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The Effect of Treatment with Frankincense on Gentamicin-Induced Nephrotoxicity in Rats

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Abstract

Drug-induced nephrotoxicity is a common cause of acute kidney injury and gentamicin is categorized under one of these nephrotoxic drugs. Using medicinal plants that can ameliorate or delay the deterioration in kidney functions is needed due to their low cost and fewer side effects.Thirty-Five healthy adult male albino rats were divided into five equal groups: (-) control group in which normal rats were fed on a basal diet as a group **(1)**, (+) control - nephrotoxicity rats in which rats were injected with gentamicin and fed on a basal diet as a group **(2)**, groups **(3,4, and 5)** nephrotoxicity rats were fed on a basal diet containing 2.5, 5, and 10% frankincense (*Boswellia sacra)* powder, respectively, for 28 days. Kidney and liver functions, minerals levels, antioxidant status, lipids profile, glucose levels, and histopathological changes were investigated. Results showed a significant increase in body weight and a significant decrease in serum level of urea, creatinine, uric acid, phosphorous, potassium, lipids, glucose, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and albumin, and total protein in groups treated with different levels of frankincense ($P \leq 0.05$). Moreover, there was a significant increase in levels of glutathione peroxidase (GPX), superoxide dismutase (SOD), and Catalase (CAT) as well as a significant decrease in levels of malondialdehyde (MDA), a biomarker of lipid peroxidation ($P \leq 0.05$). Concerning kidney histology, no histopathological alterations were seen in the kidneys of rats treated with 10 % frankincense powder. Study results demonstrated that administration of frankincense for 28 days could ameliorate kidney damage resulting from gentamicin-induced nephrotoxicity in rats.

Key words : Frankincense, Boswellia sacra, Gentamicin, Nephrotoxicity, Rats.

Introduction

The kidney is performing various important functions in the human body such as regulation of fluids outside the cells, detoxification, and excretion of toxic substances ***(Al-Naimiet al., 2019)***. Nephrotoxicity is defined as a rapid reduction in kidney functions caused by the toxic effect of medications and chemicals. The incidence of drug-induced nephrotoxicity is more common in older adults due to an increase in average life span and the increased use of medications. Medications-induced nephrotoxicity is one of the main causes of acute kidney injury (AKI), formerly called acute renal failure. AKI is a major health concern impacting ~13.3 million people worldwide per year. AKI is associated with extended hospitalization, the likelihood of progression to chronic kidney disease, and higher mortality ***(Naughton, 2008; Wang et al. 2014; and Kwiatkowska et al, 2021).***

Renal tubules, especially proximal tubule cells, are considerably influenced by drug toxicity due to their reabsorption activity. Drugs that cause cytotoxicity include aminoglycoside antibiotics, anti-retroviral, and anti-cancer drugs**(*Kim and Moon, 2012).*** Aminoglycosides (AGs) such as gentamicin are broad-spectrum antibiotics used in the treatment of various infections and primarily affect the proximal tubules ***(Naughton, 2008; and Wargo, 2014).***

Olibanum, Luban,or frankincense, a yellowish- brown oleo-gum resin, is the gum resin obtained from trees of the *Boswellia genus* (family *Burseraceae*). There are different species of these plants native to Ethiopia, India, Somalia, and the Arabic peninsula. The resin in the market is mostly taken from the *Boswellia sacra*, *Boswellia carteri*, *Boswellia serrata*, and *Boswellia papyrifera.* Several phytochemicals have been isolated from frankincense which include the boswellic acid type, triterpenoids, and non-terpenoids.These phytochemicals exhibit anti-inflammatory, antioxidant, and anti-cancer activity, among others**(*Al-Harrasi and Al-Saidi, 2008; Al-Harrasi et al., 2014;* and *Khajehdehi et al., 2022).***

The aim of this study was to determine the impact of different levels of frankincense (*Boswellia sacra*) on gentamicin-induced nephrotoxicity in rats.

Materials and Methods

Materials

Frankincense*(Boswellia sacra)* or Lubanwas obtained from the local market in Shibin-El kom City, Menoufia Governorate, Egypt. Thirty-five (Sprague-Dawley strain) adult male healthy albino rats weighting (145±5) g were obtained from the Research Institute of Ophthalmology, Animal House Department, Giza, Egypt. Gentamicin (aminoglycosides antibiotics) and other chemical kits were obtained from El-Gomhoryia Company for Preparations Chemicals and Medical Equipments, Cairo, Egypt.

