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NEPHROPROTECTIVE ACTIVITY OF CHLOROFORM EXTRACT OF *ABRUS PRECATORIUS* IN RATS

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Keywords:

Abrus precatorius, Gentamycin and Paracetamol, Histopathological studies, Nephroprotective activity

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ABSTRACT: This study seeks to evaluate the nephroprotective activity of chloroform extract of *Abrus precatorius* against gentamycin-induced nephrotoxicity in rats. Albino rats of Wistar strain of both sexes were used for the study and grouped into five, containing 6 animals. The study was performed for 14 days. For induction of nephrotoxicity, gentamycin and paracetamol were used, and the plant extract was given for 14 days. Later the animals were sacrificed, and kidneys were collected for histopathological studies. Meanwhile, blood was collected for estimation of serum parameters. All the animals treated with plant extract had shown decreased serum creatinine levels. The urea levels were also altered when compared to those of control. The histopathology studies of the kidney tissues also supported the results that the plant has a protective effect of gentamycin induced nephrotoxicity. The results of the study explored that the chloroform extract of *Abrus precatorius* has nephroprotective activity. Further studies are needed to isolate the active ingredients that have the protective effect.

INTRODUCTION: A number of environmental toxins, toxic chemicals, and drugs, including antibiotics, drugs used in chemotherapy, drastically alter the anatomy and physiology of various organs and generate adverse effects on liver, kidney, heart, pancreas, intestine, *etc.* [1] One group of antibiotics which are commonly used in these days for various bacterial infections like UTI are aminoglycoside antibiotics. Among these gentamycin is considered to be most effective in life-threatening bacterial infections and is most commonly recommended by physicians [2].

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Kidneys play an important role in eliminating various chemicals from the body through urine after metabolism. During this process, as a result of metabolism, various free radicals will be generated, and they cause damage to different parts of the nephron of the kidney. The parts which are damaged in this process include mainly the glomerulus, brush border of the convoluted tubule. This causes nephrotoxicity. Drug-induced, mainly, gentamycin, cisplatin-induced nephrotoxicity is most common in patients who have been affected with acute kidney injury. Gentamycin is thought to produce 15-30% of all nephrotoxicity cases.

In ancient medicine, these side effects are considered as most dangerous and may be life-threatening also. This is termed *Gara visa* meaning artificial poison that kills the person when accumulated in person's body for a longer period of time [3].

Abrus precatorius also known as gurivinda has been traditionally used for many ailments. The seeds of this plant are very famous for its attractive colour and is used for weighing gold in the olden days. The whole plant is having medicinal uses [4]. There has been no report for the nephroprotective activity of *Abrus precatorius*. So our study aims to report the same for it.

MATERIALS AND METHODS:

Collection of *Abrus precatorius*: The whole plant material was collected in the month of February 2017 in the areas in and around Tirupati, Chittoor district, Andhra Pradesh. Identification and authentication of the plant specimen were completed by Prof. N. Yasodamma, Department of Botany, Sri Venkateswara University, Tirupati (Specimen voucher number: KL20).

Preparation of Extract: The plant material was washed, dried under shade, and powdered. Then powdered material was preserved in an airtight container and used for future and further purposes. The powder was extracted using chloroform through soxhelation, and the extract was evaporated to dryness. The dried extract was collected and used for the experimental work. Gentamycin and paracetamol were procured from the local market, which is of standard company manufactured and marketed.

The CEAP was tested for phytochemical screening for the presence of various chemical constituents like carbohydrates, alkaloids, proteins, glycosides, flavonoids, tannins, resins, *etc*.

Animal Studies: Wistar rats of either sex weighing 150-200 grams were used for the study. They were housed in an animal house, Sree Vidyanikethan College of Pharmacy, A. Rangampet, Tirupati, maintained at 24±2 ºC under 12h light/dark cycle and fed with standard rat pellet diet and water *ad libitum.* All the animal experiments were performed after attaining Institutional Animal Ethics Committee approval (SVCP/IAEC/I-010/2017-18)

Acute toxicity studies were performed according to the OECD 423 guidelines. A single dose of 2000mg/kg, p.o was given to the rats to detect the toxicity and mortality.

