Int. J. Sci. R. Tech., 2026 3(5)
A Multidisciplinary peer-reviewed Journal
www.ijsrtjournal.com [ISSN: 2394-7063]

Original Article

Evalution Of Nephroprotective Activity Of Papaya [Carica Papaya] Seed Extract Against Gentamicin-Induced Nephrotoxicity In Albino Wistar Rats

Thummidi Harshini, Naasir Jamal, Bolla Sreeja, Jagu Sanjeev, Nadimpalli Sumanasri*

K.G.R.L. College of Pharmacy, Bhimavaram, Andhra Pradesh, India

ABSTRACT

Nephrotoxicity refers to kidney damage caused by drugs and toxic substances. The present study was conducted to evaluate the nephroprotective activity of papaya seed extract (Carica papaya) against gentamicin-induced nephrotoxicity in Wistar albino rats. Papaya seeds contain phytochemicals such as flavonoids, alkaloids, and phenolic compounds with antioxidant properties.The extract was prepared by aqueous extraction and subjected to phytochemical screening. Rats were divided into five groups and treated for 14 days. Renal function was assessed using biochemical parameters like serum creatinine, blood urea nitrogen (BUN), and uric acid, along with histopathological examination.The results showed that low-dose papaya seed extract improved kidney function and reduced renal damage, whereas the high dose showed signs of toxicity. Thus, Carica papaya seed extract exhibits nephroprotective activity at an optimal low dose due to its antioxidant properties.

Keywords: Nephrotoxicity, nephroprotective activity, Carica papaya seed extract, Gentamicininduced nephrotoxicity, antioxidant activity, renal function.

INTRODUCTION

Nephrotoxicity is defined as the adverse effect of exogenous substances such as drugs, chemicals, heavy metals, and environmental toxins on the structure and functional integrity of the kidneys. The kidneys are highly specialized organs responsible for filtration of blood, excretion of metabolic waste products, maintenance of electrolyte and acid–base balance, regulation of fluid volume, and secretion of hormones such as renin and erythropoietin. Because they receive nearly 20–25% of the cardiac output and actively concentrate substances during urine formation, the kidneys are particularly susceptible to toxic injury.

Renal toxicity can involve different anatomical components of the kidney, including the glomeruli, proximal and distal tubules, loop of Henle, collecting ducts, interstitium, and renal vasculature. Among these, the proximal tubules are most commonly affected due to their high metabolic activity and role in reabsorption and secretion. Mechanisms of nephrotoxicity include direct cytotoxic effects on tubular epithelial cells, oxidative stress due to excessive production of reactive oxygen species (ROS), mitochondrial dysfunction, inflammation, immune-mediated injury, and intratubular crystal precipitation leading to obstruction. Reduced renal blood flow and ischemia further aggravate renal damage. Clinically, nephrotoxicity often manifests as acute kidney injury (AKI), characterized by a rapid decline in glomerular filtration rate (GFR), elevated serum creatinine and blood urea nitrogen (BUN), electrolyte disturbances, and decreased urine output (oliguria). If the insult persists or is repeated, it may lead to chronic kidney disease (CKD), progressive nephron loss, interstitial fibrosis, and eventually end-stage renal disease (ESRD).

Common nephrotoxic agents include antibiotics (e.g., aminoglycosides), antiviral drugs such as Acyclovir, non-steroidal anti-inflammatory drugs (NSAIDs), chemotherapeutic agents like cisplatin, radiographic contrast media, and heavy metals. The severity of

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

nephrotoxicity depends on factors such as dose, duration of exposure, route of administration, drug interactions, hydration status, age, genetic susceptibility, and pre-existing renal impairment.

Early detection of nephrotoxicity is crucial for preventing irreversible damage. Traditional biomarkers include serum creatinine, blood urea nitrogen, and creatinine clearance. Recently, novel biomarkers such as kidney injury molecule-1 (KIM-1), neutrophil gelatinase-associated lipocalin (NGAL), and N-acetyl-β-D-glucosaminidase (NAG) have shown promise for early identification of renal injury before significant functional decline occurs.

Understanding the pathophysiology, risk factors, and diagnostic approaches of nephrotoxicity is essential for improving drug safety, minimizing renal complications, and developing protective therapeutic strategies.

STANDARD DRUG ACYCLOVIR

Acyclovir is a synthetic antiviral medication widely used in the treatment of infections caused by herpes viruses, particularly herpes simplex virus type-1 (HSV-1), herpes simplex virus type-2 (HSV-2), and varicella-zoster virus (VZV). It is a guanine nucleoside analog that selectively inhibits viral DNA synthesis, thereby preventing viral replication.

The antiviral action of acyclovir depends on its selective activation within infected cells. Initially, it is phosphorylated by viral thymidine kinase to form acyclovir monophosphate. Host cellular enzymes then convert it into acyclovir triphosphate, the active form. This active metabolite competitively inhibits viral DNA polymerase and incorporates into viral DNA, causing premature chain termination. Due to this selective mechanism, acyclovir has a high therapeutic index and minimal toxicity to normal host cells.

Pharmacokinetically, acyclovir has relatively low oral bioavailability and limited hepatic metabolism. It is primarily eliminated unchanged through the kidneys by glomerular filtration and active tubular secretion. Because of its renal excretion, high intratubular concentrations may occur, especially at high doses or with inadequate hydration.

