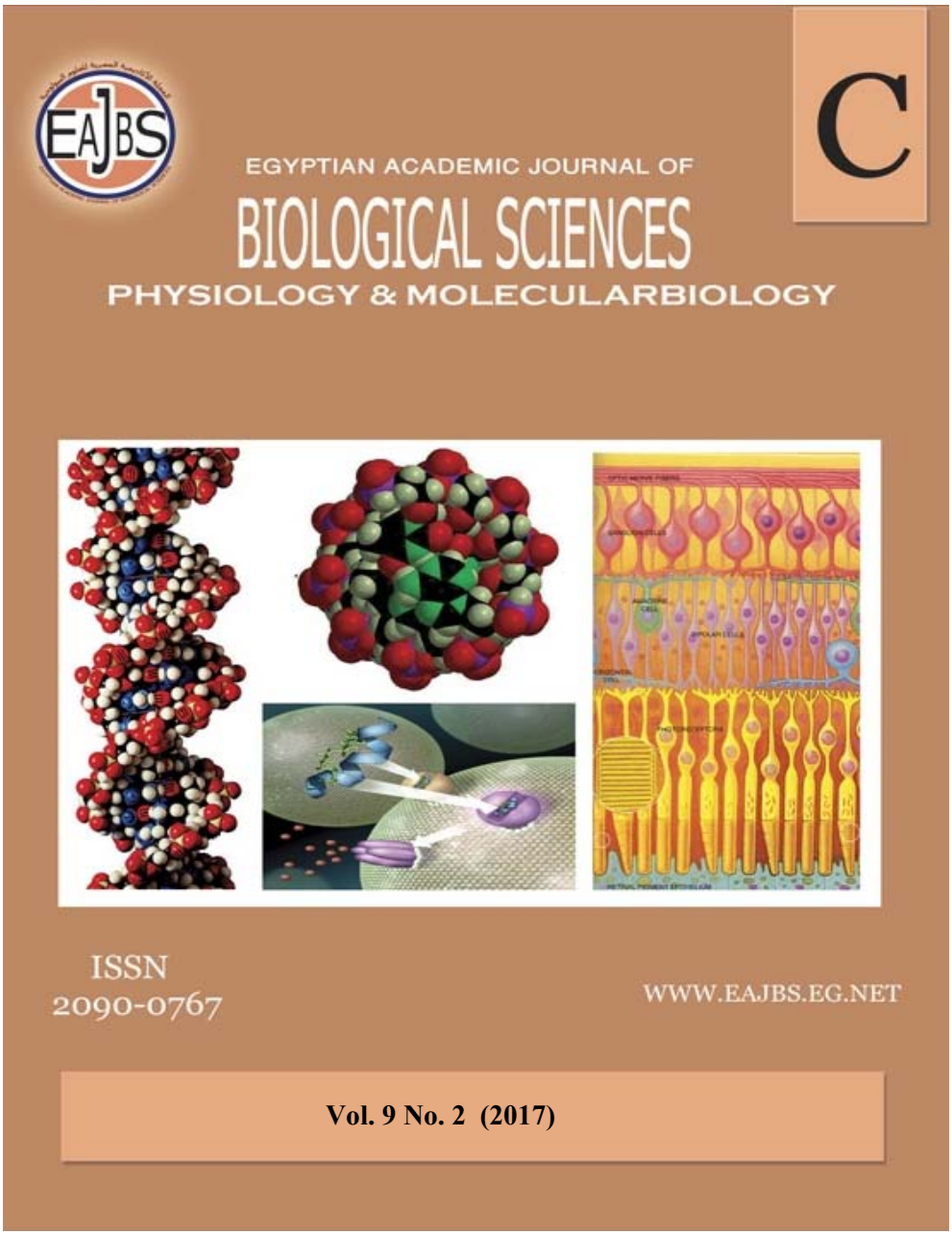

The Journal is an Egyptian journal covering the whole field of general, experimental, systematic and applied botany. Manuscripts generally should not exceed 20 pages (exceptions are possible, particularly in case of reviews, and should be negotiated in advance with the editors). Papers are considered by referees before acceptance. Authors will receive first editorial decision within 8 weeks from confirmed submission. All contributions are published in English. Authors whose mother tongue is not English are strongly urged to have their manuscripts reviewed linguistically before submission. Papers written in poor English will be returned. It is understood that manuscripts submitted to EAJBS have not been offered to any other journal for prior or simultaneous publication

www.eajbs.eg.net

Egypt. Acad. J. Biolog. Sci., 9(2): 69- 75 (2017)