Methods

Induction of kidney intoxication in rats

Kidney toxicity was induced in healthy adult male albino rats by intro-peritoneal injection of gentamicin (aminoglycosides antibiotics), (10 mg /kg/day for 10 days) subcutaneous injection once daily for 10 days ***(Farombi and Ekor, 2006).***

Experimental design and animal groups

The basal diet in the experiment consisted of corn starch (67.6%), casein (11.9%), corn oil (10%), salt mixture (4%), vitamin mixture (1%), bran (5%), methionine (0.3%) and choline chloride (0.2%) according to ***AIN, (1993).***

Sprague-Dawley strain adult male healthy albino rats (*n* = 35) weighting (145±5) g were used in this study. Rats were housed individually (each rat alone) in wire cages under hygienic conditions, a good ventilation system in the laboratory, and were fed on a basal diet for 7 consecutive days as an adaptation period. Diets were introduced to rats in a special non-scattering feeding cups to avoid feed loss and contamination, the feeding was checked and weighted daily, while rats were supplied with water through glass tubes extending through the wire cage from an inverted bottle supported on one side of the cage and checked daily.

The rats were divided into 5 equal groups(*n* per group = 7). The tested groups of rats were negative control group in which normal rats were fed on a basal diet as a group **(1)**, nephrotoxicity rats as positive control which were injected with gentamicin and fed on a basal diet as group **(2)**, while groups **(3,4, and 5)** as nephrotoxicity rats were fed on a basal diet containing 2.5, 5, and

10% frankincense (*Boswellia sacra*) powder, respectively, for 28 days.

Biological evaluation

The consumed feeding was recorded every day, body weight gain, feed efficiency ratio, and organs weight was calculated according to***Chapman et al. (1959).***

Blood sampling and organs collection

After 12 hours of food and 2 hours of water fasting, blood samples were obtained. Serum was aspirated and stored at (-20°C) until chemical analysis ***(Schermer,1967).*** Liver enzymes, serum protein fractions, renal functions, key minerals, antioxidant enzymes, lipids profile, and serum glucose were all evaluated. Each rat's organs (liver, spleen, kidney, and heart) were surgically removed, washed in saline solution, dried on filter paper, weighed, and preserved in 10% formalin for histological investigation ***(Drury and Wallington, 1980).***

Biochemical analysis of serum

Serum samples were analyzed for the determination of the following parameters: aspartate aminotransaminase (AST) and alanine aminotransferase (ALT) were measured according to ***Henry (1974)*** and ***Yound (1975),*** respectively. Also, alkaline phosphatase (ALP), AST/ALT ratio, serum gamma-glutamyltransferase (GGT) and total protein (Tp) were carried out according to the method of ***IFCC (1983); Gowenlock et al. (1988) and Spencer & Price (1977),*** respectively. Albumin (Alb), globulin (Glb), an (Alb/Glb ratio) were measured according to ***Srivastava et al. (2002).*** Urea, uric acid and creatinine were determined by the method of ***Patton& Crouch (1977); Baraham&Trinder (1972)*** and ***Henry (1974),*** respectively. Sodium (Na), potassium (K), calcium (Ca) and phosphorus (P) were measured according to ***Nicoli et al. (2003).*** Glutathione peroxidase (GPX), superoxide dismutase (SOD), catalase (CAT), glutathione s-transferases (GSTs), total antioxidant capacity (TAC) and malondialdehyde (MDA) were measured by the method of ***Zhao (2001); Sun et al. (1998); Diego(2011); Hegstedet al. (1941); Koracevic(2001); Satoh(1978)*** and ***Ohkawaet al. (1979),*** respectively.

Histopathological examination

Specimens of the internal organ (kidney) were taken immediately after sacrificing rats (all groups) and were immersed in 10% neutral buffered formalin and were dehydrated in ascending concentrations of ethanol (70, 80, 90%). The fixed specimens were trimmed and dehydrated in ascending grades of alcohol, cleared in xylene and embedded in paraffin sectioned (4-6 Mm thickness), stained with hematoxylin and eosin, and examined microscopically ***Drury & Wallington (1980) and Bancroft et al. (1996).***

Statistical analysis

The data were statistically analyzed using a computerized ANOVA. The results are presented as Mean ± SD, and differences between treatments at ($P \leq 0.05$) were considered significant ***(SAS, 2004).***

Results

As shown in **Table (1)** there was a significant ($P \leq 0.05$) decrease in (BWG/28d), (FI g/ day) and (FER) values of the nephritic positive control group as compared to the negative control group. While all nephritic rats fed on a basal diet containing 2.5%, 5% and 10% of *Boswellia sacra* showedincreasing in BWG, FI and FER, as compared to the nephritic control group. The best treatment was recorded for group 5 (nephritic rats treated with *B*. *sacra* at the level of 10%).