Clinically, acyclovir is available in oral, topical, and intravenous formulations and is commonly prescribed for conditions such as genital herpes, cold sores, herpes encephalitis, and shingles. Although generally well tolerated, adverse effects may include gastrointestinal disturbances, headache, and, in some cases, nephrotoxicity, particularly with high-dose intravenous administration. Overall, acyclovir remains one of the most effective and widely used antiviral agents for herpes virus infections.

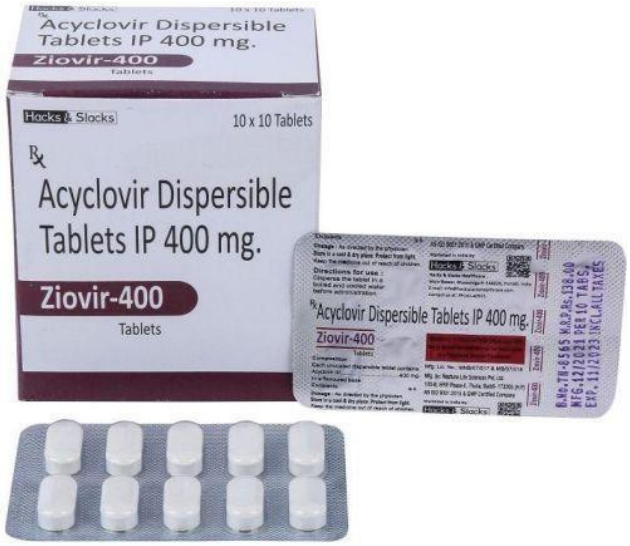


Fig.01: Acyclovir dispersible I.P.400 mg tablets

TEST DRUG PAPAYA SEEDS

Papaya seeds obtained from the fruits of *Carica papaya* have attracted considerable attention in recent years due to their diverse medicinal properties. Traditionally regarded as agricultural waste, papaya seeds are now recognized as a rich source of bioactive phytoconstituents with significant pharmacological potential. The seeds contain alkaloids such as carpaine, flavonoids, phenolic compounds, tannins, saponins, fixed oils, fatty acids, and benzyl

isothiocyanate, which contribute to their therapeutic effects.

Among their various biological activities, papaya seeds are well known for their antioxidant and anti-inflammatory properties. These properties are particularly important in conditions involving oxidative stress and cellular injury, such as drug-induced nephrotoxicity. The antioxidant components help neutralize reactive oxygen species (ROS), reduce lipid peroxidation, and protect renal tubular cells from damage. Additionally, papaya seeds have been reported to enhance endogenous antioxidant enzymes like superoxide dismutase, catalase, and glutathione, thereby strengthening the body's natural defense system.Experimental studies have also demonstrated nephroprotective potential of papaya seeds by improving renal biochemical markers such as serum creatinine and blood urea nitrogen, and by preserving normal kidney architecture in toxic models. Their natural origin, availability, cost-effectiveness, and relatively safe profile at therapeutic doses further support their selection as a test drug in experimental research.Therefore, due to their rich phytochemical composition and promising renoprotective properties, papaya seeds were selected as the test drug to evaluate their protective effect against drug-induced nephrotoxicity

Papaya seed powder from *Carica papaya* was selected because it has strong antioxidant and antiinflammatory properties. Acyclovir causes kidney damage mainly by producing harmful free radicals (oxidative stress), inflammation, and injury to kidney tubules. Papaya seeds contain natural compounds like flavonoids and phenols that help neutralize free radicals, reduce inflammation, and protect kidney cells from damage. Studies suggest that papaya seeds can improve kidney function by lowering serum creatinine and blood urea levels and by supporting natural antioxidant enzymes in the body. They are also easily available, cost-effective, and generally safe at proper doses. Therefore, papaya seed powder was considered a suitable natural option to study its protective effect against acyclovir-induced nephrotoxicity.

Fig.02: Papaya seeds

DRUG PROFILE

- **Common Name:** Papaya Seeds
- **Botanical Name:** *Carica papaya*
- **Family:** Caricaceae
- **Synonyms:** Pawpaw seeds, Papaw seeds
- **Part Used:** Seeds
- **Geographical Distribution:** Cultivated extensively in tropical and subtropical regions including India, Southeast Asia, Africa, and South America.
- **Major Chemical Constituents:** Alkaloids (carpaine), flavonoids, phenolic compounds, saponins, tannins, fixed oils, fatty acids, and benzyl isothiocyanate.
- **Pharmacological Activities:** Exhibits antioxidant, anti-inflammatory, antimicrobial, hepatoprotective, antidiabetic, and nephroprotective properties.
- **Therapeutic Applications:** Used in the management of kidney disorders (renoprotective role), liver ailments, digestive disturbances, parasitic infections, and certain metabolic disorders.

Fig.03: Papaya seed powder

MATERIALS AND METHODS

MATERIALS: -

Plant and parts used:

Papaya seeds (Carica papaya) show nephroprotective activity due to their antioxidant and anti-inflammatory phytochemicals, which reduce oxidative stress, protect renal cells, and help maintain normal kidney structure and functions

Chemicals and Reagents:-

Ferric chloride is used to detect phenols, lead acetate for toxicity studies, chloroform as an extraction solvent, concentrated sulfuric acid and hydrochloric acid for qualitative tests, magnesium ribbon for flavonoid detection, and sodium hydroxide for phytochemical analysis.

