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Nephroprotective activity of *Albizia lebeck* pods in wistar albino rats by gentamicin induced nephrotoxicity

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ABSTRACT

Background: In the Indian medicinal system, *Albizia lebeck* is known for its various therapeutic properties, including antiseptic, anti-dysenteric, anti-tubercular, anti-asthmatic, and anti-fertility effects, which have been historically linked to it. **Objective:** The objective of the present study was to evaluate the ethanolic extract of *Albizia lebeck* pods (ALPE) for its protective effects against gentamicin-induced nephrotoxicity in rats. **Materials and Methods:** The rats were divided into five groups: one receiving normal saline, another receiving gentamicin at 100 mg/kg i.p., a third group treated with Cystone at 5 ml/kg p. o. for 8 days, and two groups receiving ALPE at doses of 200 mg/kg and 400 mg/kg p. o. for 21 days, alongside gentamicin for 8 days. Serum levels of protein, creatinine, urea, and blood urea nitrogen were measured. After treatment, kidneys were collected for histological analysis. **Results:** The gentamicin treatment led to nephrotoxicity, evidenced by significant changes in blood parameters. However, the concurrent administration of the ethanolic extract of *Albizia lebeck* pods with gentamicin markedly improved all measured parameters. Histopathological examinations indicated a decrease in kidney damage when treated with the extract. **Conclusion:** The results suggest that the ethanolic extract of *Albizia lebeck* pods may be effective in preventing gentamicin-induced nephrotoxicity.

Keywords: *Albizia lebeck* pods, Gentamicin, Cystone, Nephrotoxicity.

INTRODUCTION

The kidney is the primary organ required by the human body for a variety of vital processes such as detoxification, extracellular fluid management, homeostasis and toxic metabolic excretion [1]. The terms “nephron” and “toxicity”, which refer to kidney poisoning, are combined to form the phrase “Nephrotoxicity”. Nephrotoxicity, is the buildup of waste products or toxic compounds in the kidney that interfere with normal renal function [2]. Nephron toxins are agents which cause nephrotoxicity. Globally, Chronic kidney disease (CKD) is a major cause of death and loss of years of life with a handicap, although the patient and healthcare professional awareness of this condition is poor [3].

Chronic kidney disease (CKD), which is typified by a decreased glomerular filtration rate (GFR), an increased excretion of urine albumin or both, is the primary cause of End Stage Renal Disease (ESRD) [4]. Acute Kidney Injury (AKI) leads to chronic kidney disease.

Taking the GFR into account, the CKD is divided into 5 stages. Stage 1: Damage to kidneys with a normal GFR (more than 90ml/min), Stage 2: GFR mildly reduced (60-89ml/min), Stage 3a: GFR declines moderately (45-59ml/min), Stage 3b: GFR declines moderately (30-44ml/min), Stage 4: GFR significantly lowers (15-29ml/min), Stage 5: GFR <15ml/min indicates renal failure [5]. A significant fraction of the estimated 850 million individuals with kidney disease globally do not have access to kidney disease diagnosis, prevention or treatment. The majority of these individuals reside in low- and lower-middle-income countries [6]. Dialysis is now only medical procedure that can reliably improve survival, fend off harm, or speed up recovery in case of final stages of kidney failure [7]. Nephrotoxicity is caused due to Anticancer drugs, Antibiotics, Heavy metals, Analgesic, Herbicides and pesticides Hypertension, Diabetes, Over production of Uric acid. Aminoglycosides are prescribed to treat severe gram-negative bacterial infections. However, their therapeutic application is frequently accompanied with the development of nephrotoxicity. Gentamicin, a bactericidal antibiotic from the aminoglycoside class, is efficient against gram-negative bacteria. Despite its nephrotoxicity, gentamycin is utilised clinically because of its broad spectrum of action against gram-negative bacterial infections. Gentamycin is a powerfully cationic medication that binds to negatively charged acidic phosphoinositide components of the proximal tubule's brush-border membrane, acting on the cationic receptor megalin, which is found deep at base of the brush border villi.

The resulting receptor-drug combination is promptly internalised by pinocytosis and taken by lysosomes,

where lysosomal phospholipidosis occurs, disrupting a variety of renal intracellular functions [8]. Symptoms of Nephrotoxicity Edema, Hypocalcaemia, Hypertension, Oliguria, Haematuria, Azotemia, Sleep disturbances.

