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

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**INTRODUCTION**

*Acacia senegal* 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.

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**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* (Badreldeen 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°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 4 weeks 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:
The Protective Effect of *A. senegal* gum Against Gentamicin-Induced Nephrotoxicity

Serum creatinine (Crea), Serum urea (Urea) and Uric acid (UA). Serum creatinine concentration was measured by Jaffé 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 Examination:**

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>
<thead>
<tr>
<th>Groups</th>
<th>Crea mg/dl</th>
<th>Urea mg/dl</th>
<th>UA mg/dl</th>
<th>Histology score</th>
</tr>
</thead>
<tbody>
<tr>
<td>A (control)</td>
<td>0.34±0.04</td>
<td>41.00±1.58</td>
<td>1.13±0.13</td>
<td>0</td>
</tr>
<tr>
<td>B (GM only)</td>
<td>0.78±0.04</td>
<td>48.75±1.11</td>
<td>5.24±0.30</td>
<td>4</td>
</tr>
<tr>
<td>C (GA+GM)</td>
<td>0.82±0.18&lt;sup&gt;*&lt;/sup&gt;</td>
<td>34.50±2.18&lt;sup&gt;##&lt;/sup&gt;</td>
<td>3.72±0.13&lt;sup&gt;##&lt;/sup&gt;</td>
<td>2</td>
</tr>
</tbody>
</table>

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

<sup>*</sup>Significance different from control (P< 0.05)

<sup>##</sup> Significant different from GM only group (P< 0.05)

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![Figure 1](image-url)  
**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 4 weeks 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).
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**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.

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التأثير الوقائي لصمغ الاكاسيا سيينغال ضد التسمم الكلوي بالجرذان

البيضاء

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المقدمة: صمغ الاكاسيا سيينغال أو ما يعرف بالصمع العربي هو عبارة عن أفرزات صمغية لسيفان و (Leguminosae) وأفرع شجرة الاكاسيا (Acacia senegal) التي تستخدم الصمع العربي في صناعة كلاً من المستحضرات الصيدلانية والصناعات الغذائية كمادة مستخلصة ومعلقة كما أن الصمع العربي يعد من التأثيرات الطبيعية التي تؤثر على الجهاز الهضمي، حيث أن زيادة عدد الأمراض المعدية والأمراض الجلدية بالإضافة إلى تأثيرات مختلفة على عملية الأيض الدموي والسكريات. في حالات مضافة مثل مرض الفشل الكلوي، يُستخدم الصمغ العربي للوقاية على خاصية الدهون السامة (superoxides) في الدم. الصمغ العربي قدرة على حماية كل من الكبد من سمية البارسينوم وللبطين من دوكوزوريين عند الجرذان.

الهدف من الدراسة: دراسة مدى قدرة الصمع العربي على حماية الكلوي لدى حشرة الجرذان عند الجرذان.

المولد و طريقة البحث: تم تجربة المسح العربي في ثلاث مجموعات: مجموعة (A) هي مجموعة الضابطة ومجموعة (B) هي مجموعة معالجة الحيوانات بدواء جناتينيسين فقط (80 مجم عضلي لمدة سبعة أيام) ومجموعة (C) هي مجموعة معالجة الحيوانات بالصمع العربي (10 مجم/100 مل ماء) قبل أعطاء الدواء ضار بكتيريات وبيولوجيا classe Acacia senegal (الدربي). يتم تقييم الهزائم في قشرة الدبس، في اليوم 3-4-5PRIUSKA, E. AND J. SCHACHT (1997). MECHANISM AND PREVENTION OF AMINOGLYCOSIDE OTOTOXICITY: OUTER HAIR CELLS AS TARGETS AND TOOLS. EAR NOSE THROAT J., 76:164–171.


