

## NEPHRO PROTECTIVE EFFECT OF AQUEOUS PSIDIUM GUAJAVA IN GENTAMICIN NEPHROTOXICITY

**\*Mr. Imran Hussain, Assistant Professor**

**Integral University, Lucknow, Uttar Pradesh, India.**

**ABSTRACT:** Gentamicin-induced nephrotoxicity prevention is assessed using the aqueous extract of *Psidium guajava* leaves. Serious bacterial infections are treated with gentamicin. Its medical applications are restricted by tubule degeneration and oxidative stress-induced kidney injury. The nephrotoxicity of gentamicin was investigated in animal models. Aqueous extract of *Psidium guajava* was also evaluated for its protective properties. Serum creatinine, BUN, urea, and renal tissue histology were used to evaluate kidney function. Renal function was impaired and kidney tissues were damaged by gentamicin. The metabolic changes were reduced by aqueous *Psidium guajava* extract, which restored kidney structure. *Psidium guajava*, an antioxidant and free radical scavenger, may provide kidney protection. This investigation determined that gentamicin-induced kidney toxicity may be mitigated by aqueous *Psidium guajava* extract.

**Keywords:** *Nephroprotective activity; Psidium guajava; Gentamicin-induced nephrotoxicity; Oxidative stress; Renal function; Antioxidant activity*

### 1. INTRODUCTION

Acute kidney injury (AKI) is a prevalent and hazardous medical condition that involves an abrupt cessation of renal function. This results in acid-base imbalances, metabolic waste, electrolyte imbalances, and fluid imbalances. AKI is caused by acute tubular necrosis as a result of ischemia or nephrotoxicity. AKI can be caused by ischemia-reperfusion injury, kidney-toxic medications, and sepsis.

On a global scale, kidney disease is on the rise. 850 million individuals worldwide are impacted by renal disease. This pertains to the prevention and treatment of kidney disease. Hospitalized patients who have experienced drug-induced nephrotoxicity develop acute renal failure.

Aminoglycoside-induced renal impairment is accurately modeled by gentamicin-induced acute kidney injury. In 1964, *Micromonospora purpurea* was utilized to produce gentamicin, the third clinical aminoglycoside antibiotic. Gentamicin is antibacterial and medicinal; however, its prolonged use may result in kidney injury.

In renal proximal tubular cells, aminoglycosides such as gentamicin generate reactive oxygen species (ROS) and are nephrotoxic. Renal tubules are destroyed by oxidative stress, which results in impaired kidney function. It induces mitochondrial dysfunction, inflammation, lipid peroxidation, and cell demise.

Diabetes, gastrointestinal, neurological, and kidney diseases are all treated for free by traditional medicine. Natural medicinal plants are utilized in traditional medicine and

fundamental healthcare due to their affordability, accessibility, and safety. Psidium guajava, a widely used medicinal herb, has a variety of applications.

Flavonoids, phenolic acids, tannins, terpenes, and alkaloids are present in guava leaf extract. The anti-inflammatory, anti-cancer, and antioxidant properties of these portions make them effective in the treatment of a variety of diseases. Mice are safeguarded from cyclosporine A-induced nephrotoxicity by aqueous Psidium guajava leaf extracts.

Milk thistle seed silymarin is a well-known nephroprotectant. The antioxidant and membrane-stabilizing properties of this substance have been demonstrated in numerous studies to protect rodents from drug-induced nephrotoxicity.

## 2. MATERIALS AND METHOD

The Experimental Approach of this Study was authorized by the Regional Institute of Medical Sciences (RIMS) Institutional Animal Ethics Committee (1596/GO/a/12 CPCSEA registration) in accordance with the Indian Government's Committee for the Control and Supervision of Experiments on Animals.

In Imphal, Manipur, pathology, biochemistry, and JNIMS Pharmacology collaborated.

**Collection and Identification of Psidium guajava Leaves:** In February 2023, Imphal West harvested fresh Psidium guajava foliage. The plant was discovered and verified by Mrs. Yumnam Sanatombi, a guest faculty member of Manipur University's Life Science department. The laboratory herbarium number was 001380MUMP.

**Preparation of Plant Extract:** For Psidium guajava leaves, we implemented the aqueous extraction method of Massoudi EL et al. 11. The leaves were allowed to dry in the shade for an extended period of time following their washing. Combination grinders were employed to pulverize dry leaves. Ten times more distilled water was used to soxhlet the powder. The water underwent a three-hour process of boiling and cooling. A substantial dark residue remained after the filter water dissipated. This was stored in a porcelain container at a temperature of 4°C. Continue until 20 grams of extract are obtained. The investigation employed aqueous extract of Psidium guajava.