The initial stages are treated with life style changes and using medicines such as diuretics, anti-hypertensive medications and anti-diabetic agents, AKI can result from various factors, including surgery, [8] sepsis and most drug-induced kidney injury in practice. As, a result of the intricate induction of several components of AKI and different patient groups, a number of studies have attempted to choose drugs such as dopamine [9], fenoldopam [10], to avoid the emergence of AKI. Although some results have been observed in animal models, there are no discernible clinical effects.

Herbal remedies are frequently used to treat kidney ailment in various parts of world. For generations, millions of people have relied on medicinal plants and the natural products they produce for their fundamental health care needs. Many of these therapeutic plants have had their extraordinary therapeutic efficacy confirmed and proven by science [11]. The Fabaceae family plant *Albizia Lebbeck* is often referred to as Siris, Shiris in Hindi, Lebbeck tree in English and Bhandi, Sitapuspa, Sukapriya, Mrdupuspa in Sanskrit languages. It is primarily found in tropical and subtropical regions in northern Australia, tropical Africa, Asia, Andaman Island, Myanmar, and India. Due to its variety of phytochemicals and good therapeutic abilities, *Albizia lebbeck* has been the subject of much investigation in Ayurveda [12]. Antiseptic, anti-dysenteric, anti-tubercular, anti-asthmatic, anti-inflammatory and anti-fertility properties have all been associated with it historically. Additionally, it is used to treat gonorrhoea, leucorrhoea, bronchitis, leprosy, paralysis, helminth infection and other genital illnesses. It is applied topically to wounds and ringworms. Melacidin, D-catechin, albiziahexoside, betulnic acid and echinocystic acid glycosides are the phytoconstituents found in the plants that have been linked to a number of powerful physiological and pharmacological effects. The aim of the present study was Nephroprotective activity of *albizia lebbeck pods* in wistar albino rats by gentamicin induced nephrotoxicity.

MATERIALS AND METHODS

Plant Collection and Authentication

Albizia lebbeck pods were gathered from Tirupathi A. P and authenticated by Dr. K. Madhava Chetty, Assistant Professor at Venkateshwara University, Andhra Pradesh.

Extraction by Maceration

To remove pollutants like as dirt, fresh pods were rinsed with water and dried in shade. The dried pods were ground and sieved to produce a homogenous powder. Weighed powdered plant material (1 kg) was immersed in 99% ethanol and macerated for 7 days with periodic stirring. On eighth day, the solvent was filtered through muslin cloth and evaporated in a rotary evaporator at 40°C. The extract was desiccated to eliminate residual ethanol. The dried ethanolic extract of *Albizia lebbeck pods* (ALPE) was sealed in an air tight bottle and stored in a dry place for further studies. [12]

Qualitative Phytochemical Screening

The ALPE was examined for different phytoconstituents, including carbohydrate, tannins, flavonoids, saponins, alkaloids etc.

Experimental Animals

On December 12, 2024 the Institutional Animal Ethical Committee (IAEC) approved the experimental procedure with ethical clearance No: CPSEA/1657/IAEC/CMRCP/COL-23/125. This study employed healthy adult male Albino Wistar rats weighing between 150 to 200 g. Animals were given 24hour accesses to water and normal nutritional

pellets before and after the treatment. The participants were acclimatized for 1 week in an acceptable environment (25°C±1°C temperature, 45-55 RH free access to food and water) before participating in the experiment.

Acute Toxicity Studies

A literature study revealed that acute toxicity experiments on *Albizia lebbeck pods* were conducted in accordance with OECD 423 guidelines and found to be safe for animals up to 2000 mg/kg. [13]

Evaluation of Nephroprotective activity

The animals were put into 5 groups of 6 each. (n=6)

Treatment

- ❖ **Group I- Normal:** Normal saline (10 ml/kg), *P.O.*, OD for 28 days.
- ❖ **Group II-Disease Control:** Gentamicin (100 mg/kg), *I.P.* OD for 8 days.
- ❖ **Group III-Standard Control:** Cystone (5 ml/kg), *P.O.*, OD for 28 days along with *I.P.* administration of Gentamicin for last 8 days daily for once.
- ❖ **Group IV-Test-I (200 mg/kg):** ALPE (200 mg/kg), *P.O.* for 28 days along with *I.P.* administration of Gentamicin for last 8 days daily for once.
- ❖ **Group V-Test II (400 mg/kg):** ALPE (400 mg/kg) *P.O.* for 28 days along with *I.P.* administration of Gentamicin for last 8 days daily for once.

Blood samples were taken after 24 hours after the last dose using cardiac puncture. Serum was then separated using a centrifuge. The kidneys were removed, washed in saline, and stored in 10% formalin for histopathological studies [14].