Standard Drug: -

Acyclovir is an antiviral drug used mainly in the treatment of herpes simplex virus and varicella- zoster virus infections. It works by inhibiting viral DNA synthesis, thereby preventing the replication of the virus and reducing the severity and duration of infection.

Test Animal: -

Albino rats (Rattus norvegicus) were used in the study after taking prior approval from the Institutional Animal Ethics Committee, following standard national guidelines for the care and use of laboratory animals.

Animal care and handling procedures were carried out in accordance with CPCSEA guidelines and received approval from IAEC (Approval number:2375\PO\Re\s\2025\CCSEA). In this study, thirty healthy female Albino Wistar rats weighing between 200 and 250 g are taken. The rats were housed in polypropylene cages and they were subjected to a one-week acclimatization period. During this period, they had to adapt to a new environment while adhering to standard husbandry conditions, including a (12:12 hour) light & dark cycle, humidity (30 -70%), temperature (23±2°C), and unrestricted access to their daily dietary requirements of standard pellet diet and water, all of which were provided without inducing stress.

METHODS:-

Ripe fruits of Carica papaya were collected from a local market, and the seeds were carefully separated from the pulp. The seeds were washed thoroughly with distilled water to remove adhering mucilage and impurities and then shade-dried at room temperature for about 7–10 days until completely dry. The dried seeds were powdered using a grinder and stored in an airtight container.

Extraction:-

One hundred grams of the papaya seed powder were taken in a conical flask and extracted with 1000 mL of distilled water by hot maceration. The mixture was heated on a water bath at 60– 70 °C for 2–3 hours with occasional stirring, allowed to cool, and then filtered using Whatman No.1 filter paper. The filtrate was concentrated on a water bath to obtain a semi-solid mass, which was dried and stored in an airtight container at 4 °C for further experimental use.

Test solution:-

The extract was mixed with distilled water to make 200 and 400 mg/kg solution.

TEST DRUG EXTRACT (PAPAYA SEED)

- About 100 g of dried seeds were coarsely powdered.
- Dried papaya seeds were collected, cleaned, and shade dried properly.
- The powder was passed through sieve No. 60 to obtain uniform particle size.
- The sieved powder was transferred into a clean round-bottom flask.
- 1000 mL of distilled water was added as the extraction solvent.
- The mixture was heated at 60 °C for 2 hours with continuous stirring for aqueous extraction.
- After heating, the mixture was allowed to cool to room temperature.

- The extract was filtered using Whatman No. 1 filter paper to remove solid residues.
- The filtrate was concentrated on a water bath until a semisolid mass was obtained.
- The concentrated extract was collected, stored in an airtight container, and preserved at 4 °C for further experimental use.

Fig.04 : Papaya seed Extraction

CHEMICAL TESTS:

1. DRAGENDORFF'S TEST

Papaya seed extract

⇩

Add dilute hydrochloric acid and warm gently

⇩

Cool and filter

⇩

To 2 ml of filtrate add a few drops of Dragendorff's reagent

⇩

Observation: Orange or reddish-brown precipitate

⇩

Inference: Alkaloids present

Fig.05: Test for Alkaloids

2. TEST FOR FLAVONOIDS (ALKALINE REAGENT TEST)

A small quantity of the aqueous papaya seed extract was taken to detect the presence of flavonoids.

⇩

Papaya seed extract

⇩

Add a few drops of sodium hydroxide solution (10%)

⇩

Observation: Formation of an intense yellow coloration

⇩

Add dilute hydrochloric acid

⇩

Observation: Disappearance of yellow color (becomes colorless)

⇩

Inference: Presence of flavonoids

Fig.06: Test for Flavonoids

3. TEST FOR TANNINS (FERRIC CHLORIDE TEST)

A small quantity of the aqueous papaya seed extract was taken for the detection of tannins.

Papaya seed extract

⇩

Add a few drops of 5% ferric chloride solution

⇩

Observation: Formation of blue-black or greenish-black coloration

⇩

Inference: Presence of tannins

Fig.07: Test for Tannins

4. TEST FOR TERPENOIDS (SA LKOWSKI TEST)

A small quantity of the aqueous papaya seed extract was taken for the detection of terpenoids.

Papaya seed extract

⇩

Add 2 mL of chloroform and mix well

⇩

Carefully add 1–2 mL of concentrated sulfuric acid along the side of the test tube

⇩

Allow the mixture to stand undisturbed

⇩

Observation: Formation of a reddish-brown coloration at the interface

⇩

Inference: Presence of terpenoids

Fig.08: Test for Terpenoids

STANDARD DRUG EXTRACT (ACYCLOVIR)

- Acyclovir was selected as the standard drug due to its well-known nephrotoxic potential and clinical relevance.

- The drug was procured from a reputed pharmaceutical source and was of analytical grade.
- The required quantity was accurately weighed daily using a digital analytical balance.
- The dose was calculated at 100 mg/kg body weight for each animal.
- The weighed drug was freshly dissolved in distilled water to obtain the required concentration.
- The solution was mixed thoroughly to ensure uniformity and clarity before administration.
- The prepared solution was administered orally once daily for 14 days using an oral gavage.
- The dose volume was adjusted according to the individual body weight of each animal to ensure accurate dosing.
- Animals were observed throughout the treatment period for any behavioral changes or signs of toxicity.
- Oral administration was chosen to simulate clinical exposure and maintain consistency across treatment groups for proper evaluation of nephrotoxic and nephroprotective effects.

