups when compared with the third group, noting that the fifth group gave better results than the fourth group (Figure 1,2).

3.2 The effect of gum Arabic on the level of oxidation balance

The results of our current study noted a significant increase in GSH and SOD levels in the second group, while a significant decrease (P≤0.05) was observed in the levels of the previous two enzymes in the third group compared with the control, while no significant differences appeared in the fourth and fifth groups compared with the third group. The results also indicated that there was a non-significant decrease (P≤0.05)in MDA level of the second group, while in the third group there was a significant increase in MDA level compared with the control, while a significant decrease(P≤0.05) in the level of the same indicator above was observed in the fourth and fifth groups compared with the third group. (Figure 3,4,5)

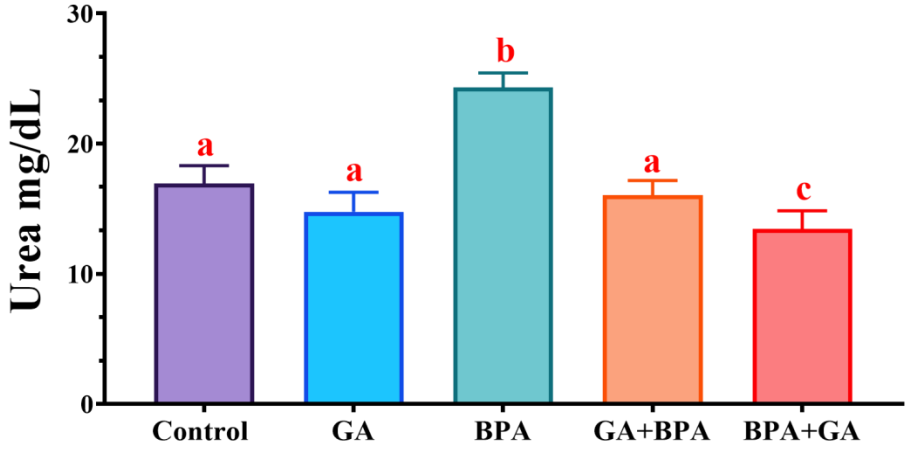

Figure -1 The effect of gum arabic on the concentration of Urea in the blood serum of male white rats treated with bisphenol A.

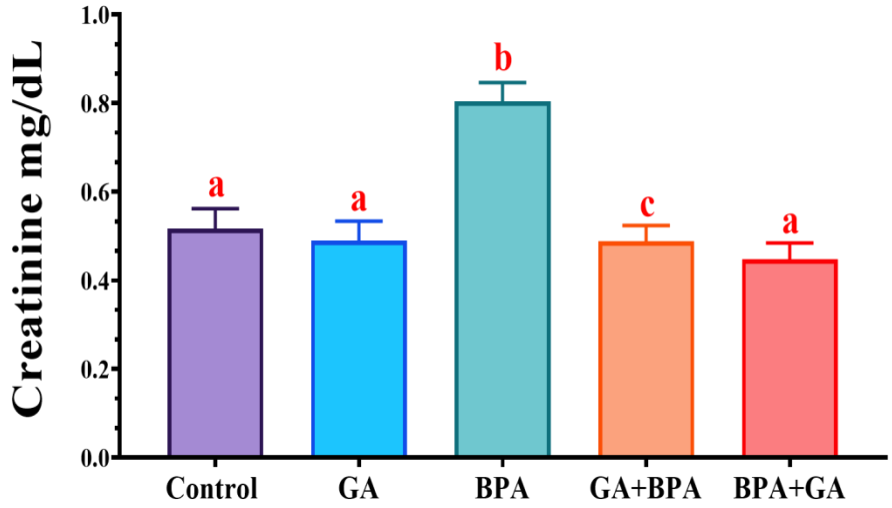

Figure -2 The effect of gum arabic on the concentration of Creatinine in the blood serum of male white rats treated with bisphenol A.