Data in **Table (2)** showed the effect of feeding *B. sacra* at different levels on liver, spleen, kidney, and heart weight of the positive control group were increased significantly ($P \leq 0.05$) as compared to the negative control group, while nephritic groups fed on a diet containing 2.5%,5% and 10% *B. sacra* revealed improvement and gradual decrease in organs weight compared to the positive control group. The best results were observed in group 5 (nephritic rats fed on a diet containing 10% *B. sacra*) which recorded nonsignificant differences in mean values of all organs weight as compared to the negative control group.

The results in **Table (3)** exhibited that levels of creatinine, urea, and uric acid in the nephritic positive control group were markedly increased significantly ($P \leq 0.05$) as compared to the negative control group. All nephritic rats fed on a diet containing 2.5%, 5% and 10% *B. sacra* showed significant decreases in levels of

kidney functions compared to the nephritic positive control group. The best treatment was recorded for group 5 (nephritic rats fed on 10% *B. sacra*).

Table (4) confirmed that all nephritic rats fed on a diet containing 2.5%, 5% and 10% *B. sacra* were markedly decreased significantly ($P \leq 0.05$) in liver enzymes as compared to the positive control group, adding to that the best treatment was recorded in group 5 (nephritic rats treated with 10% *B. sacra*).

The effects of *B. sacra* feeding *on* serum total protein, albumin, globulin, and (Alb /Glb ratio) of animals are revealed in **Table (5)**. There were significantly increased levels Tp, Alb,Glb and non-significantly increasing Alb/Glb ratio in the positive control group as compared to the negative control group. All tested groups fed on a diet containing 2.5%, 5% and 10% *B. sacra* achieved significant decreases in Tp, Alb, Glb and Alb/Glb when compared to the positive control group.

Data in **Table (6)** indicated that (Na), (Ca), (K) and (P) recorded significant differences in the nephritic positive control group when compared to the negative control group. In nephritic positive control group showed increasing in potassium and phosphorous levels and decreasing in the levels of calcium and sodium. Furthermore, all nephritic rats fed on a diet containing 2.5%, 5% and 10% *B. sacra* achieved increased significantly ($P \leq 0.05$) in (Na) and (Ca), besides decreased significantly ($P \leq 0.05$) in (K) and (P) compared to the positive nephritic control group. The best results appeared for group 5 (nephritic rats fed on 10% *B. sacra*).

Data in **(Table 7)** indicated that (GPX), (SOD) and (CAT) recorded significant differences in the nephritic positive control group when compared to the negative control group. In nephritic positive control group showed a decrease in antioxidant enzymes. Furthermore, all nephritic rats fed on a diet containing 2.5%, 5% and 10% *B. sacra* achieved a significant increase ($P \leq 0.05$) in antioxidant enzymes compared to the positive nephritic control group. The best results appeared for group 5 (nephritic rats fed on 10% *B. sacra*).

As shown in **Table (8),**glutathione transferase (GST), antioxidant capacity (TAC) and oxidant enzymatic malondialdehyde (MDA)were measured. Administration of *B. sacra* at level 10% significantly increased the mean values of (GST) and (TAC)

compared to the positive control group and the administration of the same level significantly decreased the mean values of MDA.

Data in **Table (9)** illustrated that there were significantly increasing ($P \leq 0.05$) of total cholesterol,triglycerides, (LDL-c), (VLDL-c) and (AI) besides significantly decreasing ($P \leq 0.05$) of (HDL-c) in the nephritic control group compared to the negative control group.All nephritic rats fed on a diet containing different levels of *B. sacra* revealed a significant decrease in TC, (LDL-c), and (AI) as well as a significant increase in (HDL-c). The best results appeared for thegroup (5). Concerning TG and (VLDL-c), only nephritic rats fed on a diet containing 5 % and 10 % *B. sacra* showed a significant decrease in TG and (VLDL-c) levels at the end of the experiment.

The results in **Table (10)** showed theincreasing hypoglycemic effect of *B. sacra* onnephritic rats. All nephritic rats fed on a diet containing 2.5%, 5% and10% *B. sacra* showed a significant decrease in serum glucose compared to the positive nephritic control group. The best treatment was recorded for the group (5).