Fig.09: Standard drug Extraction

PROCEDURE

Healthy albino rats of either sex, weighing about 150–200 g, were obtained from a registered animal house. The animals were housed in clean polypropylene cages under standard laboratory conditions with controlled temperature, humidity, and a 12-hour light– dark cycle. They were provided with standard pellet diet and water ad libitum and allowed to acclimatize before the start of the experiment and divided into five groups control, disease control, standard drug + gentamicin, test drug.

1. Healthy adult Wistar albino rats (150–200 g) were selected and acclimatized for 7 days under standard laboratory conditions with free access to standard pellet diet and water ad libitum.
2. After acclimatization, animals were randomly divided into five groups, each containing six rats (n = 6).
3. The total duration of the experimental study was 14 days.
4. Group I (Normal Control) received normal saline (1 ml/kg, p.o.) once daily for 14 days.
5. Group II (Disease Control) received Gentamycin 10 mg/kg (i.p.) once daily for 14 days to induce nephrotoxicity.
6. Group III (Standard Drug Group) received Gentamycin 10 mg/kg (i.p.) along with Acyclovir 200 mg/kg (p.o.) once daily for 14 days.
7. Group IV (Test Drug – Low Dose) received Gentamycin 10 mg/kg (i.p.) along with Papaya seed powder extract 100 mg/kg (p.o.) once daily for 14 days.
8. Group V (Test Drug – High Dose) received Gentamycin 10 mg/kg (i.p.) along with Papaya seed powder extract 400 mg/kg (p.o.) once daily for 14 days.
9. Body weights were recorded on Day 0 and Day 14 to assess general health status.
10. On Day 15, blood samples were collected under mild anesthesia and serum was separated for estimation of biochemical parameters such as serum creatinine, blood urea, and uric acid.
11. The animals were sacrificed, kidneys were excised, washed with ice-cold normal saline, and preserved in 10% formalin for histopathological examination to evaluate nephroprotective activity.

S.NO	GROUP	TREATMENT	DOSE	ROUTE	DURATION
1.	Normal Control	Distilled water	-	Oral (p.o.)	14 days
2.	Disease Control	Gentamicin	40 mg/kg	Intraperitoneal (i.p.)	14 days
3.	Standard Drug	Acyclovir+Gentamicin	100mg/kg+ 40 mg/kg	Oral (p.o.)	14 days
4.	Test Drug (Low Dose)	Papaya seed powder + Gentamicin	100mg/kg +40 mg/kg	Oral (p.o.)	14 days
5.	Test Drug (High Dose)	Papaya seed powder + Gentamicin	400mg/kg + 40 mg/kg	Oral (p.o.)	14 days