Egypt. Acad. J. Biolog. Sci.
C. Physiology & Molecular Biology
Email: egyptianacademic@yahoo.com

The Protective Effect of *Acacia senegal gum* against Gentamicin-Induced Nephrotoxicity In Albino Rats

Mahmoud A. Elderbi[1*], Abdel Wahab H. Mohamed[2] and Ali A. Ahmed[3]

1- Department of Pharmacology and Toxicology, Faculty of Pharmacy, Benghazi University, Benghazi, Libya

2- Department of Therapeutics, Pharmacy College, National Ribat University, Khartoum, Sudan.

3- Department of Pharmacology, Faculty of Medicine, Al-Azhar University, Assiut, Egypt

ARTICLE INFO

Article History
Received:26/8/2017
Accepted:30/9/2017

***Keywords*:**
Acacia Senegal
Nephrotoxicity
Albino Rats

ABSTRACT

Introduction: *Acacia senegal* gum is commonly known as Arabic gum or gum Arabic(GA) which obtained from the branches and stems of the trees as a dried gummy exudates. It is widely used in food and pharmaceutical industries as emulsifier and suspending agent. It has many pharmacologic effects including gastrointestinal effects such as increasing the short chain fatty acids and enhance water and electrolytes intestinal absorption but variable effects on lipid metabolism. In chronic renal failure patients, gum arabic reduces serum urea nitrogen. It is a potent superoxide scavenger so that it have a good protective activity against acetaminophen-induced hepatotoxicity and doxorubicin-induced cardiotoxicity in rats. **The Aim of study:** In the present study, we investigated the protective effect of *Acacia senegal* gum against gentamicin (GM)-induced nephrotoxicity in male albino rats. **Materials and Method:** The animals were divided into three groups A (Control), B (GM-only treated rats, 80mg/Kg, IM for 7days) and C (GA 10g/100ml water, orally for 4weeks prior to GM treatment). The nephrotoxicity was evaluated biochemically by determination level of serum Creatinine (Crea), Urea (Urea) and Uric acid (UA) level and histologically by microscopic examination the degree of proximal tubular damage. **Results:** The results showed significant increase in the level of Crea, Urea and UA in animals treated with GM only. In group (C), the level of Crea was high significant compared with the control but the level of Urea was significantly decreased compared with the control and the level of UA was significantly decreased compared with group B but higher than the control. **Conclusion:** These results suggest that *Acacia senegal* gum has some nephroprotective in rats, may be due to its antioxidant activities of GA.

INTRODUCTION

Acacia senegal gum or gum arabic (GA) is defined as a branched-chain, complex polysaccharide, either neutral or slightly acidic, found as a mixed calcium, magnesium, and potassium salt of a polysaccharidic acid obtained from the stems and branches of *Acacia senegal* (Badreldin *et al*., 2009). These types of trees are abundant in central Sudan, central Africa and in West Africa (Evans, 1989). The pharmaceutical industry use gum arabic as an emulsifier and suspending agent for insoluble drugs and in food industries as emulsifier (Rawlin, 1997).

Gum arabic undergoes complete fermentation within the cecum of rats and humans. Such fermentation promotes bacterial proliferation, and the larger bacterial mass induces increased production of short chain fatty acids linked with enlargement of the cecum (Howard *et al*., 1995).

Tulung *et al*. (1987) studied the effect of gums on the digestion in rats and found that gum arabic produced an enlargement of the caecum of rats and this leads to increasing absorption of the volatile fatty acid and electrolytes. In other studies they found that Arabic gum enhanced water, electrolyte and glucose absorption from oral rehydration salts in jejunal perfusion of healthy rats and animals with chronic diarrhea (Tulung *et al*., 1987; Kishimoto *et al*., 2006).

In chronic renal failure patients, fecal bacterial mass and fecal nitrogen content were significantly increased during supplementation with gum arabic. Also, Serum urea nitrogen was significantly decreased during supplementation with it but nitrogen balance did not change significantly (Bliss, 1996). Another study showed improvement in the quality of life and reduces or eliminates the need for dialysis in children with end-stage renal disease (Al-Mosawi, 2004).