Treatment Schedule: The animals were grouped into 5 groups (n=6). The treatment schedule was as follows.

Group I animals served as positive control and received normal saline.

Group II animals served as disease control and received gentamycin at a dose of 100mg/kg, i.p for 14 days.

Group III animals served as disease control and received paracetamol at a dose of 2g/kg, p.o for 14 days.

Group IV served as test group and received gentamycin at a dose of 100mg/kg, i.p as well as CEAP 500mg/kg, p.o for 14 days.

Group V served as test group and received paracetamol at a dose of 2g/kg, p.o as well as CEAP 500mg/kg, p.o for 14 days.

Biochemical estimations and Histopathological studies: On 7^{th} and 14^{th} day, blood was withdrawn from retro-orbital plexus under light ether anesthesia and serum was separated. Urine was also collected from the animals using the metabolic cage. The serum and urine samples were used for biochemical estimations like serum creatinine, urea, BUN, and electrolytes. All the parameters were estimated using standard assay kits using a semi-autoanalyser. At end of the study, the animals were sacrificed by cervical decapitation under ether anesthesia. The abdomen was opened and kidneys were identified, collected and kept in formalin for 24 h. After 24 h, the organs were deeply frozen. Then sectioned thinly using microtone section cutter and the sections were stained with eosin red and glycerine. Then the sections were observed under microscope for histopathological changes.

Estimation of Serum Creatinine: Creatinine levels were estimated using the standardized kits which followed the Jaffe's reaction. Creatinine reacts with alkaline picrate to produce reddish colour. The absorbance of the colour is directly proportional to creatinine concentration in sample. It was measured at 500-520 nm

Estimation of Blood Urea Nitrogen: It was estimated by measuring urea nitrogen in blood. The

enzyme urease hydrolyses the urea to ammonia which then converts into glutamate in the presence of NADH. NADH is oxidized to $NAD^{+;}$ this change was detected by decrease in absorbance at 340nm.

Statistical Analysis and Comparison: The experimental data obtained during the study was analysed using graph pad prism version 5.0. All the experimental values were expressed in mean ±SEM.

RESULTS:

Phytochemical Screening: Phytochemical screening results showed the presence of carbohydrates, glycosides, flavanoids, triterpenes, proteins and aminoacids.

Acute Toxicity Studies: Acute toxicity studies revealed the plant extract was safe at 2000mg/kg p.o also. No mortality was observed during the study. No signs of toxicity were observed during the period of 14 days. So 1/4th of the dose, *i.e.*, 500mg/kg p.o was fixed for the study.

Biochemical Estimations: The serum creatinine **Fig. 1** and serum urea levels **Fig. 2** were drastically increased in both gentamycin treated (100mg/kg i.p.) and paracetamol treated (2mg/kg p.o) group animals when compared to that in positive control group animals. The same when we observed in test-treated (500mg/kg p.o) groups along with gentamycin and paracetamol treated, the levels were significantly reduced. Similarly, the levels of blood urea nitrogen were drastically increased significantly in nephrotoxic groups when compared to that in normal group animals. Also in CEAP treated groups there was significant decrease in those levels when compared to that in group IV and V animals as observed in **Fig. 3**. The range of electrolytes Na **Fig. 4**, K **Fig. 5,** and Cl **Fig. 6** in the urine had also been observed. Ion range has been suddenly fallen in diseased animals, whereas in CEAP treated groups, those ranges were elevated to normal range. All the values were expressed in mean ±SEM for 6 animals in each group.