**The Experimental Animal Used in the Study:** 25 albino rodents weighing 150–200 grams were provided by the JNIMS animal sanctuary in Porompat, Imphal. In order to acclimate to the laboratory, they were confined to departmental polypropylene enclosures for a period of ten days. Lab rodents were provided with an unlimited supply of water and consumed a standard meal. It was both bright and dark for twelve hours. In preparation for the testing, the animals were required to fast for 18 hours and were prohibited from consuming their own excrement.

**Acute Oral Toxicity Studies:** The acute oral toxicity of Psidium guajava leaf extract was evaluated in accordance with OECD/OCED guidelines 425. The extract's safety was demonstrated by the absence of documented fatalities at 2000 mg/kg body weight orally after 14 days.

**Experimental Design:** The examination persisted for fifteen days. Twenty-five albino rats of either species, weighing 150–200 grams, were employed. We incorporated silymarin and Psidium guajava leaf extracts into 2% gum acacia. Before being randomly divided into five groups of five, the animals were weighed, recorded, and numbered.

Group (Animals)	Treatment
Group I (Normal control)	2% gum acacia administered orally
Group II (Positive control)	Gentamicin (100 mg/kg, intraperitoneal) + 2% gum acacia (oral)
Group III (Standard drug)	Gentamicin (100 mg/kg, intraperitoneal) + Silymarin (200 mg/kg, oral)
Group IV (Treatment group)	Gentamicin (100 mg/kg, intraperitoneal) + AELPG (200 mg/kg body weight, oral)
Group V (Treatment group)	Gentamicin (100 mg/kg, intraperitoneal) + AELPG (300 mg/kg body weight, oral)

The rodents were grouped and sedated with ether the following day. S. urea, S. creatinine, S. sodium, S. potassium, and S. chloride were measured in blood tests. The cervical dislocation of rodents was necessary for the collection of blood for histology liver tissue.

### 3. RESULTS

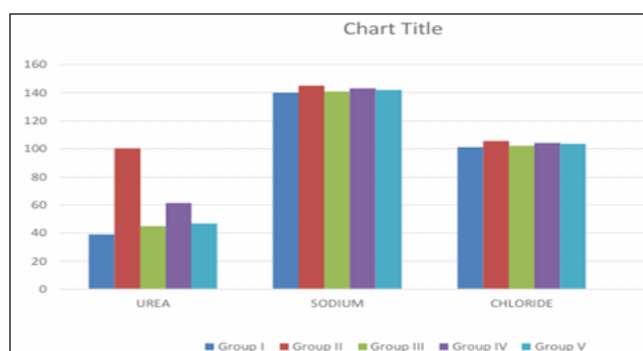
In the tables, the numbers of many parameters were shown in the right units. Along with the Mean  $\pm$  SEM (standard error of the mean), the data show five animals from each group. After a one-way ANOVA showed that there was statistical significance, we used the Tukey Kramer multiple comparisons test to compare the groups. The fact that both the F-ratio and the P value were less than 0.05 showed that the test was significant.

**TABLE 1:** Serum Level Of Urea, Creatinine, Sodium, Potassium And Chloride In All Groups (Mean $\pm$ Sem)

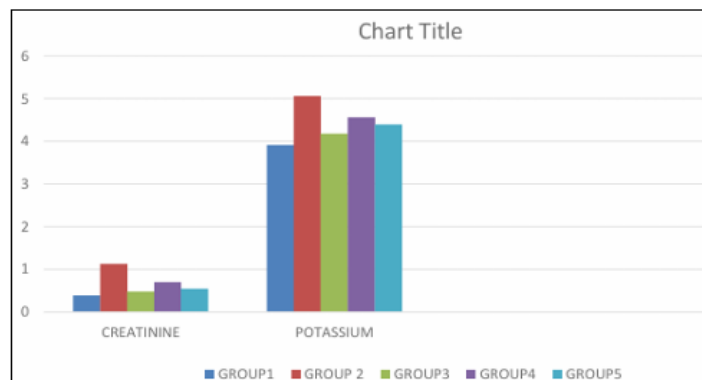
Groups	Urea	Creatinine	Sodium	Potassium	Chloride
I	38.8 $\pm$ 1.83	0.38 $\pm$ 0.04	140.0 $\pm$ 0.55	3.92 $\pm$ 0.04	101.0 $\pm$ 0.32
II	100.4 $\pm$ 1.78#	1.12 $\pm$ 0.09#	145.0 $\pm$ 0.45#	5.06 $\pm$ 0.18#	105.6 $\pm$ 0.24#
III	44.8 $\pm$ 0.37*	0.48 $\pm$ 0.04*	141.0 $\pm$ 0.63*	4.18 $\pm$ 0.08*	102.2 $\pm$ 0.37*
IV	61.4 $\pm$ 0.81*@	0.70 $\pm$ 0.03*@	143.20 $\pm$ 0.37*@	4.56 $\pm$ 0.09*@	104.2 $\pm$ 0.37*@
V	46.6 $\pm$ 1.44*	0.54 $\pm$ 0.02*	141.80 $\pm$ 0.80*	4.40 $\pm$ 0.07*@	103.4 $\pm$ 0.40*@