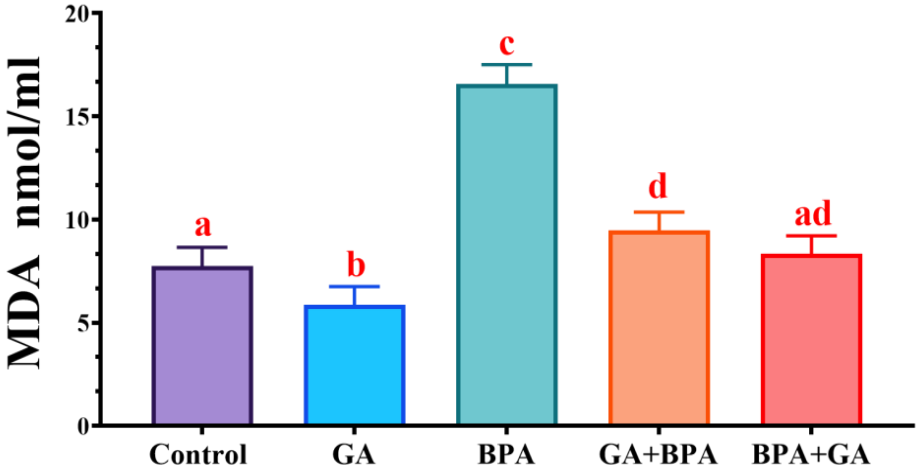

Figure -3 The effect of gum arabic on the concentration of MDA level in the blood serum of male white rats treated with bisphenol A.

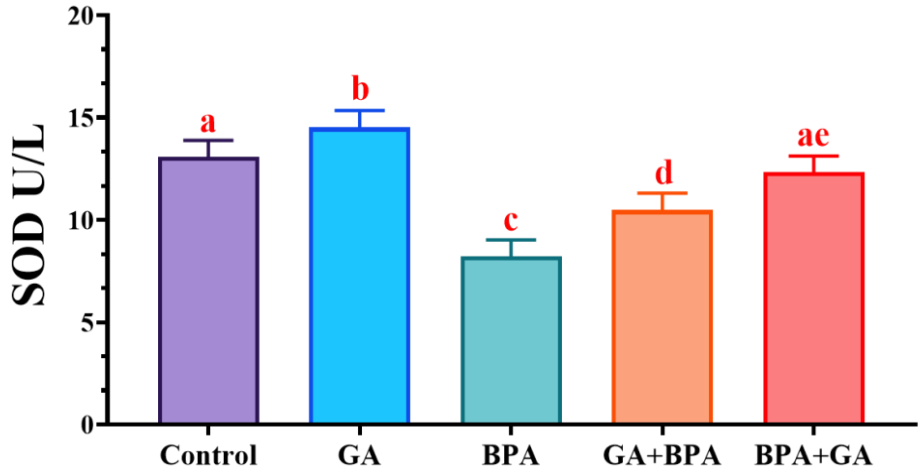

Figure -4 The effect of gum arabic on the concentration of SOD level in the blood serum of male white rats treated with bisphenol A.

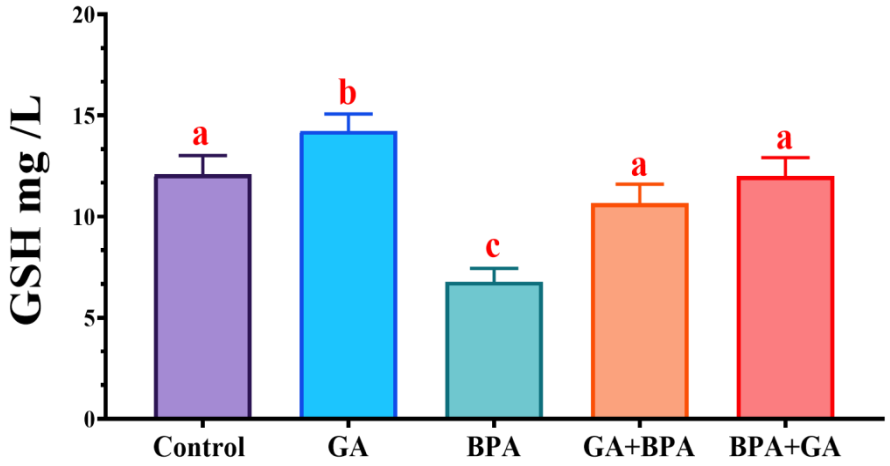

Figure -5 The effect of gum arabic on the concentration of GSH level in the blood serum of male white rats treated with bisphenol A.