Histopathological changes

The normal histological structure of renal parenchyma was demonstrated microscopically in the kidneys of rats from group 1 control (-) group (normal rats) **(Photo.1)**. Necrobiosis of epithelium lining renal tubules and vacuolation of endothelium lining glomerular tufts were found in the kidneys of rats from group 2 positive control (+) group (nephritic non-treated animals) **(Photo.2)**. However, rats in group 3 (nephritic *B. sacra* 2.5 % treated rats) had vacuolation of epithelium lining renal tubules and endothelium lining glomerular tufts in their kidneys **(Photo.3)**. The kidneys of rats in group 4 (nephritic *B. sacra* 5% treated rats) showed no histological alterations other than vacuolation of endothelial lining glomerular tuft **(Photo. 4)**. Moreover, no histopathological alterations were observed in kidneys from group 5 (nephritic B. sacra 10% treated rats) **(Photo.5).**

Discussion

Kidney diseases are a major public health challenge affecting millions worldwide. Drug-induced nephrotoxicity is a common cause of acute kidney damage and gentamicin is categorized under one of these nephrotoxic drugs. Using medicinal plants that can lessen or

delay the deterioration in the kidney functions is needed due to their low cost and fewer side effects ***(Tienda-Vázquez et al., 2022).***

In comparison to the positive control group, rats treated with different levels of *B. sacra* gained significantly more body weight and had significantly less kidney weight at the end of the experiment. Injections of gentamicin resulted in weight loss and an increase in kidney weight in untreated rats. These results are in agreement with those published by ***Saad et al., 2018*** in adenine-induced chronic renal failure in rats. In the current study, frankincense (*B. sacra*) administration to gentamicin-injected rats lessen body weight loss, which could be attributable to its ability to reduce gentamicin-induced appetite loss.

Serum urea, creatinine, and uric acid are common biomarkers for the assessment of kidney failure. Serum creatinine, urea, and uric acid levels were significanlty elevated in the positive control group than in the normal control group. Our Results showed that gentamicin increases serum urea, creatinine, and uric acid as a result of reduced urea, creatinin, uric acid renal excretion and decline in glomerular filtration rate (GFR) ***(Alotaibi et al, 2022).*** In rats treated with *B. sacra*, these indicators were significantly reduced to near-normal levels. There were no statistically significant variations in serum creatinine, urea, or uric acid between the normal control group and the group treated with 10% *B. sacra*. Our results are in agreement with ***Masoud et al, 2017***. High level of serum uric acid , namely hyperuricemia, has been shown to have a significant contribution to renal function decline in the general population. Moreover, it has been found to enhance an inflammatory process in healthy and diseased animal kidneys ***(Jung et al , 2020).***

Protein synthesis (e.g. albumin), lipid and carbohydrate metabolism , and immunomodulation are among other important functions performed by the liver. Indicators of liver damage include alkaline phosphatase (ALP), alanine aminotransferase (ALT), and aspartate aminotransferase (AST) ***(Lane et al, 2013).*** Our data showed amelioration in serum levels of total proteins, albumin, and transaminases . Our results are in parallel with **Asad *and Alhumoud, 2015.***

Hypoalbuminemia and hypoproteinemia seen in the gentamicin-untreated group could be attributed to reduced albumin synthesis by the liver and to the leaking of albumin into the urine. Acute kidney injury has been viewed as an acute systemic disease

with significant effects on other organs such as the liver in a process named organ crosstalk ***(Lane et al, 2013 and Makris & Spanou, 2016).***

Some lipid abnormalities are also caused by changes in liver metabolism. Our data showed that rats fed on a diet containing different levels of *B. sacra* revealed significant decrease in TC, (LDL-c), and (AI) as well as a significant increase in (HDL-c).

Our data are in the same line as with ***Pandey et al, 2005*** who showed that water extract of *Boswelliaserrata* has hypocholesterolemic properties in rats. Moreover, ***Ahangrapour et al, 2014*** reported that *Boswellia serrata* supplementation for six weeks at 900 mg daily significantly ameliorates HDL, LDL, and TC levels in type 2 diabetic patients.However, only nephritic rats fed on a diet containing 5 % and 10 % *B. sacra* showed a significant decrease in TG and (VLDL-c) levels at the end of our experiment.Concering serum glucose levels, significant improvements were observed in rats treated with *B. sacra* in agreement with the above mentioned studies.

In the current study, rats treated with gentamicin (nephritic positive control) exhibited hyperphosphatemia with hypocalcemia. Renal phosphate excretion is impaired as renal function deteriorates, resulting in a rise in serum phosphate levels. Because serum calcium is inversely correlated with serum phosphate levels, serum calcium levels fall ***(Blaine et al., 2015).*** Hyponatremia, low sodium levels in the blood, and hyperkalemia, high levels of potassium in the blood, are other effects of the decline in kidney function in the present study. Hyperkalemia may be attributed to impaired potassium excretion in urine, a condition that can lead to cardic arrest and death ***(Alotaibi et al., 2022).*** Low sodium levels in the blood may be due to sodium reabsorption inhibition in the renal tubules and hence increased sodium loss. Serum sodium levels have been linked to a higher risk of death in acute kidney injury patients ***(Li et al, 2021).***

The administration of frankincense improves P, Ca, K, and Na levels, indicating that it has a beneficial effect on renal disease progression.