## One-way ANOVA

Parameter	F value	df	p value
Urea	331.38	4, 20	< 0.05
Creatinine	35.71	4, 20	< 0.05
Sodium	11.37	4, 20	< 0.05
Potassium	76.78	4, 20	< 0.05
Chloride	—	4, 20	< 0.05



**Fig. 1:** Bar Diagram Showing Serum Levels Of Urea, Sodium And Chloride In All Groups. Each Value Is Expressed As Mean ± Sem



**Fig. 2:** Bar Diagram Showing Serum Levels Of Creatinine And Potassium In All Groups. Each Value Is Expressed As Mean ± Sem

The results show that the levels of urea ( $100.4 \pm 1.78$ ), creatinine ( $1.12 \pm 0.09$ ), sodium ( $145.0 \pm 0.45$ ), potassium ( $5.06 \pm 0.18$ ), and chloride ( $105.6 \pm 0.24$ ) were significantly higher ( $p < 0.05$ ) in group II, which was given gentamicin to make the kidney damage worse. In group III, which received silymarin (200 mg/kg) along with gentamicin, blood levels of urea ( $44.8 \pm 0.37$ ), creatinine ( $0.48 \pm 0.04$ ), sodium ( $141.0 \pm 0.63$ ), potassium ( $4.18 \pm 0.08$ ), and chloride ( $102.2 \pm 0.37$ ) were all significantly lower than those in group II ( $p < 0.05$ ). The levels of urea ( $61.4 \pm 0.81$ ), creatinine ( $0.70 \pm 0.03$ ), sodium ( $143.2 \pm 0.37$ ), potassium ( $4.56 \pm 0.09$ ), and chloride ( $104.2 \pm 0.37$ ) were all much lower in group IV (200 mg/kg of AEPGL) than in groups II and III ( $p < 0.05$ ). When 300 mg/kg of AEPGL was given to group V, their levels of urea ( $46.6 \pm 1.44$ ), creatinine ( $0.54 \pm 0.02$ ), sodium ( $141.8 \pm 0.80$ ), potassium ( $4.40 \pm 0.07$ ), and chloride ( $103.4 \pm 0.40$ ) were all significantly lower ( $p < 0.05$ ) than those in group II. The only important difference between groups V and III was the amount of potassium and salt present.

Serum urea, creatinine, sodium, potassium, and chloride levels were much lower in the groups that were given AEPGL compared to the positive control group II.

#### 4. HISTOPATHOLOGICAL FINDINGS

**Gross Features:** None of the groups, not even the ones that were given silymarin, the poisonous control, the normal control, or the extract-treated groups at different doses, showed any major changes. The kidneys were the right size, form, color, surface, and contour.