3.3 Histological Changes in the Kidney

The results of our current histological study of the control group showed that the kidney cortex contains renal glomeruli, and each glomerulus is surrounded by the capsular space, then by Bowmann's capsule, in addition to the presence of proximal convoluted tubules lined with pyramidal cells, and the lumen of the tubules is serrated, in addition to the presence of distal convoluted tubules lined by simple cuboidal cells with a wide lumen, As shown in Image. (1), the kidney medulla contained renal tubules lined with simple epithelial cuboidal cells, and the interstitium contained some bundles of colloidal fibers and infiltrated white blood cells, fibroblasts, and some phagocytic cells.

As shown in Image (2) in the second group, the histological pattern of the kidney cortex and medulla is almost similar to that of the control group.

While in the third group that was treated with bisphenol A, severe histological changes were observed, represented by the presence of blood congestion between the urinary tubules, and degeneration of the cells lining the proximal and distal convoluted tubule was observed, as well as the presence of necrosis of some lining cells, with the presence of infiltration of inflammatory cells noted in Image (3,4). While in the fourth group, which is the preventive group, it was observed that there were histological changes represented by the presence of a small amount of blood congestion with degeneration and necrosis of a number of cells lining the urinary tubules in Image (5,6), while the histological sections of the fifth group, which is the therapeutic group, showed that the results were better than the rest of the groups, as a recurrence of the histological pattern was observed. To the normal appearance, close to the control group, with some histological effects, including degeneration of a limited number of cells lining the urinary tubules, with a very limited blood congestion observed in Image (7,8).

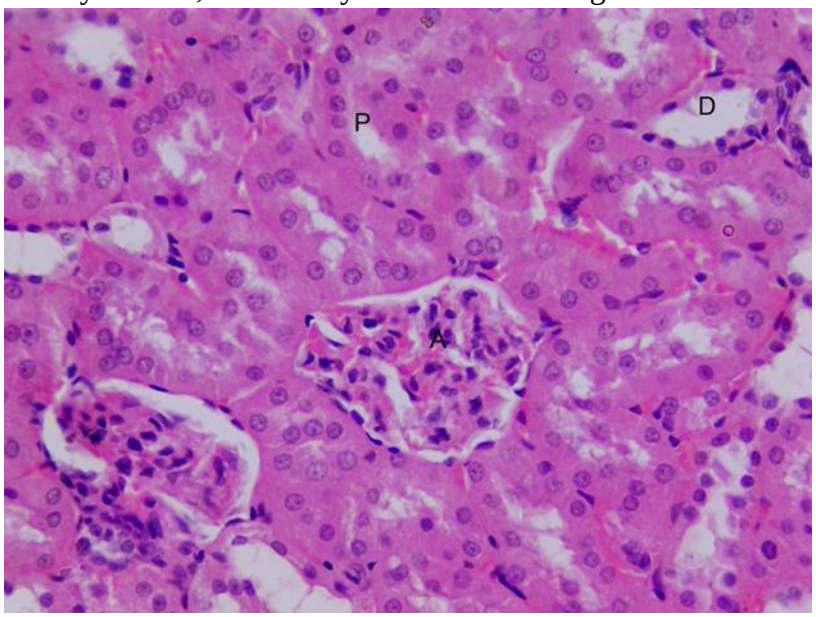

Image -1 A cross-section of the kidney of a control animal showing the histological structure consisting of glomeruli (A) surrounded by proximal (P) and distal (D) tubules, H&E (40X).

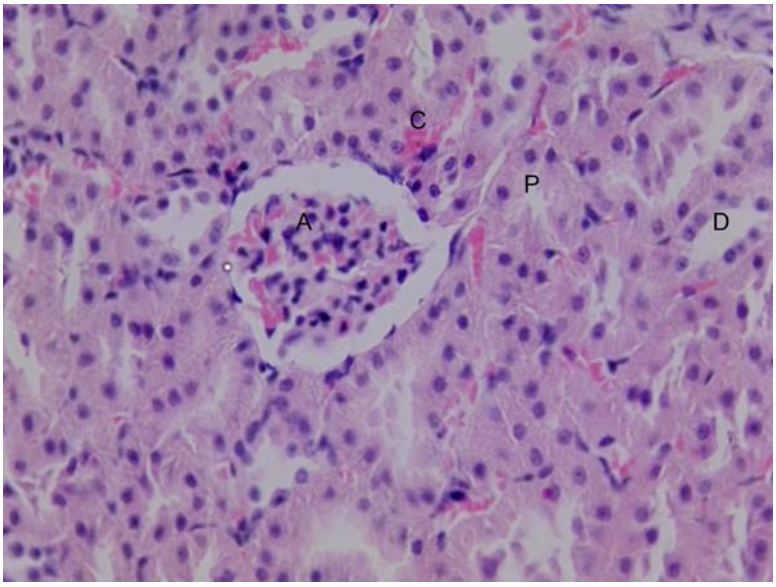

Image-2 A cross-section of a kidney in an animal treated with gum arabic extract, showing the histological appearance close to normal, with the presence of blood congestion (C) in the blood vessels , H&E (40X)

