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PRECLINICAL EVALUATION OF ANTINEPHROTOXIC EFFECT OF GAMBHARI (GMELINA ARBOREA.ROXB) IN GENTAMICIN INDUCED NEPHROTOXICITY IN WISTAR RATS.

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ABSTRACT

Introduction: This study evaluated the anti-nephrotoxic activity of Gambhari (Gmelina arborea.Roxb) fruit ksheerapaka, an *ayurvedic* formulation, against Gentamicin induced nephrotoxicity in Wistar rats.

Methods: A total of 24 rats were divided in four groups: Normal control, Disease control (Gentamicin induced), Test group 1 (Low dose of *Gambhari* fruit *ksheerapaka*) and Test group 2 (High dose of *Gambhari* fruit *ksheerapaka*)

Discussion and Conclusion: Over a period of 7 days, parameters such as body weight-kidney weight, clinical parameters, biochemical parameters, histopathological changes were assessed. Results showed that *Gambhari* fruit *ksheerapaka* significantly reduced gentamicin-induced kidney damage from the improved biochemical parameters and reduced histopathological alterations as compared to the disease control group. This study concluded that *Gambhari (Gmelina arborea.Roxb)* fruit *ksheerapaka*, both low dose and high dose show anti nephrotoxic effects against the gentamicin-induced nephrotoxicity in Wistar rats.

Keywords: Gentamicin, Nephrotoxicity, *Gambhari (Gmelina arborea.Roxb)* fruit.

INTRODUCTION

Ayurveda, the traditional system of Indian medicine, has been known since the Vedic period. This system of medicine involves the use of plant parts, animal products, minerals, and metals.

Among the various body organs kidney is the organ which is highly susceptible to toxic effects and actions of drugs and medications. As the kidney has more vascularity, there is a concentration of drugs, thus exposing the renal tubules. Therefore, if drug accumulation occurs, then it can cause severe toxic manifestations like renal insufficiency and nephritis.[1]

Nephrotoxicity manifests as damage to the renal tubules, resulting in loss of urine concentration and low glomerular filter rate. A broad spectrum of therapeutic drugs and environmental pollutants frequently induces nephrotoxicity. Drugs that cause direct nephrotoxicity are aminoglycosides, NSAIDs, and heavy metals. From the causes stated above, aminoglycosides produce high nephrotoxicity. The leading cause of aminoglycoside-induced nephrotoxicity is tubular toxicity, which is caused by apoptosis and necrosis of renal tubular epithelial cells. Aminoglycosides attain high concentration in the renal cortex, and the toxicity is related to the total amount of the drug received by the patient. Renal damage caused by aminoglycosides is reversible, provided the drug is promptly discontinued, although aminoglycoside nephrotoxicity can occur even with proper monitoring. Nephrotoxicity has been traced to marked accumulation and retention of aminoglycosides in the proximal tubular cells.[2]

Several studies have shown that the simultaneous administration of different herbal medications along with various nephrotoxic drugs so reduces the incidence of kidney injury.

Accordingly, this study was planned to investigate the possible renal damage caused by gentamicin in an experimental rat model, so Gambhari fruit was used to assess its anti-nephrotoxic effect.

MATERIALS AND METHODS

Sample Preparation.

1. *Gambhari* fruit *ksheerapaka*:[3] One part of *Gambhari* fruit coarse powder will be mixed with eight parts milk and 32 parts waters appropriately mixed, boiled up till it is reduced to the amount of milk then it will be filtered with a cotton cloth, and it will be administered to the animals.

2. Gentamicin Administered at a dose of 100mg/kg i.p.

Dose Calculation

The human dose will be extrapolated for rats with an extrapolation factor of 0.018. It was calculated using a human dose(40ml) adjusted for 200gm of rats with the extrapolation factor 0.018, resulting in a dose of 0.72ml/200gm for a single dose administration.[5]

Study Design

The study included 24 Wistar rats, equally divided by gender and weighing between 180 and 220 gms. The rats were acclimatized to the laboratory conditions for 7 days prior to the experiment's initiation and randomly divided into four groups, with six rats in each group.

- **Group I (Normal Control):** received normal water.
- **Group II (Disease Control):** Administration of Gentamicin (100 mg/kg i.p) daily for 8 days.
- **Group III (Test Group 1):** Gentamicin + *ksheerapaka* of *Gambhari* fruit (1ml).
- **Group IV (Test Group 2):** Gentamicin + *ksheerapaka* of *Gambhari* fruit (3ml).

All animals were observed individually after doing at least once during the first 30 minutes for any immediate signs for a total of 8 days and weighed before and after the study. At the end of the study, biochemical parameters, including serum urea, serum blood urea nitrogen, serum creatinine, serum total proteins, urinary creatinine, and urinary albumin, were assessed. Two animals of each group underwent histopathological analysis of the kidney.