**FIG. 3:** Gross Kidney Specimen Of Albino Rats

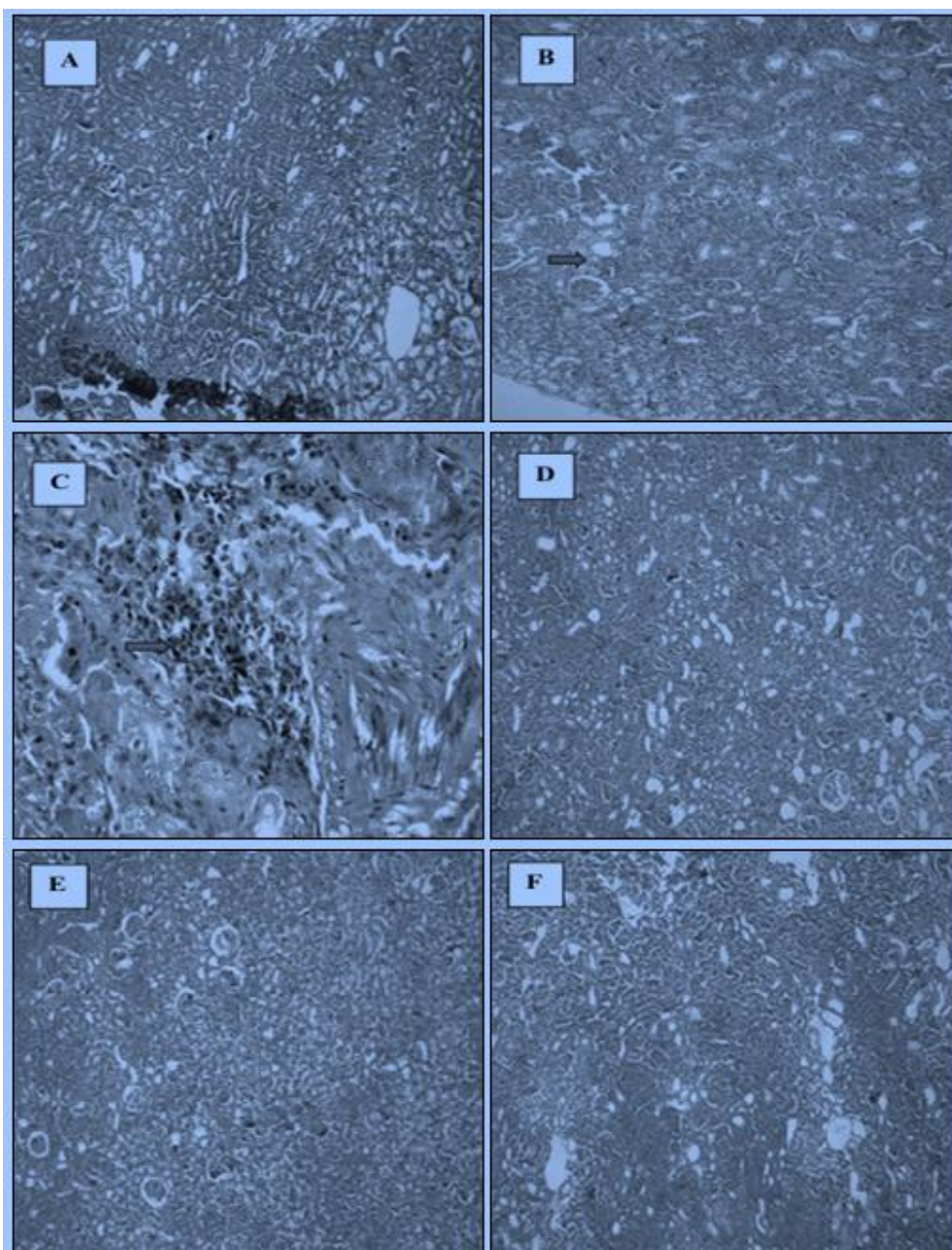
**Microscopic Findings:** In the control group (group I), the kidney histology showed that the tubules and glomeruli were normal (Fig). In the gentamicin-treated group (group II), acute tube necrosis, degeneration of proximal tubular epithelial cells, and sloughing of the lumen were seen.



**Fig. 4:** Dissected Kidney of Albino Rats

The kidney interstitium became inflamed when gentamicin was used. When 200 mg/kg of silymarin was given to Group III, there was no damage to the interstitial spaces and only a few tubules with damaged epithelial cells. The number of inflamed cells went down in Group IV, and some damage was seen in the proximal tubular epithelial cells. On the other hand, people in Group V fully recovered from interstitial nephritis and acute tubular necrosis. The results of all of these studies show that the AEPGL protected the kidneys when preparations and gentamicin were given to rats.





**Fig. 5:** Histopathology of rat kidney (H&E) showing tubular necrosis in gentamicin group and improvement with silymarin and AELPG treatment.

## 5. CONCLUSION

This research demonstrates that the aqueous extract of *Psidium guajava* leaves significantly safeguards the kidneys of albino rats against nephrotoxicity induced by gentamicin. Flavonoids, alkaloids, tannins, saponins, and phenolic compounds are bioactive chemicals in *Psidium guajava* that may be responsible for its nephroprotective properties. These substances enhance the activity of antioxidant enzymes, neutralize free radicals, and fortify renal tissue. These factors may elucidate the renal preservation attributes of *Psidium guajava*. The study indicates that the aqueous extract of *Psidium guajava* may serve as an effective nephroprotective agent. Further research with a purer form of the extract is necessary to elucidate its cellular and molecular mechanisms, assess the safety and efficacy of its active constituents, and evaluate its potential as a nephroprotective agent in the future.

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