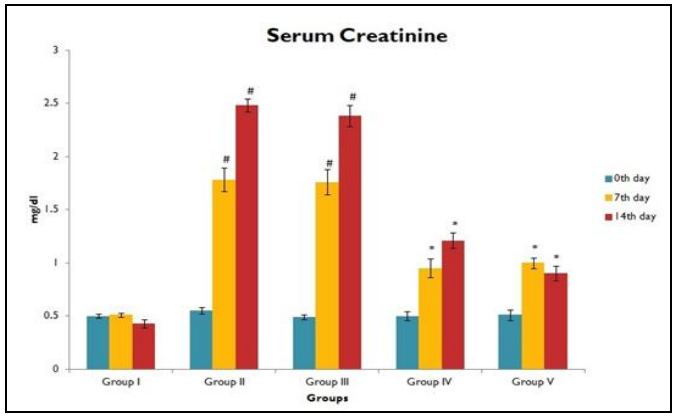

FIG. 1: GRAPH REPRESENTING SERUM CREATININE LEVELS. Significance: #p<0.05 compared with Group I, *p<0.05 compared with Group II & Group III respectively.

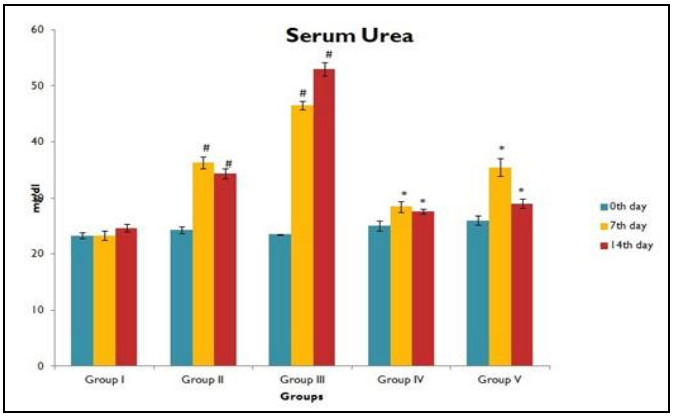

FIG. 2: GRAPH REPRESENTING SERUM UREA LEVELS. Significance: #p<0.05 compared with Group I, *p<0.05 compared with Group II & Group III respectively.

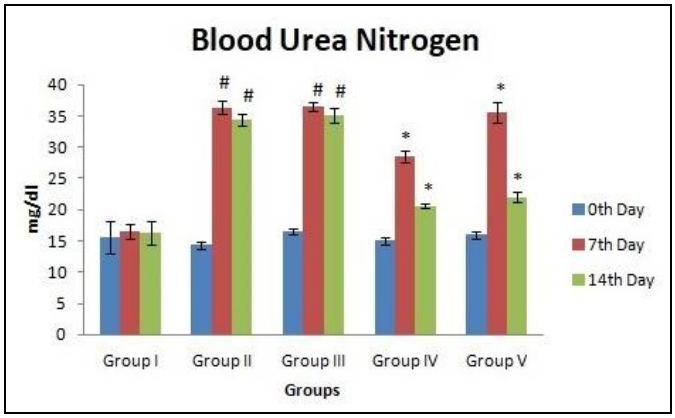

FIG. 3: GRAPH REPRESENTS THE BLOOD UREA NITROGEN LEVELS. Significance: #p<0.05 compared with Group I, *p<0.05 compared with Group II & Group III respectively.

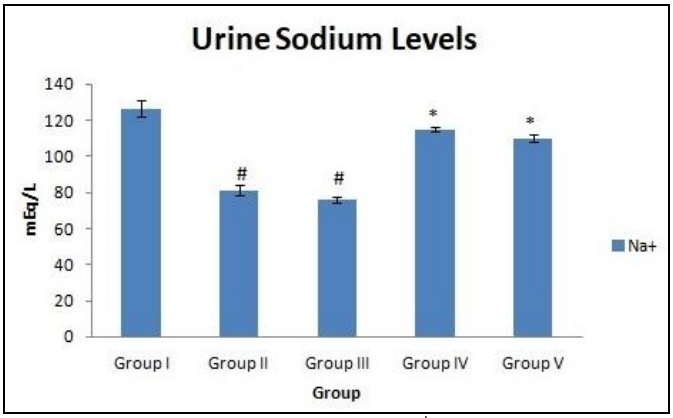

FIG. 4: GRAPH REPRESENTING Na^+ LEVELS IN URINE. Significance: #p<0.05 compared with Group I, *p<0.05 compared with Group II & Group III respectively.