Histopathological studies

A 10% formalin-fixed kidney sample was studied histologically. The kidney segment was imbedded in a paraffin wax, 4-6 µm in size, stained with haematoxylin and eosin and photographed.

Statistical Analysis

The findings were analysed using One-Way ANOVA and Dunnett's multiple comparison test [15].

RESULT

Preliminary Phytochemical Screening

The results of phytochemical screening were revealed in Table 1.

Table 1: Results of Preliminary Phytochemical screening

S. No.	Phytoconstituent	ALPE
1	Alkaloids	+
2	Flavonoids	+
3	Tannins	-
4	Saponins	+
5	Steroids	+
6	Amino acids	+
7	Carbohydrates	+

+ Means positive and - means negative

The phytochemical screening identified alkaloids, flavonoids, saponins, steroids, amino acids, carbohydrates in ALPE.

Serum Parameters

The results of serum parameters were revealed in Table 2.

Table 2: Effects of ALPE on Biochemistry

S. No.	Treatment groups	Creatinine (mg/dl)	Uric acid (mg/dl)	Urea (mg/dl)	BUN (mg/dl)	Total Protein (g/dl)	Albumin (g/dl)	Globulin (g/dl)
1.	Normal control	0.664± 0.0026	3.28± 0.23	35.7± 2.37	17.2± 0.23	7.97± 1.216	9.033± 0.216	8.44± 0.215
2.	Disease control	2.34± 0.033	5.35± 0.18	60.2± 3.97	52.5± 1.87	4.35± 1.176	4.301± 0.002	3.36± 0.180
3.	Standard control	0.705± 0.0024***	3.55± 0.38***	40.3± 2.61***	23.1± 2.17***	7.29± 1.471***	8.110± 0.001***	7.79± 0.044***
4.	ALPE 200 mg/kg	1.696± 0.0025***	4.12± 0.18***	52.2± 1.47***	31.2± 1.94***	5.32± 1.489***	7.482± 0.567***	5.67± 0.512***
5.	ALPE 400 mg/kg	1.17± 0.0026***	3.73± 0.16***	44.7± 2.42***	26.4± 1.26***	6.95± 1.186***	7.991± 0.044***	7.18± 0.033***

Values are represented as Mean ± SEM. Statistical analysis was done by one way ANOVA followed by post hoc Dunnett's multiple comparison test. ***p<0.0001, **p<0.001, and *p<0.05 vs Disease control.