In an experimental model of chronic renal failure (CRF) using rat kidney remnant model, Ali, (2004) showed that treatment of rats with gum arabic was not effective in either reversing the decrease in body weight or the increases in creatinine and urea observed 2 weeks after the surgical induction of the CRF.

By using a lipid model system, one study found that Arabic gum protects against lipid peroxidation in the skin in a dose-dependent manner (Trommer and Neubert, 2005). More recently, however, Cindoruk *et al*. (2007) reported that gum arabic was ineffective in ameliorating hepatocellular damage in cholestasis induced by fenofibrate in rat.

Gum arabic was reported as a potent superoxide scavenger so that it give protective effect against both Paracetamol-induced hepatotoxicity and doxorubicin-induced cardiotoxicity in mice (Gamal el-din *et al*., 2003; Abd-Allah *et al*., 2002) but it fails to protect the kidney from damage effect of cisplatin (Al-Majeed *et al*., 2003).

This study was conducted to investigate the protective effect of gum arabic against gentamicin-induced nephrotoxicity in rats.

MATERIALS AND METHOD

Experimental Animals:

Fifteen Adult male rats weighing 250-350 g were obtained from the animal house of Omar Al-Mukhtar University. Normal rat-feed, water *ad libitum* was provided under 12-hour light and 12-hour dark schedule at room temperature (25^{o}C).

Experimental design:

The rats were divided randomly into 3 groups of 5 animals each. The first group (A) as control. The second group (B) received gentamicin (GM; 80 mg/kg daily for 7 consecutive days, IM), and the third (C, GA+GM) received gum arabic (10g/100ml in drinking water for 4weeks before GM administration). At the end of experiment, the rats were sacrificed, 2 ml of blood was collected in clean test tubes and centrifuged (4000 x *g* for 5 min). The serum obtained was stored at 0-4◦C for measurement the indices of nephrotoxicity. The kidneys were excised, blotted on a filter paper. The cortex was dissected out, cut to portions and immediately fixed in formalin 10% for subsequent histological processing.

Biochemical measurements:

The following parameters were measured to evaluate nephrotoxicity:

Serum creatinine (Crea), Serum urea (Urea) and Uric acid (UA). Serum creatinine concentration was measured by Jaffè reaction (Henry, 1984). Serum urea concentration was measured by enzymatic colorimetric method by Berthelot modified method (Berthelot, 1959). Uric Acid (UA) determination is based on modified Praetoriuos and Poulson (1927).

Histopathological Examinaton:

Small portion of cortex of the representative kidneys were fixed in 10% formalin, dehydrate in graded alcohol and embedded in paraffin wax, sectioned (5 μm) thickness and stained with Hematoxylin and Eosin (H&E) for light microscopic examination. Renal proximal tubular damage was assessed on the basis of arbitrary score (Teixeira, 1982) as follows: 0 for no cell necrosis; 1 for mild, usually single cell necrosis in sparse tubules; 2 for moderate, sparse tubules showing more than one cell involvement; 3 for marked, tubules in almost every power field exhibiting total necrosis; and 4 for massive, total necrosis.

Statistical analysis:

The results obtained from the experiments were represented as mean ± SEM (P value <0.05). Data were analyzed by one-way analysis of variance (ANOVA) using SPSS computerized program.

RESULTS

The biochemical and histological changes in the kidney were summarized in (Table 1) for different groups. In group A, the rats were administered gentamicin intramuscularly to made nephrotoxic model and the results showed significant elevation in Crea, Urea and UA level in rats (Fig. 1-3). This assumption was supported by histological observation of the H&E stained transverse sections through the renal cortex, which suggested massive damage to the proximal tubules (score 3) of these groups of rats (Fig. 4b).

Table 1: Effect of gentamicin and GA on the biochemical parameters and histology of kidney.

Groups	Crea mg/dl	Urea mg/dl	UA mg/dl	Histology score
A (control)	0.34±0.04	41.00±1.58	1.13±0.13	0
B (GM only)	0.78±0.04*	48.75±1.11*	5.24±0.30*	4
C (GA+GM)	0.82±0.18*	34.50±2.18*#	3.72±0.13*#	2

All data are expressed as Means ± SE (n=5)

*Significance different from control (P< 0.05)

Significant different from GM only group (P< 0.05)