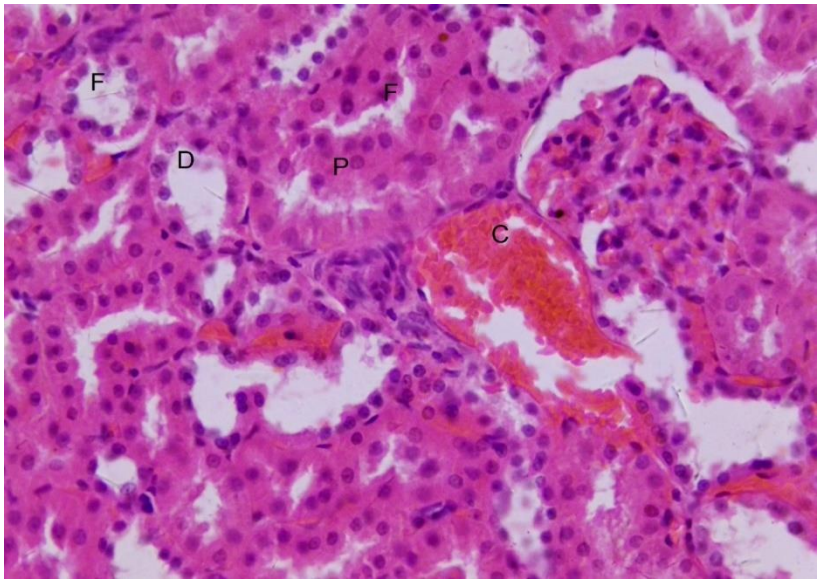

Image -3 A cross-section of a kidney in a bisphenol-treated animal showing the presence of blood congestion (C) and degeneration (D) in the cells lining the proximal and distal tubules (P), H&E (40X).

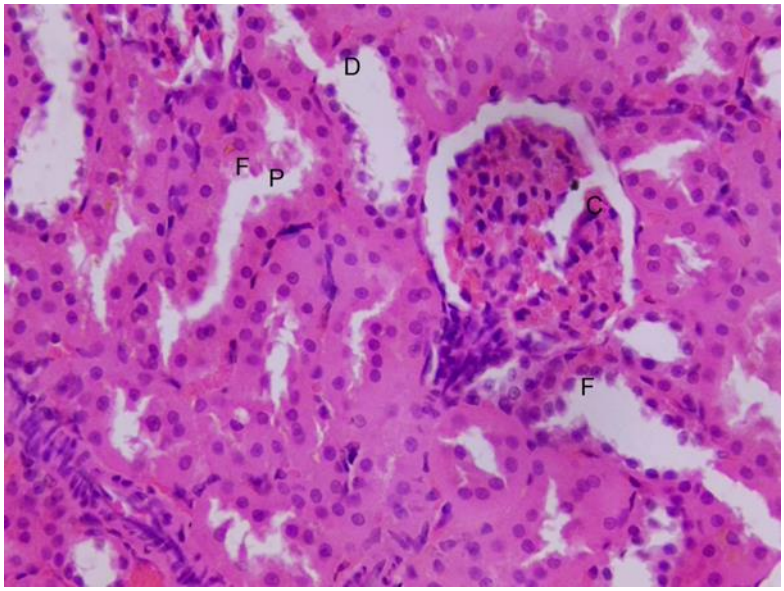

Image -4 A cross-section of the kidney of an animal treated with BPS shows the presence of blood congestion (C), degeneration(D) and necrosis(F) in some cells lining the proximal and distal tubules (P) with infiltration of inflammatory cells (M). , H&E (40X)