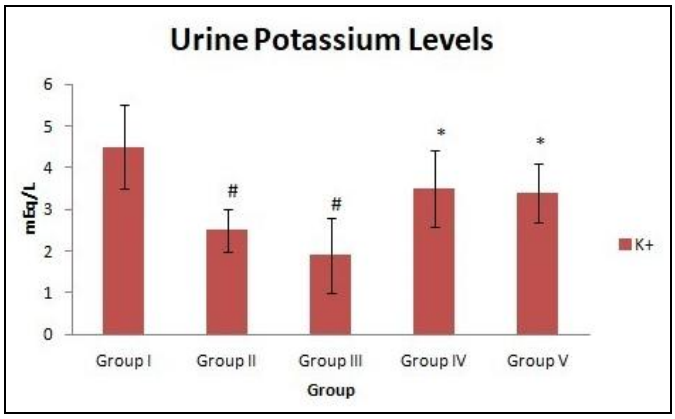

FIG. 5: GRAPH REPRESENTING K^+ LEVELS IN URINE.
Significance: #p<0.05 compared with Group I, *p<0.05 compared with Group II & Group III respectively.

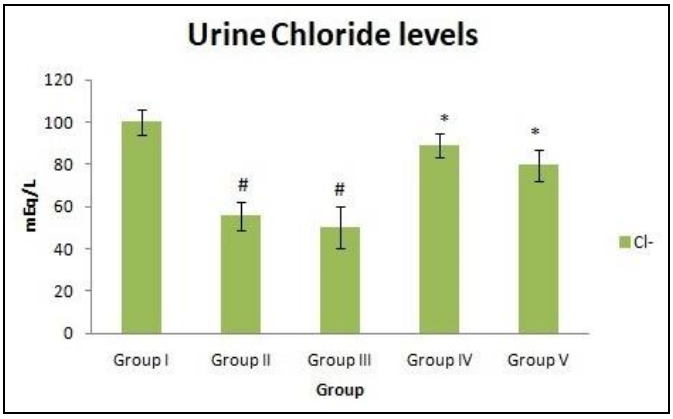

FIG. 6: GRAPH REPRESENTING CL^- LEVELS IN URINE.
Significance: #p<0.05 compared with Group I, *p<0.05 compared with Group II & Group III respectively.

Histopathological Studies: The histopathological changes in each kidney were observed for changes in glomerular congestion, interstitial congestion, tubular hemorrhage, colloids, inflammatory cell infiltrates, dilated capillaries, ruptured, and degeneration of cells.