Oxidative stress is known to induce inflammation and both processes are deeply connected to kidney diseases ***(Sureshbabu et al, 2015).*** Our data showed a significant increase in glutathione peroxidase (GPX), superoxide dismutase (SOD), catalase (CAT), and

glutathione -S- transferase (GSH) levels compared to the positive nephritic group. Moreover, there was a decrease in malondialdehyde levels, a lipid peroxidation biomarker. These effects might be due to frankincense anti-inflammatory and anti-oxidant properties. According to ***Biggs et al. (2016),*** frankincense is a rich source of total phenolics, flavonoids, triterpenes, monoterpenes, diterpenes, and saponins, suggesting that it has antioxidant qualities. In agreement, ***Bertocchi et al. (2018),*** reported that *B. sacra*extract contains a considerable amount of natural antioxidants (e.g. flavonoids) which play a role in controlling oxidation and increasing total antioxidant capacity.

In addition, a kidney histopathology analysis to evaluate the protective effects of frankincense on kidney injury was performed. In groups of rats treated with 2.5, 5, and 10% *B*. *sacra* powder, pathological abnormalities in kidney tissues improved significantly, with the effect being most pronounced in group 5 (nephritic rats fed on 10 % *B. sacra*). These improvements can be linked to the antioxidant bioactive molecules in frankincense, boswellic acid, that inhibit oxidative stress, hence, attenuating histopathological abnormalities ***(Ebrahimpour et al., 2017).***

In summary, administration of frankincense for 28 days could ameliorate kidney damage resulting from gentamicin-induced nephrotoxicity in rats.

Table (1): Effect of treatment with some levels of *Boswellia sacra* on nutritional parameters of rats with nephrotoxicity

Group	Parameters		
	BWG(g/28d)	FI (g/d)	FER
Negative control(G_1)	40.50^{a}±5.10	14.9^{a}±2.55	0.097^{a} ±0.05
Positive control (G2)	19.05^{e} ±1.70	8.93^{c}± 1.81	0.076^{c}±0.004
Rats fed on 2.5% Boswellia sacra (G3)	22.25^{d}±1.49	9.02^{c}±1.35	0.089^{b}±0.021
Rats fed on 5% Boswellia sacra(G4)	29.08^{c}±1.34	10.95^{b}±2.79	0.095^{a} ±0.002
Rats fed on 10% Boswellia sacra(G5)	35.38^{b}±2.90	12.8^{b}±2.31	0.098^{a} ±0.022
LSD	3.87	1.98	0.004

Means in the same column with different letters are significantly different ($P \leq 0.05$).

Table (2): Effect of treatment with some levels of *Boswellia sacra* on organs weight of rats with nephrotoxicity

Group	Parameters			
	Liver	Spleen	Kidney	Heart
Negative control ($G_{1)}$	4.09^{d} ±0.12	0.24^{c}± 0.013	0.63^{d}± 0.040	0.29^{e} ±0.003
Positive control (G2)	5.53^{a}±0.22	0.55^{a}± 0.029	1.35^{a} ±0.06	0.83^{a} ±0.015
Rats fed on 2.5% *Boswellia sacra* (G3)	5.33^{a} ±0.23	0.49^{a} ±0.018	0.96^{b} ±0.07	0.64^{b} ±0.012
Rats fed on 5% *Boswellia sacra* (G4)	5.02^{b}±0.38	0.40^{b} ±0.014	0.81^{c} ±0.09	0.53^{c} ±0.06
Rats fed on 10% *Boswellia sacra* (G5)	4.56^{c}±0.15	0.30^{b} ±0.120	0.68^{d} ±0.034	0.42^{d} ±0.011
LSD	0.34	0.12	0.11	0.10

Means in the same column with different letters are significantly different (P ≤0.05).

Table (3): Effect of treatment with some levels of *Boswellia sacra* on kidney functions of rats with nephrotoxicity

Group	Parameters		
	Creatinine (mg/dl)	Urea (mg/dl)	Uric acid(mg/dl)
Negative control ($G_{1)}$	0.42^{d}±0.031	17.12^{d}±0.712	1.30^{d}±0.57
Positive control (G2)	1.46^{a}±0.04	32.65^{a}±1.351	3.51^{a}±0.16
Rats fed on 2.5% Boswellia sacra (G3)	1.25^{b}±0.03	28.50^{b}±1.172	2.40^{b}±0.11
Rats fed on 5% Boswellia sacra (G4)	0.93^{c}±0.07	24.22^{c}±1.012	1.96^{c}±0.078
Rats fed on 10% Boswellia sacra (G5)	0.47^{d}±0.02	17.75^{d}±0.943	1.41^{d}±0.061
LSD	0.094	1.96	0.23

Means in the same column with different letters are significantly different (P ≤0.05).