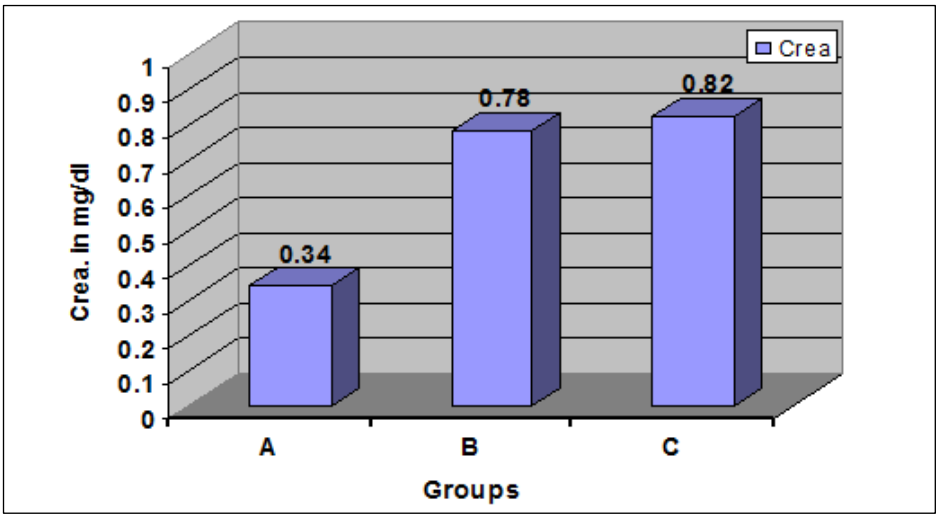

Fig. 1: Effect of GM on the Crea. level before (B) and after GA administration(C)

To examine the protective effect of GA against GM-induced nephrotoxicity rats were given GA orally for 4weeks before gentamicin administration and at end of the study the results showed that the Level of urea was decreased significantly compared with the control (Fig. 2). The level of UA in group C was decreased significantly compared with control and group B on another hand, the level of Crea., in group C was remain significantly high compared with control (Figs. 2, 3).

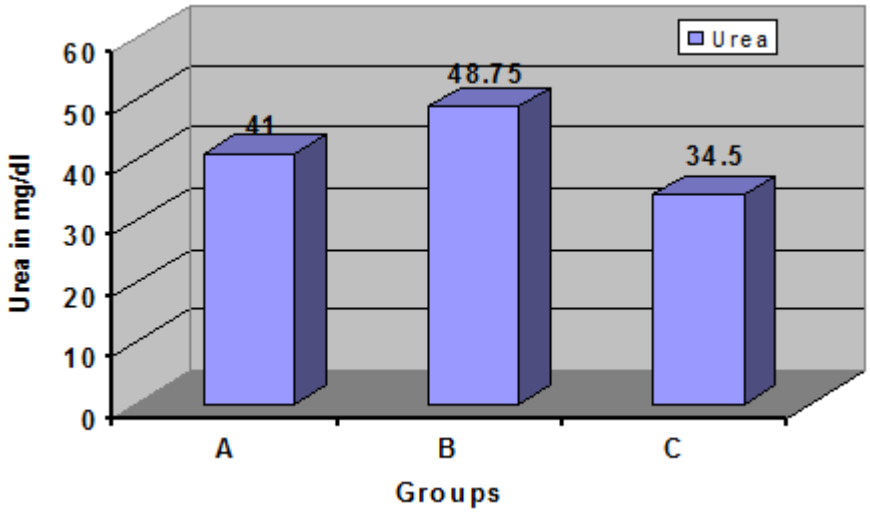

Fig. 2: Effect of GM on the level of Urea before GA treatment (B) and after GA administration(C)

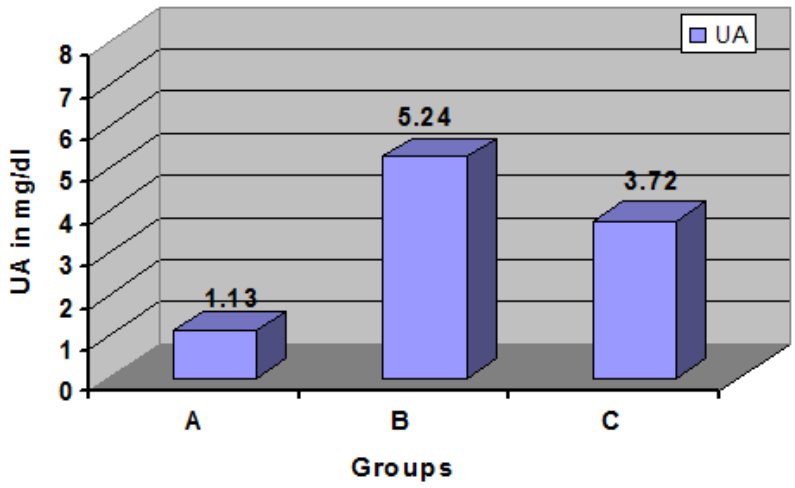

Fig. 3: The level of uric acid(UA) in GM-treated group (B) and GA+GM treated group(C).