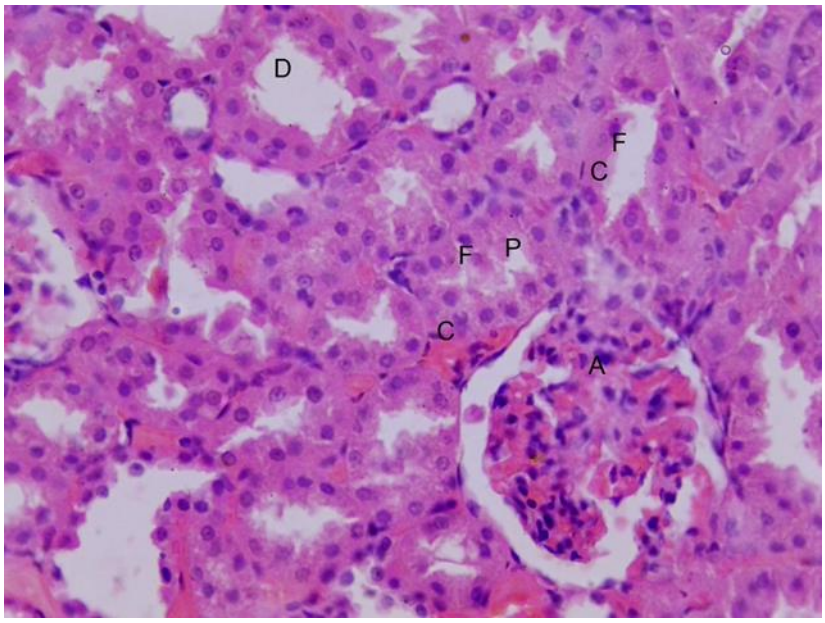

Image -5 A section of the kidney of an animal treated with the GA + BPS, showing the presence of very slight degeneration in the cells lining the tubules (P) and (D) with blood congestion (C), , H&E (40X)

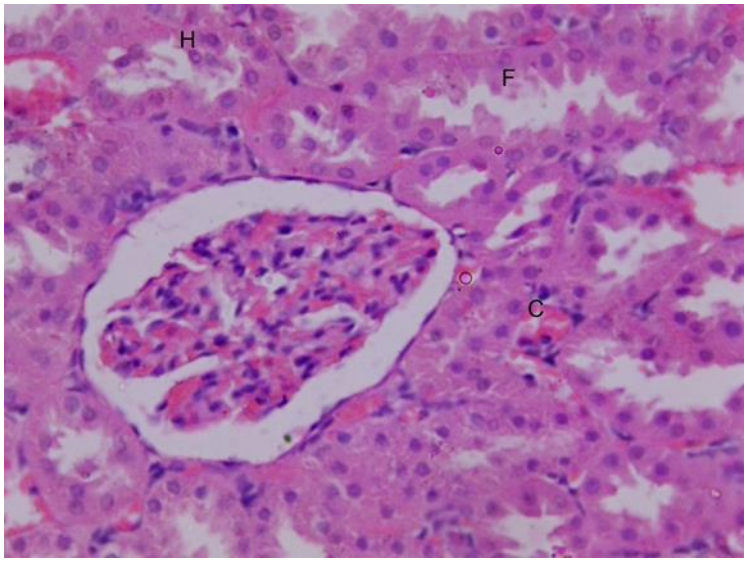

Image -6 A cross-section of a kidney in an animal treated with the GA + BPS, showing the presence of blood congestion (C), with degeneration (F) and necrosis of the cells lining the proximal and distal tubules (D), , H&E (40X)