Table (4): Effect of treatment with some levels of *Boswellia sacra* on liver functions of rats with nephrotoxicity

Groups	Parameters				
	AST(U/L)	ALT(U/L)	ALP(U/L)	AST/ALT(ratio)	GGT(U/L)
Negative control ($G_{1)}$	39.56^{e} ±2.56	37.34^{e} ±1.16	70.23^{e} ±2.44	1.06^{c} ±0.53	3.12^{c} ±0.88
Positive control (G2)	65.87^{a} ±2.81	60.99^{a} ±7.90	106.65^{a} ±9.13	1.08^{c} ±0.08	5.99^{a} ±0.42
Rats fed on 2.5% B. sacra (G3)	60.76^{b} ±2.22	55.96^{b} ±6.02	93.97^{b} ±2.07	1.86^{a} ±0.02	5.08^{a} ±0.17
Rats fed on 5% B.sacra (G4)	54.55^{c} ±5.05	48.63^{c}±1.91	88.54^{c} ±1.20	1.21^{b} ±0.07	4.26^{b} ±0.09
Rats fed on 10% B. sacra (G5)	45.22^{d} ±5.10	41.32^{d} ±1.25	79.76^{d} ±1.71	1.09^{c} ±0.01	3.91^{b} ±0.05
LSD	3.94	2.96	3.20	0.11	0.92

Means in the same column with different letters are significantly different (P ≤0.05).

Table (5): Effect of treatment with some levels of *Boswellia sacra* on total protein, albumin, globulin, and (Alb /Glb ratio) of rats with nephrotoxicity

Group	Parameters			
	Tp (g/L)	Alb (g/L)	Glb (g/dl)	Alb/Glb ratio
Negative control ($G_{1)}$	66.34^{e} ±2.20	37.98^{e} ±4.18	33.45^{c} ±2.49	1.14^{a} ±0.53
Positive control (G2)	90.76^{a} ±2.41	59.76^{a} ±3.90	50.65^{a} ±3.33	1.18^{a} ±0.78
Rats fed on 2.5% Boswellia sacra (G3)	85.32^{b} ±2.22	55.54^{b} ±1.52	47.43^{a} ±2.57	1.17^{a} ±0.02
Rats fed on 5% Boswellia sacra (G4)	79.76^{c} ±5.75	50.32^{c} ±1.51	41.65^{b} ±1.20	1.21^{a} ±0.07
Rats fed on 10% Boswellia sacra (G5)	70.54^{d} ±5.50	45.76^{d} ±1.27	36.43^{c} ±1.71	1.26^{a} ±0.01
LSD	4.94	3.96	4.20	0.22

Means in the same column with different letters are significantly different (P ≤0.05).

Table (6): Effect of treatment with some levels of Boswellia sacra on some minerals of rats with nephrotoxicity

Group	Parameters			
	Na(mmoL/L)	K (mmoL/L)	Ca (mmoL/L)	P (mmoL/L)
Negative control ($G_{1)}$	0.44^{a}±0.011	18.22^{d}±0.712	2.31^{a}±0.057	5.71^{e}±0.114
Positive control (G2)	0.22^{c}±0.074	33.75^{a}±1.351	1.02^{d}±0.176	9.91^{a}± 0.196
Rats fed on 2.5% B. sacra (G3)	0.26^{b}±0.063	28.50^{b}±1.172	1.41^{c}±0.121	8.94^{b}± 0.325
Rats fed on 5% B. sacra (G4)	0.34^{b}±0.047	24.32^{c}±1.012	1.67^{b}±0.098	7.62^{c}±0.206
Rats fed on 10% B. sacra (G5)	0.40^{a}±0.024	19.85^{d}±0.943	1.82^{b}±0.071	6.90^{d}± 0.169
LSD	0.094	2.96	0.25	0.35

Means in the same column with different letters are significantly different (P ≤0.05).

Table (7): Effect of treatment with some levels of Boswellia sacra on antioxidant enzymes of rats with nephrotoxicity

Group	Parameters		
	GPX (ng/dl)	SOD (U/L)	CAT (mmoL/L)
Negative control ($G_{1)}$	80.03^{a}±2.25	53.05^{a}±1.85	70.74^{a}±2.87
Positive control (G2)	50.07^{e}±5.55	30.14^{d}±2.02	39.31^{d}±3.66
Rats fed on 2.5% *B. sacra* (G3)	60.02^{d}±2.05	42.03^{c}±1.91	55.90^{c}±2.70
Rats fed on 5% *B. sacra* (G4)	69.15^{c}±1.51	46.07^{b}±2.15	62.04^{b}±6.15
Rats fed on 10% *B. sacra* (G5)	72.78^{b}±2.27	52.53^{a}±1.61	69.05^{a}±2.54
LSD	2.97	3.35	3.96

Means in the same column with different letters are significantly different (P ≤0.05).