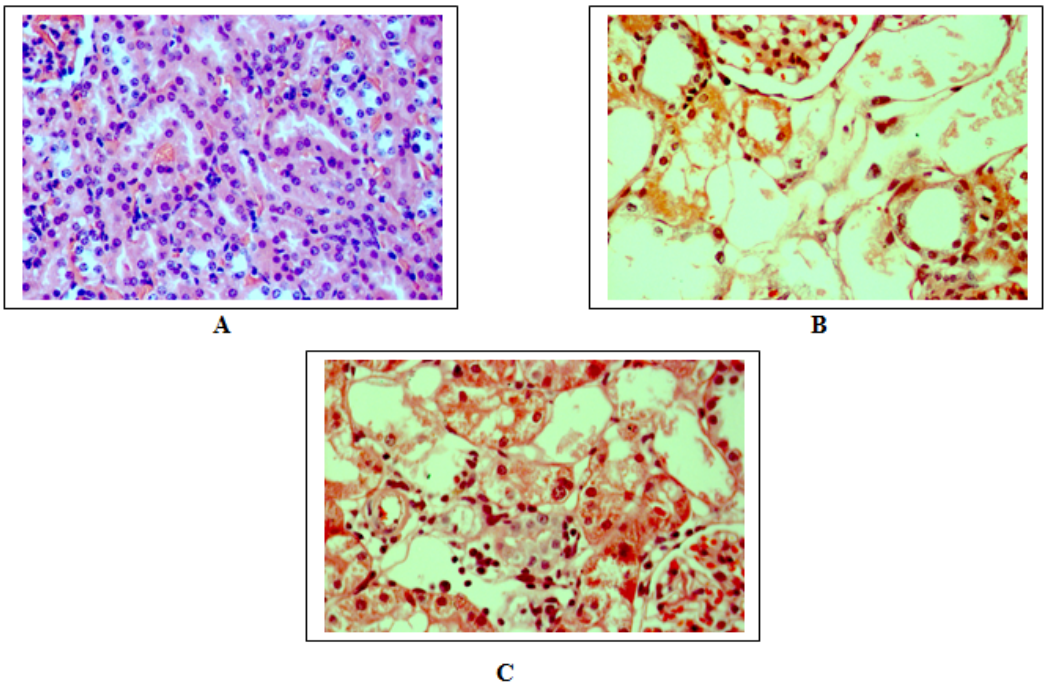

Fig. 4: Representative photograph of sections of renal cortex under light-microscope of rats treated with (a) distilled water; (b) gentamicin (80 mg/kg/day for 7 days (showing massive damage to the proximal tubules); (c) GA treated animals (10 g/100ml/day for 4weeks) prior gentamicin administration.(H&E 40 x).

DISCUSSION

Gentamicin is an important aminoglycoside antibiotic commonly used in treating life-threatening gram-negative infections. However its usefulness is limited by signs of nephrotoxicity, which may occur in 13-30% of treated patients. Lipid peroxidation may occur in the course of gentamicin administration, giving rise to free radicals, which are highly toxic to tissue and causing nephrotoxicity (Ali *et al*., 2003).

In the present study, nephrotoxicity induced by gentamicin was evidenced by increases in serum creatinine, serum uric acid and serum urea concentrations. This was supported by proximal tubular histology suggestive of gross tubular damage. These observations were similar to those of Ali (2004) who reported similar biochemical and histological changes suggestive of nephrotoxicity. In animals, high dose of gentamicin (40 mg/kg or more) is rapidly induced extended cortical necrosis and overt renal dysfunction. At this stage, a large number of structural, metabolic, and functional alterations are observed in tubular cells (Table 1), and several of these alterations have been claimed to be responsible for cell death or dysfunction. The mechanism of this necrosis is explained by different hypotheses, one of these assumes that gentamicin exert its toxicity in direct relation to their local storage of gentamicin in lysosomes as non-toxic but it becomes nephrotoxic once it released from lysosomes. In this connection, gentamicin was shown to chelate mitochondrial iron, forming a very oxidant Fe (II)-gentamicin complex and free oxygen radicals capable of causing hair cell death (Parker *et al*., 1982; Priuska and Schacht, 1997).