RESULTS

Effect of *Gambhari* fruit *ksheerapaka* on Body weight and Kidney weight:

The results clearly showed a significant decrease in body weight in gentamicin-induced nephrotoxic rats, while the co-treatment with Gambhari fruit ksheerapaka protected from the nephrotoxic effects of gen-

tamicin, as indicated by no significant impact in treatment compared to gentamicin control. On the other hand, kidney weights were also changed by gentamicin induction, while protection was seen by *Gambhari* fruit *ksheeraapaka* treatments.

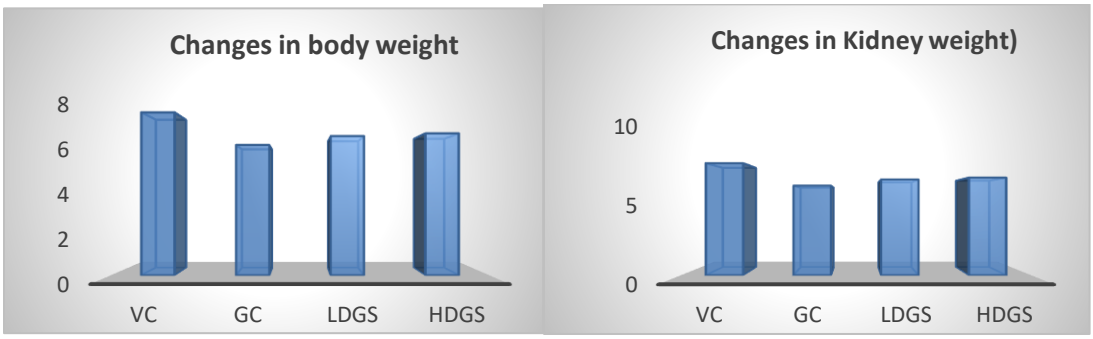


Figure No.1 Graphical Representation of changes in body weight and kidney weight.

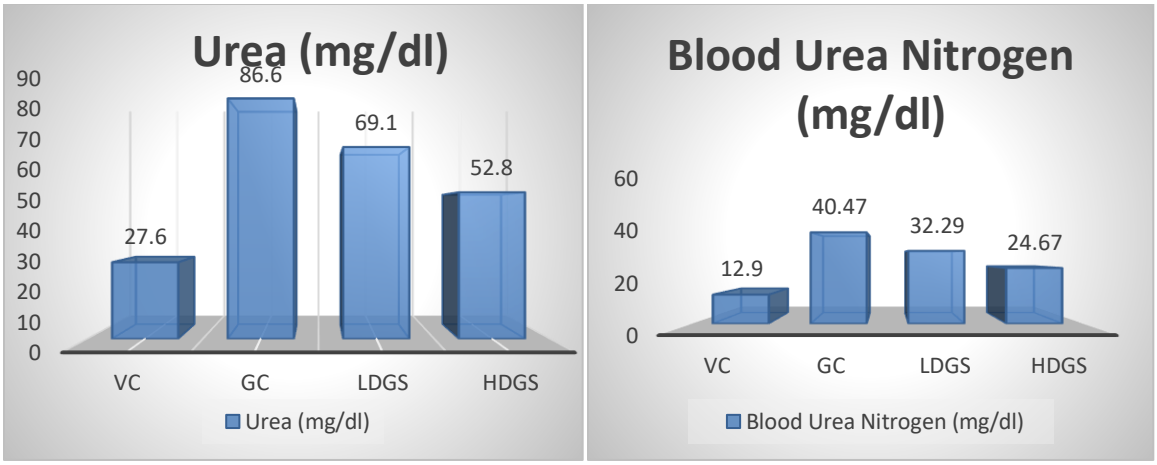
Clinical Signs and Symptoms:

Animals in all groups were evaluated for signs of toxicity, such as Hyperactivity, Irritability, and tremors. Salivation was seen more in the Gentamicin control (disease control) group, while the rest of the groups were normal. Only Diarrhoea was not noted in any of the groups.

Effect on Biochemical Parameters:

The effect of Gambhari fruit ksheerapaka on blood parameters such as blood urea nitrogen (BUN), urea, serum creatinine, and total protein levels against gentamicin-induced animals. There was a marked increase in blood urea nitrogen (BUN), urea, and serum creatinine levels in gentamicin-induced nephrotoxic animals compared to vehicle control, while co-administration of Gambhari fruit ksheerapaka decreased the respective blood parameters.

The urine creatinine and albumin levels increased in the gentamicin control group compared to vehicle control animals. At the same time, co-administration with Gambhari fruit ksheerapaka decreased the respective levels compared to the gentamicin control group.