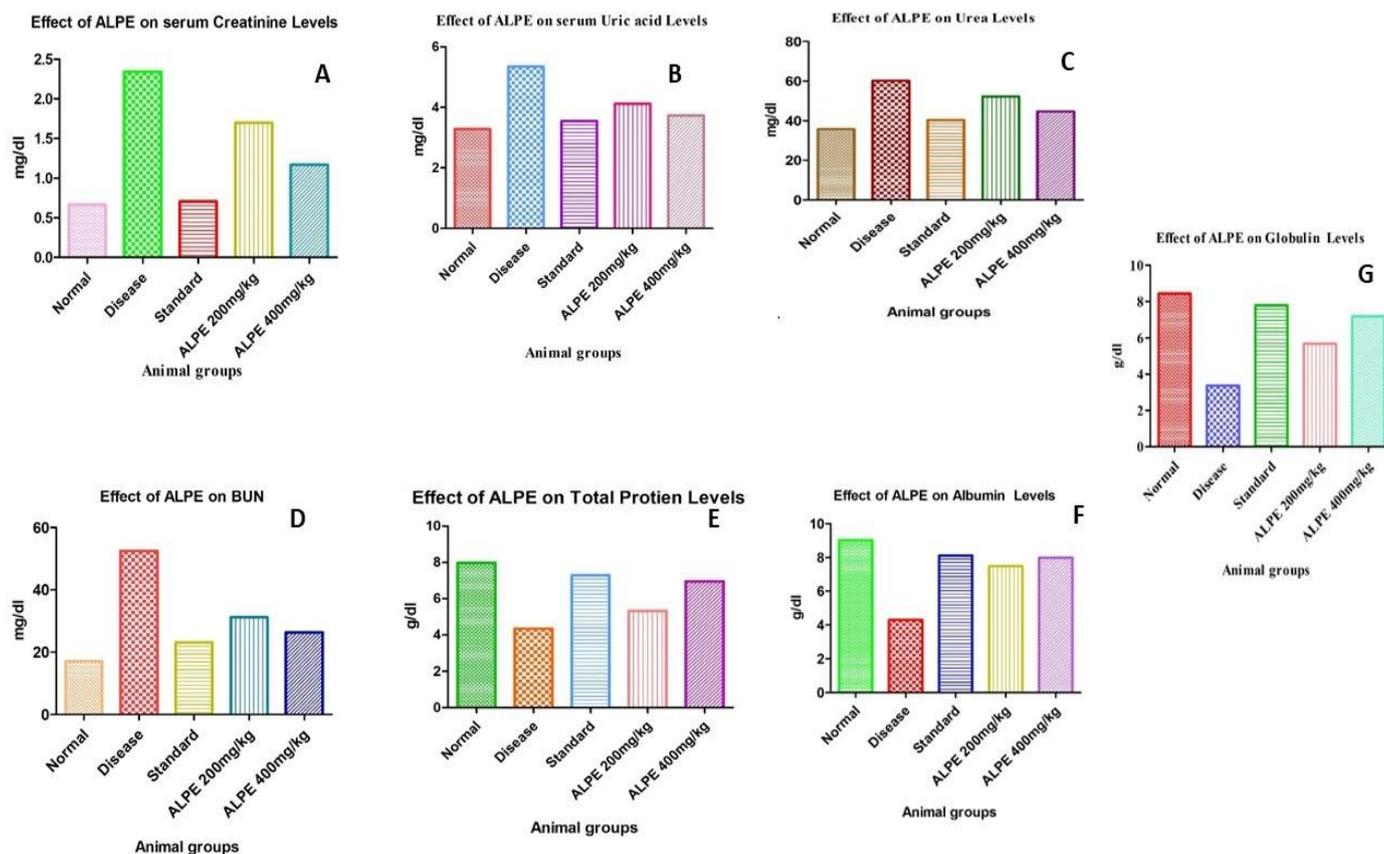


Figure 1: Effect of ALPE on Serum A. Creatinine, B. Uric acid, C. Urea, D. BUN, E. Total Protein, F. Albumin, G. Globulin Parameters

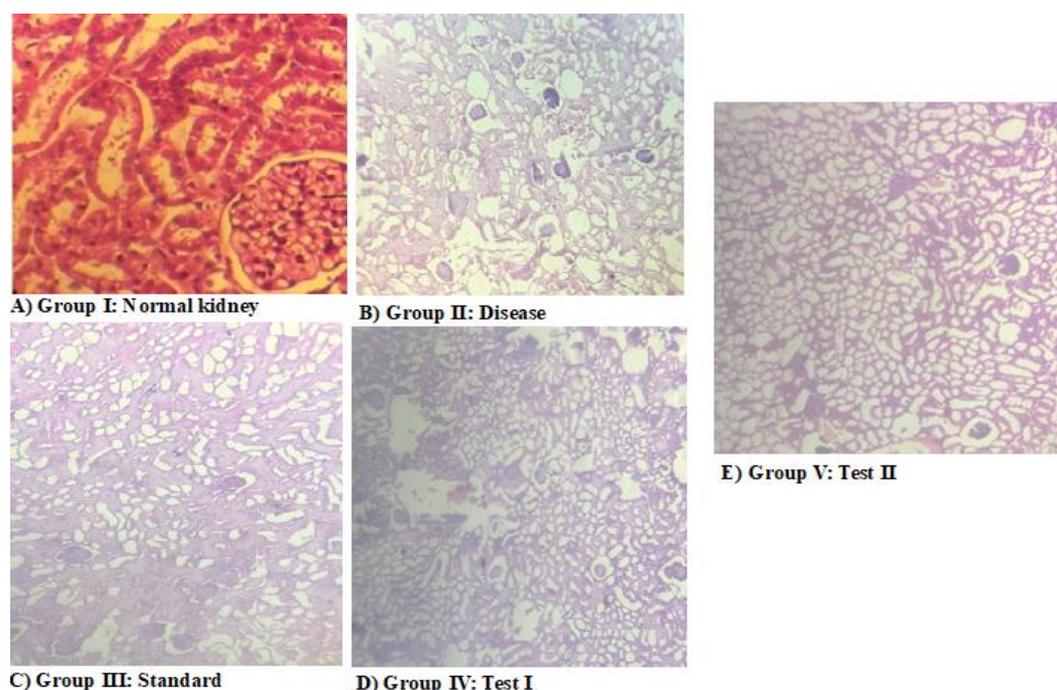


Figure 2: Light Microscopy study (H&E) of renal tissue in various experimental groups.