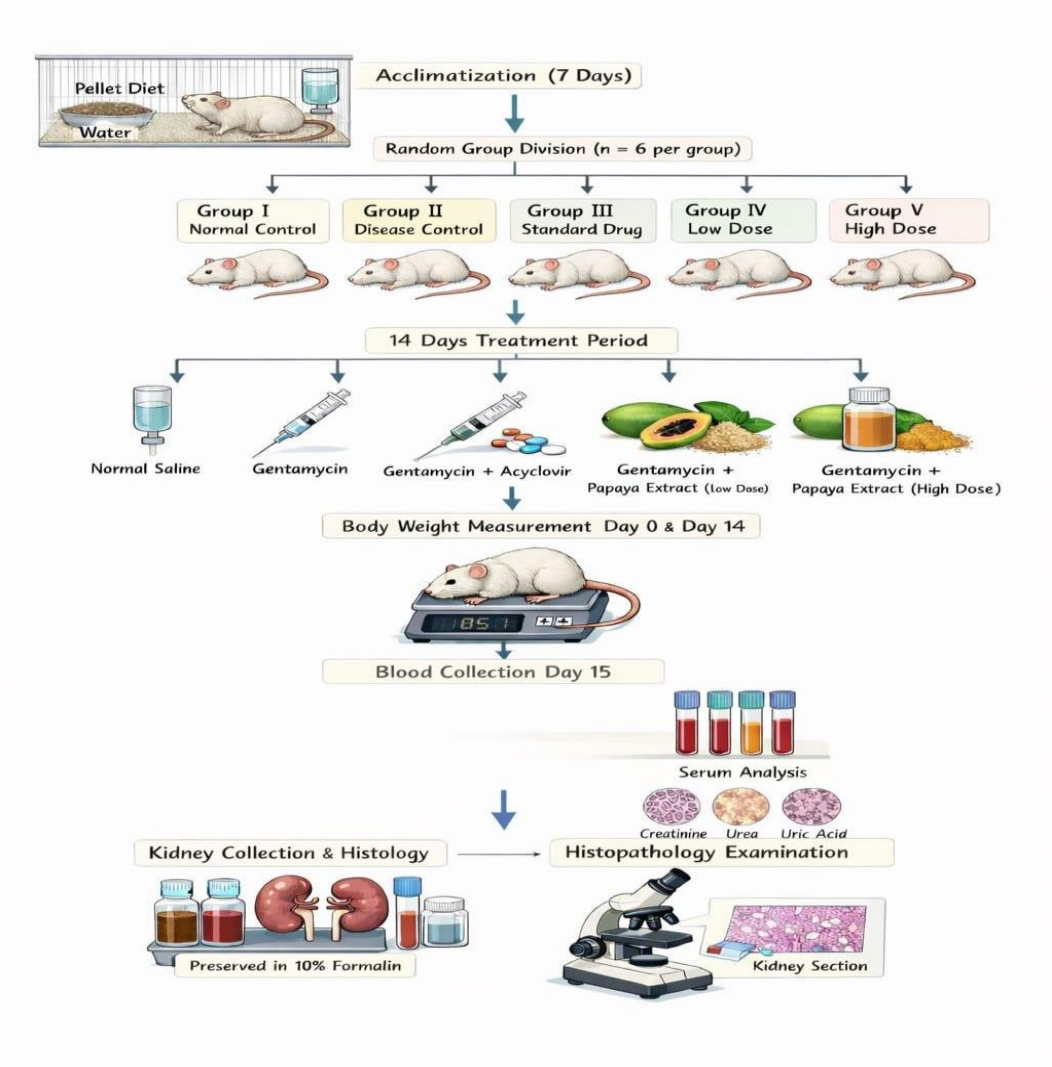


Fig.10: Protocol

CHEMICAL TESTS FOR PAPAYA SEED POWDER

S.No	Phytochemical Tests	Result
1.	Test For Alkaloids	Positive
2.	Test For Flavonoids	Positive
3.	Test For Flavonoids	Positive
4.	Test For Tannins	Positive
5.	Test For Terpenoids	Positive

