Some Physiological Effect of Acacia Gum on Acute Renal Failure Induced by Gentamicin in Male Rabbits

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Abstract

Renal failure a case characterized by the impairment of the kidney to filter waste products from the body. The study aims to evaluate the potential effect of Acacia gum in the prevention of induced Acute renal failure in the rabbit model. Eighteen healthy male domestic rabbits (Lepus cuniculus) were divided into three groups. Group 1: normal rabbits as control, Group 2: animals were injected (70mg/kg. B.W) of intramuscular gentamicin daily for 14 days for induction of acute renal failure, Group 3: animals were treated with intramuscular injection (70mg/kg B.W) gentamicin daily and offered 15% Acacia gum with drinking water for 14 days. At the end of the experiment Serum urea, uric acid, creatinine, blood urea nitrogen, calcium, sodium, and malondialdehyde were measured in addition to Urine analysis. The results showed that the treatment of Acacia gum improved significantly serum uric acid, creatinine, urea, blood urea nitrogen, electrolyte, and proteinuria. Also reduced malonaldehyde, urine Specific gravity, and pH levels. Our findings conclude that GA can protect the kidney by enhancing antioxidant efficiency, and may be useful in improving acute renal failure.

Keywords: *Acacia gum, Acute renal failure, Gentamicin.*

Introduction

Acute renal failure (ARF) recently called Acute kidney injury (AKI). It characterized as a sudden reduction (within hours) in kidney function involving both injury (structural damage) and disability (function loss). The ARF is a condition that seldom has clear, distinct pathophysiology [1,2]. Kidney failure is categorized as either acute kidney failure that occurs quickly and reversible and chronic kidney failure that progresses slowly and irreversible condition. Symptoms may include swelling of the legs, feeling fatigued, vomiting, loss of appetite and confusion. In a medical condition, kidneys operate at less than 15% of normal in renal failure [3]. Acute renal failure clinically observed as a severe reversible rise in nitrogen waste products – measured by blood urea nitrogen (BUN) and serum creatinine levels over hours to weeks [2]. Gentamicin is an important aminoglycoside antibiotic that commonly prescribed for the treatment of life-threatening Gram-negative bacterial infections, because of their efficiency and low cost. But its related adverse effects of oxidative stress and kidney damage limit its long-term clinical use [4,5]. Acacia Gum (AG) also called gum Arabic is the dried gummy exudates derived from stems and branches Acacia Senegal (Linne‘) or other similar African species of Acacia (Fam. Leguminosae) (Phillips 2009). Acacia Gum is a natural complex polysaccharide contain calcium, magnesium, and potassium. Which a highly fermentable dietary fiber with proven prebiotic properties [6]. The AG has been used in the traditional treatment of a several diseases including renal insufficiency, improve digestive systems, increasing appetite and antidiarrheal. Experimental studies of Acacia gum yielded use the potential to change the physiological state for hepatic and cardiac failure, anemia and diabetes mellitus. It also has anti-inflammatory and antioxidant properties [7-10].

Materials and Methods

Experiment Animal: A total of eighteen healthy male domestic rabbits (*Lepus cuniculus*) were brought from Basra / Local markets. Animals weigh (1375-1750) grams and age between (8-12) months. The

rabbits were housed under observation for ten days in an animal house at the University of Basra College of Veterinary Medicine. A healthy rabbit diet was given consisting of green leaves, fodder and water *ad libitum*. The procedures for the handling of animals were carried out according to ethical norms.

Experimental Design: The animals were divided into: three groups (6 rabbit).

Group 1: normal rabbits were served as control. Group 2: animals were treated with intra muscular injection (70mg/kg. B.W) gentamicin (Florence/Italy) daily for 14 days.

group 3: animals were treated with intra muscular injection (70mg/kg b.w) gentamicin daily and offered 15% Acacia gum with drinking water for 14 days.

Biochemical Analysis:

Blood and Urine Collection Analysis**:** At fifteens day of the experiment, blood samples were collected from heart puncture and were poured in a gel tube for serum biochemical analysis by using commercial kits such as urea, uric acid creatinine, Calcium and Sodium (Biolabo/France). Serum malodialdehyde (MDA) was determined according to Yiğit,*etal* (11) . The urine was collected directly from the urinary bladder by syringe and was poured in a plain tube. Urine analysis was done by using urinalysis reagent strips (ACON Laboratories/ San Diego/USA).