Effect on Serum Biochemistry

Rats from the Gentamicin alone group exhibited significantly decreased ($p < 0.05$) levels of total protein and albumin compared to the control group (Figure 1). In contrast, ALPE treatment prevented decreases in these parameters; with ALPE 200 mg/kg and ALPE 400 mg/kg resulting in nearly normal levels of total protein and albumin (Table 2). Table 2 shows that serum urea and creatinine were significantly increased ($p < 0.05$) in the Gentamicin alone group compared to the control group. Notably, experimental rats treated with ALPE 200 mg/kg and ALPE 400 mg/kg had significantly ($p < 0.05$) lower levels of urea and creatinine compared to Gentamicin alone group. Similar results were observed for creatinine clearance. There was significant decrease in the level of creatinine clearance in the Gentamicin alone group compared to control group. This decrease was prevented in treatment groups, with a significant increase in the creatinine clearance levels in the ALPE 200 ($p < 0.01$) and ALPE 400 ($p < 0.001$) groups compared to Gentamicin alone group, suggesting that treatment with the ALPE extract may protect renal tissue from further damage. Data from BUN/creatinine ratio indicate no significant changes with all the tested groups after treatment.

Histopathological Studies

The normal control group (A) had normal glomeruli and tubules, but the disease control group (B) showed acute tubular necrosis, peritubular inflammation, interstitial haemorrhage (Figure 2). The kidney sections from standard, Test I, Test II showed normal glomerulus, minor interstitial congestion, peritubular inflammation and interstitial congestion. Pretreatment with ALPE considerably reduced histological changes when compared to Gentamicin alone.

DISCUSSION

Gentamicin produces nephrotoxicity by blocking lysosomal hydrolases such sphingomyelinase and phospholipases, which leads to renal phospholipids and oxidative stress [16]. Gentamicin-induced nephrotoxicity causes direct tubular necrosis, primarily in the proximal tubules. Gentamicin's toxicity is linked to the production of reactive oxygen species in the kidney. The condition involves elevated plasma creatinine and urea levels, significant proximal tubular necrosis, and eventual renal failure. These are the biochemical markers used to investigate drug-induced nephrotoxicity in animals

and mammals [17]. Gentamicin was injected intraperitoneally once daily for 8 days to evaluate drug-induced nephrotoxicity. Gentamicin reaches proximal tubules after glomerular filtration, causing injury and renal circulation abnormalities. *Albizia lebbek pod* extract is thought to protect nephrons against gentamicin-induced nephrotoxicity due to its strong antioxidant properties due to presence of flavonoids; multiple animal research studies have shown a link between oxidative stress and nephrotoxicity. The current investigation includes phytochemical and pharmacological assessments of nephroprotective effect of ethanolic extract of *Albizia lebbek pods* at doses 200 mg/kg and 400 mg/kg of body weight. An initial phytochemical examination of ALPE revealed the presence of alkaloids, flavonoids, saponins, carbohydrates, steroids, amino acids.

In this experiment the ALPE protected gentamicin-induced nephrotoxicity. ALPE decreased serum creatinine, uric acid, urea, and BUN levels while increased total proteins, albumin, and globulin. These results indicate that ALPE improves renal function.

According to analysis, the plant possesses secondary metabolites, flavonoids, and phenolic compounds that operate as anti-oxidants. These might occur responsible for kidney protection. The normal control group had normal glomeruli and tubules, but the disease control group showed acute tubular necrosis, peritubular inflammation, and interstitial haemorrhage. The kidney sections from standard, Test I, Test II showed normal glomerulus, minor interstitial congestion, peritubular inflammation and interstitial congestion. Pretreatment with ALPE considerably reduced histological changes when compared to Gentamicin alone. Histopathological data suggest the ALPE protects against gentamicin-induced nephrotoxicity. The study suggests that ethanol extract of *Albizia lebbek pods* could be used as a nephroprotection. Further research is needed to understand the mechanisms of action and develop new therapeutic medicines for kidney disorders.

CONCLUSION

The current study obtained and validated *Albizia lebbek pods* from the family *Fabaceae*. The pods were pulverised to create coarse powder. The coarse powder was extracted with 95% ethanol using maceration technique. The extract was filtered and dried using a desiccator's dried ALPE was safely stored for phytochemical screening and nephroprotective studies.

ALPE's phytochemical screening proven alkaloids, flavonoids, saponins, carbohydrates, amino acids, steroids, carbohydrates and phenolic compounds. ALPE has been shown in literature to be safe at doses as high 2000 mg/kg, with no documented fatalities. ALPE shown immense preventive effect against renal damage caused by gentamicin, Flavonoids, alkaloids, saponins and phenolic compounds may be responsible for ALPE's renoprotective properties, either alone or in combination. According to the literature, flavonoids, alkaloids may have significant nephroprotective properties due to positive effects on renal system.

Conflict of interest

The authors declared no conflict of interest.

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