Fig.11: Graphical representation of urine creatine levels

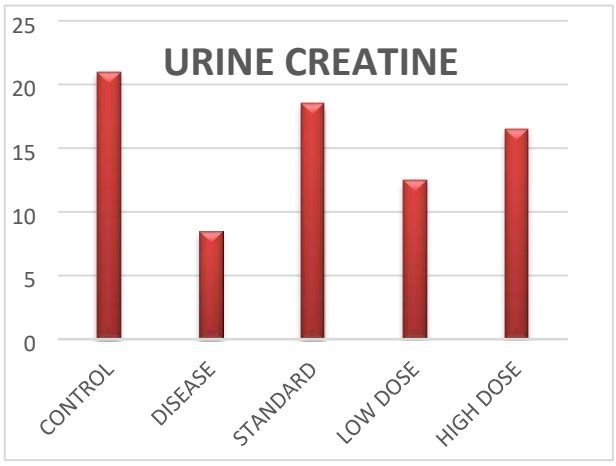


Fig.12: Graphical representation of urine protein levels

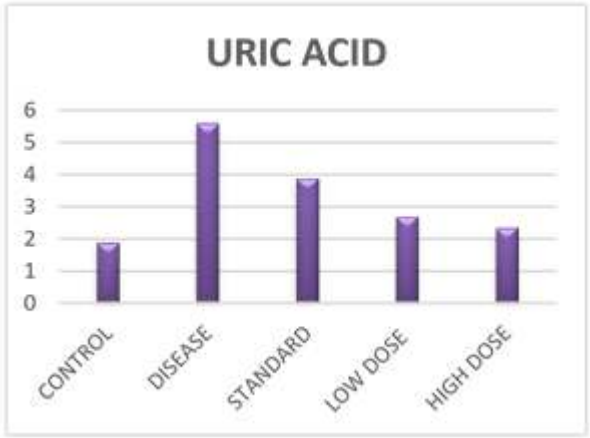


Fig.13: Graphical representation of Uric acid levels

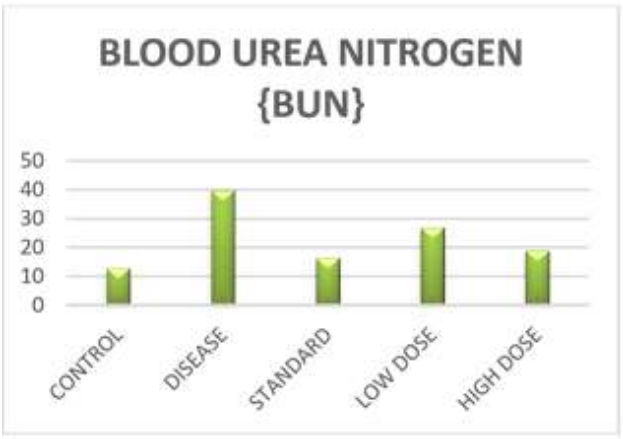


Fig.14: Graphical representation of Blood Urea Nitrogen levels

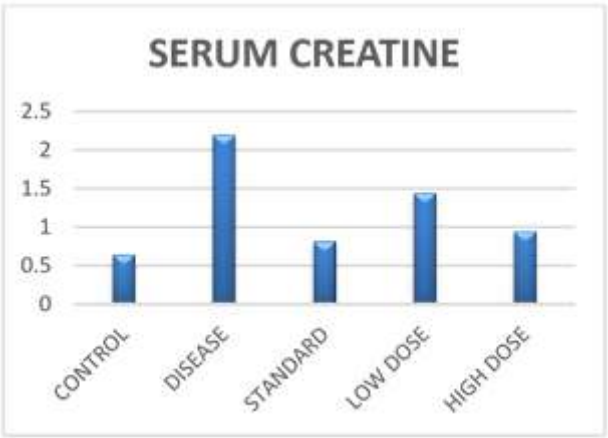


Fig.15: Graphical representation of Creatine levels

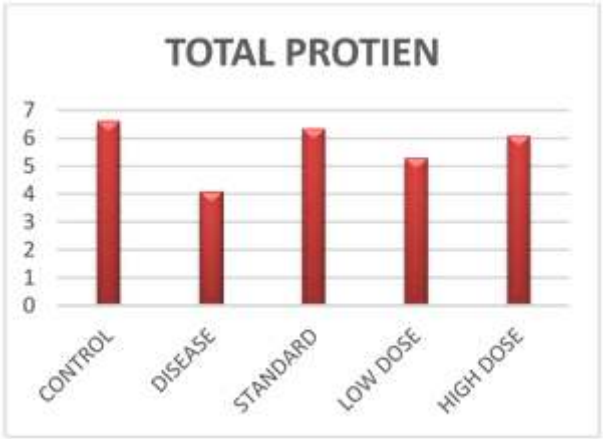


Fig.16: Graphical representation Serum Total Protein levels

MORPHOLOGICAL CHANGES IN KIDNEYS

In the normal group, kidneys appear smooth, reddish-brown, and maintain normal size and structure. In the

toxic group, kidneys show visible alterations such as enlargement, pale discoloration, and irregular surface, indicating damage caused by nephrotoxic agents. In the treatment groups, the low dose shows slight improvement with reduced swelling and better appearance, while the high dose exhibits near-normal morphology with restoration of size, color, and surface, suggesting protective effects.

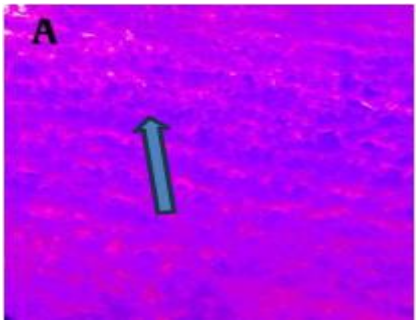
Fig.17: Control group Kidneys

Fig.18: Disease group Kidneys

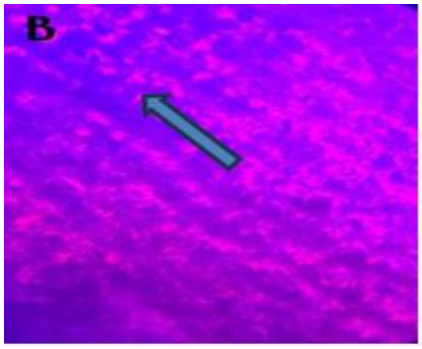
Fig.21: Low dose group Kidneys

Histopathology of Kidneys

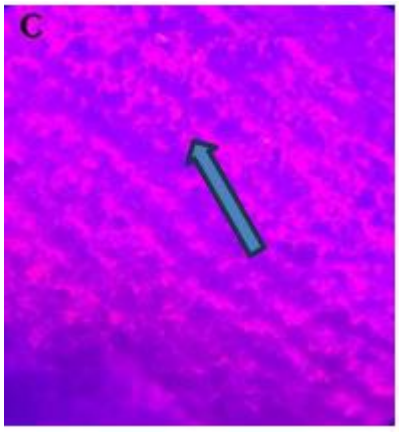
Microscopic examination of the normal group shows intact glomeruli, Bowman's capsule, and well-arranged renal tubules without any abnormalities [Fig:-22A]. In the toxic group, severe changes such as tubular necrosis, glomerular damage, inflammatory cell infiltration, tubular dilatation, and cast formation are observed due to oxidative stress and cellular injury [Fig:-22B]. In the treatment groups, the low dose shows mild damage with reduced inflammation and partial recovery of tubular structure [Fig:-22C], whereas the high dose demonstrates significant improvement with near-normal architecture and minimal histological alterations, indicating strong nephroprotective activity [Fig:-22D].



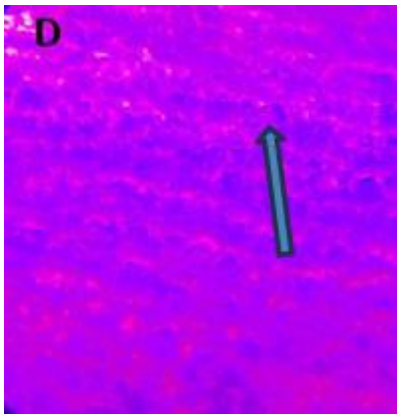
CONTROL



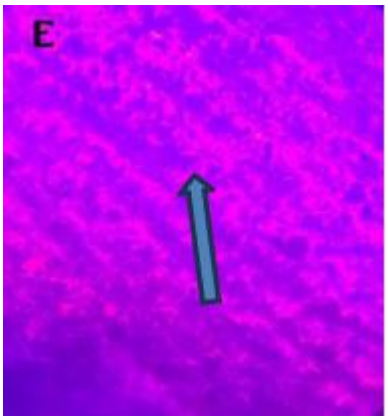
DISEASE



STANDARD



HIGH DOSE



LOW DOSE

DISCUSSION :-

The present study was carried out to evaluate the nephroprotective activity of Carica papaya seed extract against gentamicin-induced nephrotoxicity in Wistar albino rats. Gentamicin is known to induce renal damage mainly by accumulating in proximal tubular epithelial cells, where it generates reactive oxygen species (ROS), leading to oxidative stress, lipid peroxidation, mitochondrial dysfunction, and ultimately tubular necrosis. In this study, the normal control group showed normal biochemical parameters such as serum creatinine, blood urea, and uric acid within physiological limits, indicating proper renal function.

Histopathological examination of kidney sections from this group revealed normal renal architecture with intact glomeruli, well-defined Bowman's capsule, and normal proximal and distal convoluted tubules, confirming the healthy condition of renal tissues.