To reduce or to protect against gentamicin nephrotoxicity, the most consistent effects have been observed with the use of antioxidants. On the basis of the finding that gentamicin forms complexes with mitochondrial iron to catalyze the formation of free oxygen radicals; the nephroprotection is possible by using antioxidants. Gum Arabic was

reported by Gamal el-din *et al*., (2003) as a potent superoxide scavenger so that the superoxide scavenging effect of GA may explain the protective effect against gentamicin-induced nephrotoxicity.

REFERNCES

Abd-Allah AR, Al-Majed AA, Mostafa AM, Al-Shabanah OA, Din AG and Nagi MN. (2002). Protective effect of arabic gum against cardiotoxicity induced by doxorubicin in mice: a possible mechanism of protection. J Biochem Mol Toxicol., 16(5):254-9.

Al-Majed AA, Abd-Allah AR, Al-Rikabi AC, Al-Shabanah OA and Mostafa AM.. (2003). Effect of oral administration of Arabic gum on cisplatin-induced nephrotoxicity in rats; J. Biochem Mol Toxicol., 17(3):146-53.

Al-Mosawi A. J. (2004). Acacia gum supplementation of a low-protein diet in children with end-stage renal disease. Pediatr Nephrol., 19(10):1156-9.

Ali B.H. (2004). Does G.A. have an antioxidant action in rat kidney? Ren. Fail. 26: 1–3.

Ali B. H., Al-Qarawi AA, Haroun EM and Mousa HM. (2003). The effect of treatment with gum arabic on gentamicin nephrotoxicity in rats: a preliminary study. Fundam Clin Pharmacol, 25(1):15-20.

Ali H. Badreldin, Amal Ziada and Gerald Blunden. (2009). Biological effects of gum arabic: A review of some recent research Food and Chemical Toxicology, 47(1):1-8

Berthelot, MPE, (1959). Repert Chim. Appl. 284,

Bliss, D. Z., Stein, T. P., Schleifer, C. R., Settle, R. G. (1996). Supplementation with G.A. fiber increases fecal nitrogen excretion and lowers serum urea nitrogen concentration in chronic renal failure patients consuming a low-protein diet. Am. J. Clin. Nutr., 63: 392–398.

Cindoruk, M., Kerem, M., Karakan, T., Salman, B., Akin, O., Alper, M., Erdem, O., Unal, S. (2007). Peroxisome proliferators-activated alpha agonist treatment ameliorates hepatic damage in rats with obstructive jaundice: an experimental study. BMC Gastroenterol., 28- 44.

Evans WC. (1989). Drugs of biological origin in: Trease and Evan`s pharmacognosy, 13th ed. (part 6): 371-373.

Gamal el-din AM, Mostafa AM, Al-Shabanah OA, Al-Bekairi AM and Nagi MN. (2003). Protective effect of arabic gum against acetaminophen-induced hepatotoxicity in mice. Pharmacol Res., 48(6):631-5.

Henry JB. (1984). Clinical dignosis and management 17th edition, Sauders Publisher,

Howard, M. D., Gordon, D. T., Garleb, K. A., Kerley, M. S. (1995). Dietary fructooligosaccharide, xylooligosaccharide and gum arabic have variable effects on cecal and colonic microbiota and epithelial cell proliferation in mice and rats. J. Nutr., 125: 2604–2609.

Kishimoto, A., Ushida, K., Phillips, G.O., Ogasawara, T., Sasaki, Y. (2006). Identification of intestinal bacteria responsible for fermentation of gum arabic in pig model. Curr. Microbiol., 53: 173–177.

Parker, R. A., W. H. Bennett, and Porter G. A. (1982). Animal models in the study of aminoglycoside nephrotoxicity, p. 235–267. *In* A. Whelton and H. C. Neu (ed.), The aminoglycosides: microbiology, clinical use and toxicology. Marcel Dekker, Inc., New York, N.Y.