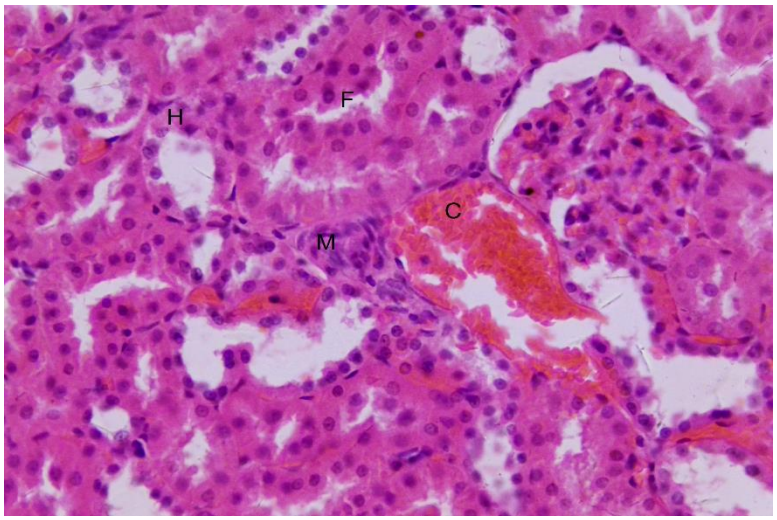

Image -7 A section of a kidney from a therapeutic animal (BPS + GA) showing the near-to-normal shape of the proximal (P) and distal (D) urinary tubules H&E (40X)

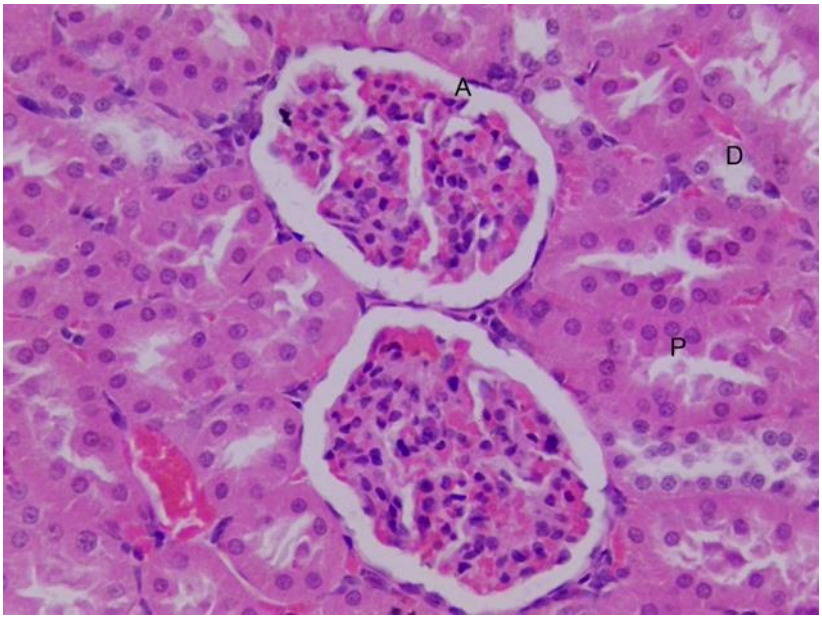

Image -8 A cross-section of the kidney of a therapeutic animal(BPS + GA) showing slight blood congestion (C) and slight degeneration in some cells lining the urinary tubules (F), , H&E (40X)

4. Discussion

The current study, which included measuring renal functions in animals dosed with bisphenol A, showed a significant increase in the concentration of both urea and creatinine. These results are consistent [12]who found serum creatinine levels were significantly elevation. An elevation in creatinine level is due to a decreased ability of the kidney to remove toxic metabolites[18].

An increase in the levels of urea and creatinine in the group treated with BPA is a sign of decreased kidney function, which plays a crucial role in purifying the blood of wastes[19]. When the kidneys are damaged, their ability to effectively filter these wastes decreases, leading to their accumulation in the blood[20].

Bisphenol A can cause kidney damage in several ways, including oxidative stress, as bisphenol can cause an increase in free radicals in the body, leading to oxidative stress. This stress can cause damage to kidney cells[21]. Exposure to bisphenol may also lead to an inflammatory response in the kidneys, causing kidney tissue damage and decreased function[22]. Bisphenol is known to be a substance similar to the effect of estrogen, this hormonal interference can affect overall body functions, including kidney function[23].

Many toxic materials that cause Toxic effect on kidney function can change the glomerular basement membrane and Thus, the efficiency of the glomerular filtration rate changes, Toxic effect on renal function are explained by the accumulation of poisonous metabolites of BPA and Hence, renal dysfunction[24]. The poisonous metabolites of BPA accumulate and the kidney's ability to excrete these toxic substances decreases[25].

Gum arabic can protect the kidneys from damage resulting from bisphenol and other toxins because it contains effective compounds, especially flavonoids, phenols, and alkaloids, in addition to being rich in amino acids, including hydroxyproline, proline, serine, leucine, isoleucine, threonine, and histidine[9]. The fiber found in GA can also help improve kidney function in general by improving metabolism and reducing the accumulation of waste in the body[26]. Gum arabic can also bind to some toxins in the intestines, reducing their absorption

and transmission into the blood circulation, thus reducing the negative impact of these toxins on the kidneys[27].