Statistical Analysis

A data was done using a significant level of ($P<0.05$) using the one-way Analysis of Variance (ANOVA). Relevant group differences were calculated using version 22 of the computerized SPSS (Statistical System for Social Sciences) software using the least significant differences (LSD).

Results

The results of the present study showed that a significant increase ($p< 0.05$) in the serum levels of uric acid, creatinine, urea and BUN after gentamicin injection as compared to normal rats. While there was a significant decrease in treatment with Acacia gum and gentamicin as compared with the gentamicin group, and no significant difference in uric acid between acacia gum group and control as shown in (Table -1).

Table 1: Effect of Acacia Gum and gentamicin on serum uric acid, creatinine, urea and blood urea nitrogen (BUN)

Parameter Group	Uric acid mg/dl	Creatinine mg/dl	Urea mg/dl	BUN mg/dl
Control	0.345 ± 0.72 b	1.15 ± 0.75 c	32.05 ± 1.29 c	14.88 ± 0.61 c
Gentamicin	1.32 ± .0.95 a	5.36 ± 0.33 a	282 ± 49.9 a	131.16 ± 23.79 a
Gentamicin + Acacia gum	1.108 ± 0.41 b	4.33 ± 0.41 b	208 ± 22.5 b	96.5 ± 10.47 b

Values (mean ± SD), n = 6/group, letters (difference with in groups (P<0.05).

The results of (Table -2) indicated that the injection of gentamicin caused a significant decrease (P<0.05) on serum Ca and Na concentration in the gentamicin group as compared to the control group. Treatment with gentamicin and acacia gum group showed a significant increase (p<0.05) in the serum Ca and Na concentration as compared to the gentamicin group. However, gentamicin injection produced a significant increase (p < 0.05) in serum MDA levels as compared to control rats. Administration of acacia gum treatment significantly (p < 0.05) restored the levels of serum MDA compared to the gentamicin group.

Table 2: Effect of Acacia Gum and gentamicin on serum Ca, Na and malondialdehyde (MDA)

Parameter Group	Ca mg/dl	Na mmol/l	MDA nmol/l
Control	11.7 ± 0.17 a	160.8 ± 7.2 a	0.258 ± 0.27 b
Gentamicin	11.05 ± 0.58 b	139 ± 6.88 b	2.425 ± 0.32 a
Gentamicin + Acacia gum	11.79 ± 0.55 a	145 ± 11.82 b	0.411 ± 0.66 b

Values (mean ± SD), n = 6/group, letters (difference with in groups (P<0.05).

Depending on the statistical analysis, the result revealed that the treatment of rats with Acacia gum and gentamicin showed a significant decrease(p<0.05) on urine Specific gravity and pH levels as compared to the gentamicin group. Also, the result did not show any significant differences between the gentamicin plus acacia gum group and control group. On the other hand, the urine protein concentration results indicate that a significant increase (P<0.05) in the gentamicin group as compared to control. While a significant decrease (P<0.05) in protein concentration was recorded in the gentamicin plus acacia gum group as compared to the gentamicin group (table-3).

Table 3: Effect of Acacia Gum and gentamicin on urine specific gravity, pH and protein

Parameter Group	Specific gravity	pH	Protein mg/dl
Control	1.025 ± 0.004 a	7.01 ± 0.36 a	10.66 ± 8.32 c
Gentamicin	1.0061 ± 0.006 b	5.01 ± 0.66 b	180 ± 24.4 a
,,Gentamicin + Acacia gum	1.030 ± 0.044 a	7.41 ± 0.58 a	45.8 ± 18.5 b

Values (mean ± SD), n = 6/group, letters (difference with in groups (P<0.05).