Praetorious E. and Poulsen H. (1927). Enzymatic determination of uric acid with detailed directions. Scandinav J. Clin Lab Investigation. 1953, 3:273-280. Mac Kay EM Mac Kay LLJ Clin Invest, 4:295

Priuska, E. M., and J. Schacht. (1997). Mechanism and prevention of aminoglycoside ototoxicity: outer hair cells as targets and tools. Ear Nose Throat J., 76:164–171.

Rawlin E. A. (1997). Tablet and capsules .In Bentley`s textbook of pharmaceutics, 8th ed. (Ch 19):274.

Teixeira RB, Kelley J, Alpert H, Pardo V. and Vaamonde CA. (1982). Complete protection from gentamicin-induced acuterenal failure in diabetes mellitus rats. Kidney Int., 21: 600-12

Trommer, H., Neubert, R.H. (2005). The examination of polysaccharides as potential antioxidative compounds for topical administration using a lipid model system. Inter. J. Pharm. , 298: 153–163.

Tulung, B., Rémésy, C., Demigné, C. (1987). Specific effect of guar gum or gum Arabic on adaptation of cecal digestion to high fiber diets in the rat. J. Nutr., 117: 1556–1561.

ARABIC SUMMARY

التأثير الوقائي لصمغ الاكاسيا سينيغال ضد التسمم الكلوي للجنتاميسن بأستخدام الجرذان البيضاء

محمود عبدالله الدربي[1] وعبدالوهاب حسن محمد[2] و علي عبدالسلام احمد[3]

1- قسم الادوية و السموم- كلية الصيدلة- جامعة بنغازي- بنغازي- ليبيا.

2- قسم العلاجيات- كلية الصيدلة- جامعة الرباط الوطني- الخرطوم- السودان.

3- قسم الادوية- كلية الطب- جامعة الازهر- أسيوط - مصر.

المقدمة: صمغ الاكاسيا سينيغال أو ما يعرف بالصمغ العربي هو عبارة عن أفرازات صمغية لسيقان و أفرع شجرة الاكاسيا (Acacia senegal) و الانواع الافريقية المماثلة لها من عائلة (Legumenosae) . يستخدم الصمغ العربي في صناعة كلا من المستحضرات الصيدلانية و الصناعات الغذائية كمادة مستحلبة و معلقة كما أن للصمغ العربي العديد من التأثيرات الدوائية منها تأثير الصمغ على الجهاز الهضمي ، حيث أنه يزيد من الاحماض الدهنية القصيرة السلسلة كما يزيد قدرة الجهاز الهضمي على أمتصاص الماء و الاملاح بالاضافة الى تأثيرات مختلفة على عملية الايض للدهون و السكريات. في حالات مرضى الفشل الكلوي. للصمغ العربي قدرة عالية على خفض اليوري في الدم . للصمغ العربي القدرة على التخلص من (superoxides) و لهذا لدى الصمغ العربي قدرة على حماية كلا من الكبد من سمية البارسيتمول و القلب من دوكسوروبيسن عند الجرذان.

الهدف من الدراسة: دراسة مدى قدرة الصمغ العربي على حماية الكلى من التسمم الناتج عن جنتاميسن عند الجرذان.

المواد و طريقة البحث: يتم تقسيم الحيوانات الى ثلاثة مجموعات: المجموعة (A) وتمثل المجموعة الضابطة و مجموعة (B) ويتم معالجة الحيوانات بدواء جنتاميسن فقط (80 مج حقن عضلي لمدة سبعة أيام متواصلة) و المجموعة (C) وفيها يتم معالجة الحيوانات بالصمغ العربي (10مج/100مل ماء) قبل أعطاء الجنتاميسن. يتم تقييم التسمم الكلوي عن طريق قياس كلا من الكرياتنين و اليوريا و حمض اليوريك في الدم بالاضافة الى التحليل النسيجي للكلى.

النتائج: أظهرت النتائج زيادة ذات دلالة في كلا من الكرياتنين و اليوريا و حمض اليوريك في المجموعة (B) ولكن أظهرات النتائج في المجموعة (C) أرتفاع فى نسبة الكرياتنين و أنخفاض في نسبة اليوريا ذات دلالة مقارنة مع المجموعة (B) و لكن أعلى من تلك في المجموعة (A)

الخلاصة: هذه النتائج تثبت أن الصمغ العربي لديه بعض القدرة على حماية الكلى من التسمم بالجنتاميسن و ذلك لوجود خواص مضادة للاكسدة يمتلكها الصمغ العربي.