Table (8): Effect of treatment with some levels of *Boswellia sacra* on GST, TAC, and MDA of rats with nephrotoxicity

Group	Parameters		
	GST(mmoL/L)	TAC(nmoL/L)	MDA(nmoL/L)
Negative control ($G_{1)}$	34.07^{a}±2.98	1.99^{a}±0.61	17.17^{e}±2.08
Positive control (G2)	17.84^{e}±1.47	0.82^{c}±0.02	34.03^{a}±1.80
Rats fed on 2.5% *B.sacra* (G3)	21.35^{d}±1.18	0.89^{c}±0.05	30.01^{b}±1.11
Rats fed on 5% *B.sacra* (G4)	25.02^{c}±2.56	0.99^{b}±0.01	27.02^{c}±3.66
Rats fed on 10% *B.sacra* (G5)	29.08^{b}±1.44	1.09^{b}±0.41	23.91^{d}±5.95
LSD	2.56	0.15	2.96

Means in the same column with different letters are significantly different (P ≤0.05).

Table (9): Effect of treatment with some levels of *Boswellia sacra* on lipid profile and AI of rats with nephrotoxicity

Group	Parameters					
	TG (mg/dl)	TC (mg/dl)	HDL-c (mg/dl)	LDL-c (mg/dl)	VLDL-c (mg/dl)	AI (ratio)
Negative control ($G_{1)}$	91.5 ^{d}±2.45	106.4 ^{e}±4.22	59.7^{a} ±2.45	28.4^{e} ±0.58	18.3^{d} ±0.45	0.79^{d} ±0.09
Positive control (G2)	125.5 ^{a} ±4.43	148.6^{a} ±3.11	41.6^{e} ±2.44	81.6^{a} ±1.82	25.1^{a} ±0.55	2.61^{a} ±0.14
Rats fed on 2.5% *B. sacra* (G3**)**	123.5 ^{a} ±3.55	132.8 ^{b}±4.33	50.3^{d} ±3.65	57.8^{b} ±0.93	24.7^{a} ±0.25	1.64^{b} ±0.07
Rats fed on 5% *B. sacra* (G4)	113.5 ^{b}±3.22	120.6 ^{c}±2.78	52.6^{c} ±2.84	45.3^{c} ±1.51	22.7^{b} ±0.32	1.28^{c} ±0.05
Rats fed on 10% *B.sacra* (G5)	101.5 ^{c}±5.95	112.5 ^{d}±5.89	56.6^{b} ±4.59	35.6^{d} ±0.88	20.3^{c} ±0.13	0.98^{d} ±0.09
LSD	5.05	5.66	2.04	3.51	1.25	0.19

Means in the same column with different letters are significantly different (P ≤0.05).

Table (10): Effect of treatment with some levels of *Boswellia sacra* on serum glucose of rats with nephrotoxicity

Group	Serum glucose
Negative control ($G_{1)}$	96.98^{a}±2.81
Positive control (G2)	157.98^{b}± 2.74
Rats fed on 2.5% *Boswellia sacra* (G3)	130.34^{c}± 1.97
Rats fed on 5% *Boswellia sacra* (G4)	125.67^{d}± 2.13
Rats fed on 10% *Boswellia sacra* (G5)	119.77^{e}± 1.57
LSD	3.91

Means in the same column with different letters are significantly different (*P* ≤0.05).

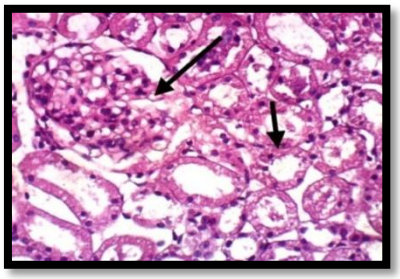

Photo (1):
The kidney of a rat from group 1 (normal rats) had normal renal parenchyma histological structure (H & E X 400).

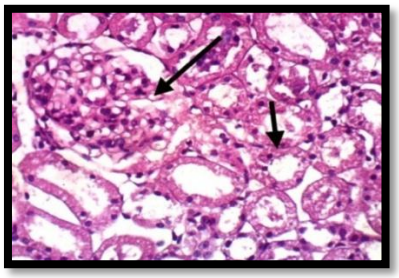

Photo (2):
Necrobiosis of epithelium lining renal tubules and vacuolation of endothelium lining glomerular tufts were seen in the kidney of rats from group 2 (nephritic non-treated animals) (H & E X 400).