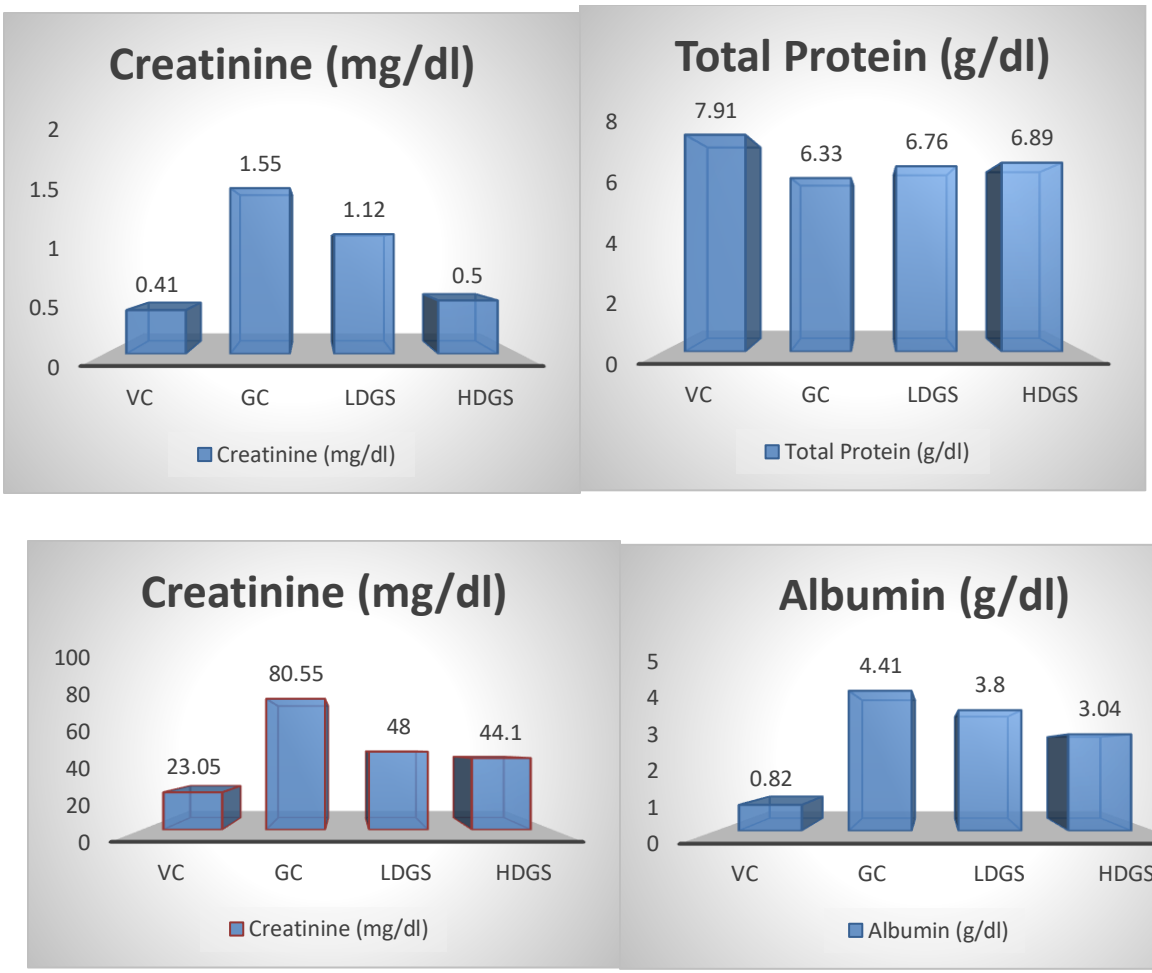


Figure No.2 Graphical Representation of Effect on biochemical parameters.

Histopathological Analysis:

Kidney: There was a marked increase in tubular degeneration tubular necrosis, varying degrees of necrosis were seen along with loss of brush-border and a wide lumen was seen with congested glomerular blood vessels and epithelial cell degeneration in gentamicin-induced nephrotoxic animals compared to vehicle control. At the same time, co-administration of *Gambhari* fruit *ksheerapaka* decreases the above respective parameters. Meanwhile, regenerative changes were seen in the group treated with Gambhari fruit ksheerapaka at a high dose.

DISCUSSION

The study evaluates that *Gambhari* fruit *ksheerapaka* shows significant anti-nephrotoxic effects against gentamicin-induced nephrotoxicity in Wistar rats, comparable to those of gentamicin. The reduction in serum biochemical parameters and improvement in histopathological outcomes suggest that Gambhari fruit ksheerapaka alleviates gentamicin-induced kidney damage through antioxidant and anti-nephrotoxic mechanisms.

CONCLUSION

This animal study indicates that serum urea, BUN, creatinine, total proteins, urinary creatinine, and albumin are the biomarkers used in this experiment for gentamicin-induced nephrotoxicity in Wistar rats. The increased serum urea, BUN, creatinine urinary creatinine and albumin changes were noticed in gentamicin-treated animals compared to the Gambhari fruit ksheerapaka low dose and high dose. The levels of the above biomarkers decreased considerably. Hence, using these biomarkers in preclinical and clin-

ical studies to assess nephrotoxicity can be recommended.

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