The current study found that when BPA was taken orally, there was a significant decrease in SOD and GSH and a significant increase in MDA. This imbalance causes a condition known as oxidative stress and damage to organs, Based on these indicators, these observations showed that the process of oxidative stress resulting from treatment with BPS causes damage at the cellular level to liver and kidney tissue[28].

In hemodialysis patients with BPA-containing polysulfone dialysis, there is an association between elevated serum BPA levels and increased markers of oxidative stress[29]. Oxidative stress creates an imbalance between the production of reactive oxygen species and antioxidant defenses, leading to oxidative damage[30]. [31]showed that exposure to BPA decreased antioxidant GSH and SOD and increased MDA levels. This disease caused renal oxidative stress and kidney injury.

Gum arabic helps enhance the activity of antioxidant enzymes such as SOD and GSH, which enhances the body's defenses against free radicals and reduces oxidative damage, also effective role in this may be due to the fact that gum arabic possesses effective chemical compounds such as polyphenolic compounds and flavonoids, which inhibit the formation of free radicals and work to remove them. They also work to increase the activity of liver antioxidant enzymes such as catalase, superoxide dismutase (SOD) and glutathione peroxidase (GPX), which all work to inhibit the oxidation and peroxidation of fats and prevent the production of MDA.. MDA is an end product of lipolysis and can be considered an indicator of oxidative stress[32]. Eating GA may help reduce the production of free radicals, which indicates a reduction in oxidative damage in the body[33]. Therefore, GA can have a positive effect in reducing the harmful effects of BPA by enhancing the body's antioxidant system, providing protection against oxidative stress and improving overall health[34]. Recent data show that GA exerts anti-inflammatory, antioxidant and anti-apoptotic activities to reduce kidney damage in several animal models of kidney damage. , this method is similar to text[35]. There is also evidence that oral administration of GA improves kidney injury in chronic renal illness through anti-inflammatory and antioxidant mechanisms, consistent with[36]. Recent studies in both patients with CKD stage 3–4, and hemodialysis patients, suggests that daily supplementation with GA reduces measures of oxidative stress and inflammatory markers[37]. GA, given orally, has been utilized in the treat-men of CKD in several developing countries such as Iraq and Sudan.

Our study's renal histopathology is consistent with that of [12], who found that mononuclear cell infiltration, Renal capsular atrophy with retraction of the glomerular bunch, expansion of urinary spaces, degenerative changes of renal tubules, and atrophy of renal tubules. The ability of BPA to generate ROS can explain this, thus leading to mitochondrial damage, which contributes significantly to apoptosis.[38] found that the intraperitoneal injection of bisphenol A at a dose of 50 mg/kg for 5 weeks increased the cytoplasm and foot processes in podocytes and increased the presence of thick chromatin.[39] explained that exposure to BPA is linked with thickness for the basement membrane of Bowman's capsule, which was confirmed by Schiff's acid [PAS] intensity of the periodontal acid.

Many nephrotoxic toxins can alter the glomerular basement membrane and influence the glomerular filtration. Also, treatment of rats with BPA induced oxidative damage in the liver tissue[40]. The cytotoxic effect of hepatic and renal cells resulting from the intake of BPS leads to the occurrence of what is known as an imbalance in oxidation between oxidants and

antioxidants, and are characterized by biochemical and histopathological alterations, therefore, we should avoid exposure to bisphenol[41]. More research is needed to characterize Exposure to BPA and clarification of the link between BPA damage to the kidney and liver[25]. GA may work to protect renal cortical tubular epithelial cells from damage caused by free oxygen radicals and prevent the formation of oxidants, supported by GA increased more demand for free radicals , is also beneficial for kidney function, related to its anti-inflammatory and antioxidative effects[42] . The antioxidant properties of GA are due to its compounds, flavonoids and other polyphenols, and these plant compounds have been reported to have antioxidant lipids and antioxidant activity[43]. The conclusion of the study is that the administration of GA to rats by drinking water for 90 days reduced the effects of nephrotoxicity caused by BPS by inhibiting free radicals and increasing kidney function.

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