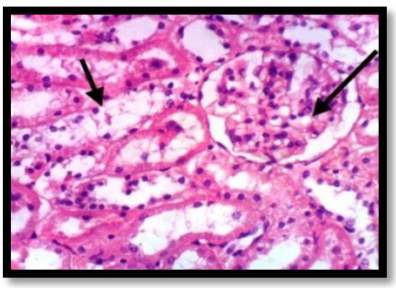

Photo (3):
Kidney of rat from group 3 (nephritic rats treated with 2.5 % *B. sacra*) showed vacuolation of epithelial lining renal tubules andthe endothelial lining glomerular tuft (H & EX 400)

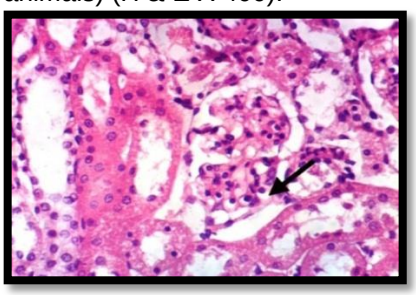

Photo (4) :
Kidney of rat from group 4 (nephritic rats treated with 5 % *B. sacra*) demonstrated vacuolation of endothelial lining of glomerular tuft (H & E X 400).

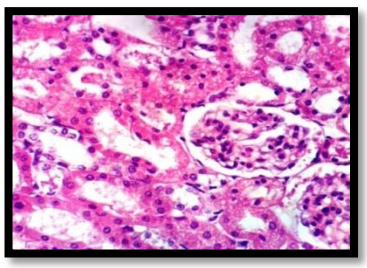

Photo (5) :
Kidney of rat from group 5 (nephritic rats treated with 10 % *B. sacra*) revealed no histopathological change (H & E X 400).

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تأثير اللبان المُر علي السمية الكُلوية بالجنتاميسين في الفئران

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السمية الكُلوية التي تسببها الأدوية تعتبر سبب شائع لإصابة الكلي الحادة ويتم تصنيف الجنتاميسين كأحد هذه الأدوية السامة للكلي. استخدام النباتات الطبية التي يمكن أن تحسن أو تؤخر التدهور في وظائف الكلي أصبح أمر ضروري لتكلفتها المنخفضة وآثارها الجانبية الأقل. تم تقسيم 35 من ذكور الفئران البيضاء البالغة السليمة إلي خمس مجموعات متساوية : مجموعة ضابطة سالبة تغذت فيها الفئران علي النظام الغذائي الأساسي ، مجموعة ضابطة موجبة ، تم حقن الفئران بالجنتاميسين وتم تغذيتها علي النظام الغذائي الأساسي ، مجموعة 3 ، 4 ، 5 تم تغذية الفئران المصابة بالسمية الكُلوية علي نظام غذائي أساسي يحتوي علي 2.5 ، 5 ، 10 في المئة من مسحوق اللبان المر ، علي التوالي ، لمدة 28 يوم. تم فحص وظائف الكلي ، وظائف الكبد ، مستويات المعادن ، مضادات الأكسدة ، مستويات الجلوكوز ، مستويات الدهون ، والتغيرات النسيجية للكلي. أظهرت النتائج زيادة معنوية في وزن الجسم وانخفاض معنوي في مستوي اليوريا ، حمض اليوريك ، الكرياتينين ، الفوسفور ، البوتاسيوم ، الدهون ، الجلوكوز ، إنزيمات الكبد ، الألبيومين ، والبروتين الكلي في الدم في المجموعات المعالجة بمستويات مختلفة من مسحوق اللبان المر. علاوة علي ذلك ، أظهرت النتائج زيادة معنوية في مستويات مضادات الأكسدة الإنزيمية (انزيم الكاتاليز والسوبرأوكسيد ديسميوتيز والبيروكسيديز) مع انخفاض معنوي في مستويات malondialdehyde ، مؤشر حيوي علي أكسدة الدهون. فيما يتعلق بنسيج الكلي ، لم يلاحظ أي تغيرات نسيجية مرضية في الكلي من الفئران المعالجة بمسحوق اللبان المر بنسبة 10 %. أظهرات نتائج الدراسة أن إعطاء اللبان المر لمدة 28 يوم قد يخفف من إصابة الكلي الناتجة عن السمية الكُلوية التي يسببها الجنتاميسين في الفئران.

الكلمات الدالة : اللبان المُر ، الجنتاميسين ، السمية الكُلوية ، الفئران