Discussion

Renal failure induced by gentamicin has been extensively studied in the past and has become one of the known models of nephrotoxicity induced by drugs. The animal models are often used to understand the pathophysiology of ARF and to examine drug therapies. In our study gentamicin injection for 14 days causes significant increase in the serum levels of kidney markers function such as uric acid, creatinine, urea and BUN in rabbits, these finding agree with previous study [5]. Serum uric acid is the final metabolite of purine, thus, any change in the rate of glomerular filtration can cause serum uric acid to rise. On another side, it has been proposed that proximal convoluted tubules damage caused by gentamicin decreases the tubular capacity to reabsorb $HCO3^-$which is essential to uric acid excretion out [11].ic acid can decrease the endothelial capacity to produce nitric oxide [12]. Uric acid has been reported to play a role in the development of the pathophysiology of chronic renal disease and probably, in acute renal injury [13]. Creatinine is essential for clinically testing renal function and GFR. Creatinine is secreted by the liver and proximal kidney tubules and then transferred through the blood to the muscles. Creatinine undergoes glomerular filtration and tubular secretion to a lesser degree. Such elevated serum creatine levels can be associated with drug-induced oxidative alteration of mitochondrial or cytosolic creatine kinases, oxidative damage-prone enzymes [14]. Blood urea nitrogen is a metabolic waste product excreted in urine by the kidneys. Urea flows from the blood to the glomerular filtrate during glomerular filtration, the liquid that is the urine precursor. The urea will not correctly get filtered into the urine in the case of kidney damage [5]. Acacia gum ‘s reno-protective effect can be related to its sorbent effect, which helps eliminate some of the creatinine and urea from the blood without necessarily altering major physiological factors like glomerular filtration rate and creatinine clearance. Several theories are explaining how dietary fibers such as Arabic gum decreases serum urea nitrogen. It has been reported that colonic bacteria can ferment dietary fibers to provide them with energy for growth and excretion of nitrogen [15]. Another suggestion in animal models of experimental chronic renal failure showed that consuming diets containing fermentable carbohydrates results in a higher rate of transmission of urea nitrogen from the blood to cecal lumen, where it is hydrolyzed by bacterial urease before the subsequent metabolism and proliferation of microflora, which results in a high excretion of fecal nitrogen, together with a decrease in urinary nitrogen excretion and plasma urea concentration. The kidneys are essential organs with important roles to control the hydroelectrolyte balance and remove waste products from the blood and maintain the acid base balance of the body. The present study demonstrates that gentamicin-induced changes in plasma electrolyte (Ca^{2+} and Na^+). Gentamicin may negatively affect sodium/potassium ATPase and thus, decrease the sodium-driven basolateral gradient sodium and calcium exchanger. Provided the probable location of the Sodium-calcium exchanger in nephron [16]. plasma electrolyte improved in treated acacia gum group that enhanced the Ca^{2+}-sensing receptor with subsequent inhibition of the Na^+, K^+, $2Cl^–$ cotransport in the thick ascending limb [17].

After gentamicin injection, renal oxidative stress as illustrated by increased measuring MDA significantly. Gentamicin has been shown to stimulate the development of free radicals, like relative oxygen species (ROS), which induce kidney injury through peroxidation of cell membrane lipids, protein denaturation and DNA damage. Treatment with acacia gum attenuated the gentamicin-induced oxidative damage by reduced MDA levels substantially. This may be attributed to the acacia gum’s excellent antioxidant properties and scavenging ROS via metallothionein synthesis zinc-induced [18,19]. the previously mentioned study Acacia gum has antioxidant and anti-inflammatory properties [20]. Such findings implied that the effective antioxidant property of acacia gum could be used in numerous clinical conditions and diseases caused by increased lipid peroxidation and injury to the tissue.

The results revealed rises in the blood acidity, as shown by reductions in pH levels for rats treated with gentamicin. This may be attributed to the hydrogen ion retention in the blood due to renal failure. While

treatment with Arabic gum restoring pH to its normal value this result agree with Nasir,*etal* [21].The high dose of gentamicin causing overproduction of nitric oxide (NO) that decreases in number and size pore in the glomerulus of endothelial cells. These changes lead to decreased filtration and lack of selectivity membranes causing proteinuria [22,23]. Treatment with acacia gum diminished proteinuria and increases the glomerular filtration rate. Mechanism of action Acacia Gum either GA modifies NO release, acting as a scavenger of NO and as a competitive inhibitor of NO synthase [22]. We conclude that the treatment of Acacia gum improved serum uric acid, creatinine, urea, blood urea nitrogen, urine electrolyte, and proteinuria. Also reduced lipid peroxidation, urine Specific gravity, and pH levels. So, the treatment of GA may be of use in the reduction of oxidative stress and improvement of acute renal failure in rabbits.

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Conflict of Interest: None to declare.

Ethical Clearance: All experimental protocols were approved under the College of Veterinary Medicine and all experiments were carried out in accordance with approved guidelines.

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