In contrast, the disease group treated with gentamicin showed a significant increase in biochemical parameters, indicating impaired kidney function. Histopathological findings further supported these results, showing severe renal damage characterized by tubular degeneration, necrosis, epithelial cell desquamation, interstitial inflammation, and glomerular alterations. These changes confirm the successful induction of nephrotoxicity and are mainly due to oxidative stress and cellular injury caused by gentamicin. The standard-treated group showed significant protection, with biochemical parameters approaching normal values. Histopathological studies revealed improved renal architecture with minimal damage, confirming its nephroprotective effect and validating the experimental model.

The group treated with Carica papaya seed extract at a high dose (400 mg/kg) showed significant improvement in biochemical parameters compared to the toxic control group. Histopathological examination revealed reduced tubular damage, mild degeneration, and near-normal glomerular structure, indicating recovery of renal tissues. The positive effect observed at this dose can be attributed to the presence of antioxidant phytoconstituents such as flavonoids and phenolic compounds, which help in scavenging free radicals, reducing oxidative stress, and protecting renal cells from damage.

However, the low dose group (200 mg/kg) did not show protective effects and instead exhibited signs of toxicity. The biochemical parameters remained elevated, indicating persistent renal damage. Histopathological observations showed noticeable structural alterations such as increased tubular degeneration, cellular swelling, and possible necrosis, suggesting that higher doses of the extract may

aggravate kidney injury. This negative effect may be due to pro-oxidant activity at higher concentrations, metabolic overload, or inherent toxicity of certain phytochemicals present in the extract

CONCLUSION

Carica papaya seed extract shows nephroprotective activity at high dose (400 mg/kg). The low dose (200mg/kg) exhibits toxicity and is not safe. Therefore, the extract is effective only within an optimal dose range and should be used cautiously.

REFERENCES

1. Drug-induced nephrotoxicity is a major cause of acute kidney injury. Many medications damage renal tubules through oxidative stress and inflammation.
   Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC6436396.
2. The kidneys receive nearly 20–25% of cardiac output, making them highly vulnerable to toxic substances. This high blood flow increases exposure to drugs and toxins.
   Link: https://www.ncbi.nlm.nih.gov/books/NBK557847.
3. Gentamicin is commonly used to induce nephrotoxicity in experimental animal models. It damages proximal tubular cells through oxidative stress.
   Link: https://pubmed.ncbi.nlm.nih.gov/25087119.
4. Natural plant compounds have shown protective effects against drug-induced kidney damage. Their antioxidant properties help prevent renal injury.
   Link: https://www.frontiersin.org/articles/10.3389/fphar.2020.00384.
5. Papaya seeds contain phytochemicals such as flavonoids and phenolic compounds. These compounds exhibit antioxidant and anti-inflammatory activities.
   Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC4480493.
6. Experimental studies suggest papaya seed extract can improve kidney function markers. It reduces serum creatinine and blood urea nitrogen levels.
   Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC11082695.
7. Oxidative stress is a major mechanism involved in nephrotoxicity. Reactive oxygen species damage renal cells and lead to tubular necrosis.
   Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC6621352.
8. Kidney injury molecule-1 (KIM-1) is an important biomarker for early detection of kidney injury. It increases significantly during tubular damage.
   Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC3794522.
9. Acyclovir is a widely used antiviral drug for herpes infections. High doses may lead to renal toxicity due to crystal formation in renal tubules.
   Link: https://www.ncbi.nlm.nih.gov/books/NBK542200.
10. Histopathological examination of kidney tissues helps detect structural changes caused by nephrotoxic agents. It confirms biochemical findings in renal studies.
    Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC5741114.
11. Medicinal plants are widely studied for their renoprotective activity. Their bioactive compounds help reduce oxidative stress in kidney tissues.
    Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7259412.
12. Flavonoids are natural antioxidants that protect cells from oxidative damage. They are important in preventing kidney injury caused by toxins.
    Link: https://www.mdpi.com/1420-3049/24/21/3888.
13. Serum creatinine is a commonly used biomarker for evaluating kidney function. Increased levels indicate impaired glomerular filtration.
    Link: https://www.kidney.org/atoz/content/kidneytests.

14. Reactive oxygen species generated by drugs can cause lipid peroxidation in kidney cells. This leads to inflammation and renal dysfunction.
Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC4200866.
15. Herbal extracts have gained attention for their nephroprotective potential. Many plants contain compounds capable of reducing renal oxidative stress.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7601852.
16. Papaya (Carica papaya) is widely used in traditional medicine. Different parts of the plant possess antioxidant and antimicrobial properties.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5452224.
17. The proximal tubule is the most common site of drug-induced kidney injury. Many nephrotoxic drugs accumulate in these cells.
Link: https://www.ncbi.nlm.nih.gov/books/NBK470352.
18. Kidney diseases are increasing worldwide due to exposure to drugs and environmental toxins. Early detection helps prevent severe renal damage.
Link: https://www.who.int/news-room/fact-sheets/detail/kidney-disease.
19. Antioxidant enzymes such as catalase and superoxide dismutase protect cells from oxidative stress. Their activity is reduced during nephrotoxicity.
Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC6769704.
20. Papaya seed extract has demonstrated hepatoprotective and nephroprotective activities in animal studies. These effects are attributed to phenolic compounds.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6237296.
21. Acute kidney injury results in a rapid decline in glomerular filtration rate. It can be caused by drugs, toxins, infections, or ischemia.
Link: https://www.kidney.org/atoz/content/acute-kidney-injury.
22. Chronic kidney disease occurs due to progressive loss of nephron function. Long-term exposure to nephrotoxic substances contributes to this condition.
Link: https://www.kidney.org/atoz/content/chronic-kidney-disease.
23. Nephrotoxicity may involve glomeruli, tubules, and renal interstitium. Damage to these structures impairs kidney filtration functions.
Link: https://www.ncbi.nlm.nih.gov/books/NBK551707.
24. Gentamicin accumulates in renal tubular cells causing mitochondrial dysfunction. This leads to cell death and renal injury.
Link: https://pubmed.ncbi.nlm.nih.gov/27889773.
25. Plant-derived antioxidants are effective in reducing oxidative damage in kidney tissues. These compounds neutralize harmful free radicals.
Link: https://www.sciencedirect.com/science/article/pii/S0891584917302815.
26. Nephrotoxicity can lead to electrolyte imbalance and fluid retention. Severe damage may progress to kidney failure.
Link: https://www.ncbi.nlm.nih.gov/books/NBK563249.
27. Experimental nephrotoxicity studies help evaluate protective effects of natural drugs. Animal models are commonly used for this purpose.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8063442.
28. Papaya seeds contain benzyl isothiocyanate, an important bioactive compound. It contributes to antimicrobial and antioxidant activities.
Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4003676.
29. Inflammation plays a key role in kidney injury caused by toxins. Anti-inflammatory agents can help reduce renal damage.

Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8538856.

30. Renal oxidative stress leads to lipid peroxidation and membrane damage. Antioxidant therapy can protect kidney tissues.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8829973.
31. Natural phytochemicals have shown promising therapeutic potential in renal disorders. Their mechanisms involve antioxidant and anti-inflammatory effects.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9029052.
32. Drug-induced kidney injury accounts for a large percentage of hospital-acquired renal failure cases. Monitoring kidney function during therapy is essential.
Link:
https://pubmed.ncbi.nlm.nih.gov/24130922.
33. Kidney tissues are sensitive to toxic damage because they concentrate drugs during filtration. This increases the risk of nephrotoxicity.
Link:
https://www.ncbi.nlm.nih.gov/books/NBK482435.
34. Experimental animal models help identify potential nephroprotective drugs. They allow evaluation of biochemical and histological changes.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9180472.
35. Phytochemicals such as tannins and alkaloids possess antioxidant activity. These compounds help protect tissues from oxidative damage.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9391288.
36. Papaya seeds have been reported to improve antioxidant enzyme levels in animal studies. This helps protect kidney tissues from injury.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9605968.
37. Nephrotoxicity often results in elevated serum creatinine and urea levels. These markers indicate reduced kidney filtration capacity.
Link:
https://www.kidney.org/atoz/content/kidneytests.
38. Plant extracts rich in phenolic compounds are effective free radical scavengers. They reduce oxidative damage in biological tissues.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9742834.
39. Antioxidant therapy is considered an important strategy to prevent kidney damage. It helps restore normal cellular function.
Link:
https://www.sciencedirect.com/science/article/pii/S0273230018300375.
40. Kidney injury leads to structural damage in renal tubules and glomeruli. Histopathology helps visualize these changes.
Link:
https://pmc.ncbi.nlm.nih.gov/articles/PMC6237296.
41. Herbal medicines have gained popularity in nephroprotective research. They provide safer alternatives to synthetic drugs.
Link:
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7601852.
42. Renal oxidative stress is associated with increased lipid peroxidation. This damages cell membranes and organelles.
Link:
https://pmc.ncbi.nlm.nih.gov/articles/PMC6769704.
43. Acyclovir nephrotoxicity is mainly caused by crystal precipitation in renal tubules. Adequate hydration helps prevent this complication.
Link:
https://www.ncbi.nlm.nih.gov/books/NBK542200.
44. Nephroprotective agents reduce kidney damage by improving antioxidant defense mechanisms. They also reduce inflammatory responses.
Link:
https://www.frontiersin.org/articles/10.3389/fphar.2020.00384.

45. Papaya seeds have been traditionally used for digestive and medicinal purposes. Modern research supports their pharmacological potential. Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5452224.
46. Kidney diseases affect millions of people worldwide. Prevention and early diagnosis are crucial for effective treatment. Link:https://www.who.int/news-room/fact-sheets/detail/kidney-disease.
47. Experimental nephrotoxicity studies measure biochemical parameters such as creatinine and urea. These markers indicate renal function status. Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC8063442.
48. Reactive oxygen species are generated during drug metabolism. Excessive production can damage renal tissues. Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC4200866.
49. Medicinal plants are a valuable source of therapeutic compounds. Many are being studied for kidney protective effects. Link: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7259412.
50. Renal histopathology is an important method for evaluating structural kidney damage. It confirms the protective effect of therapeutic agents. Link: https://pmc.ncbi.nlm.nih.gov/articles/PMC5741114.

HOW TO CITE: Thummidi Harshini, Naasir Jamal, Bolla Sreeja, Jagu Sanjeev, Nadimpalli Sumanasri*, Evalution Of Nephroprotective Activity Of Papaya [Carica Papaya] Seed Extract Against Gentamicin-Induced Nephrotoxicity In Albino Wistar Rats, Int. J. Sci. R. Tech., 2026, 3 (5), 802-816. https://doi.org/10.5281/zenodo.20343599