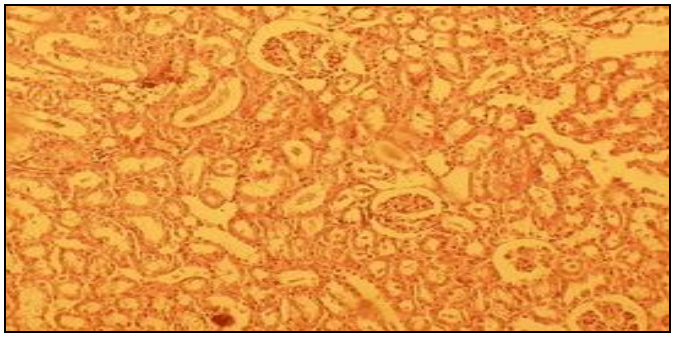

FIG. 7: REPRESENTS THE POSITIVE CONTROL GROUP

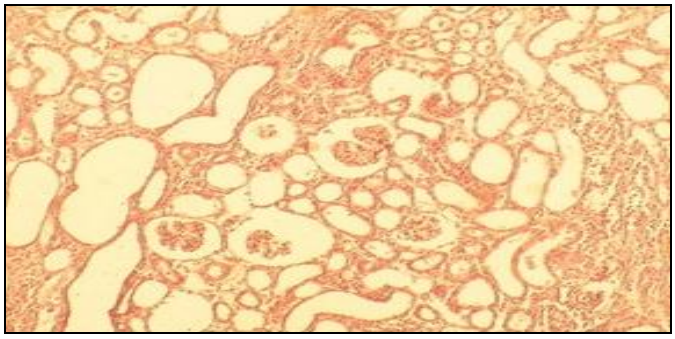

FIG. 8: REPRESENTS THE GENTAMYCIN INDUCED NEPHROTOXICITY

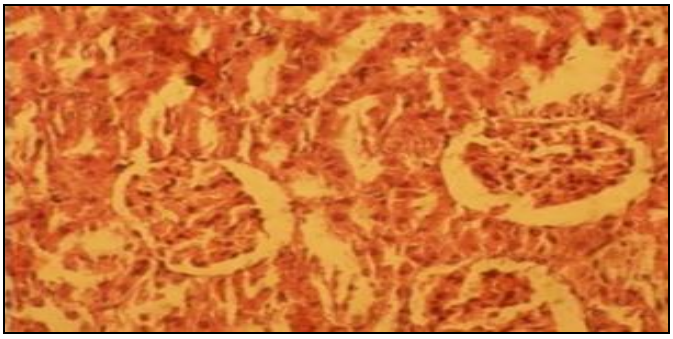

FIG. 9: REPRESENTS THE PARACETAMOL INDUCED TOXICITY IN KIDNEY

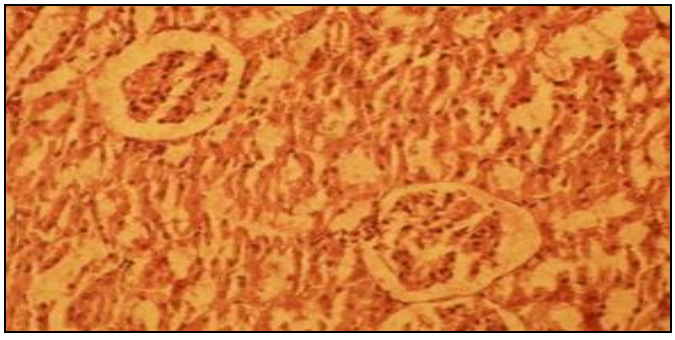

FIG. 10: REPRESENTS THE RECOVERY OF DAMAGED GLOMERULUS IN CEAP TREATED GROUPS INDUCED WITH GENTAMYCIN

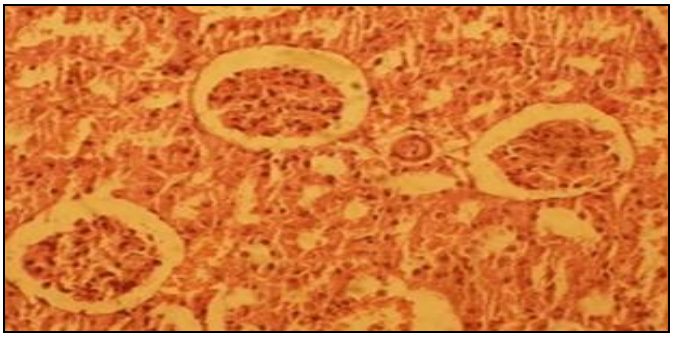

FIG. 11: REPRESENTS THE RECOVERY OF DAMAGED GLOMERULUS IN CEAP TREATED GROUPS INDUCED WITH PARACETAMOL

In gentamycin **Fig. 8** and paracetamol **Fig. 9** treated groups, the parameters were observed and compared to that with normal **Fig. 7** group animals. There was severe damage in those parameters along with atrophy of cells, nephrons, and kidney. The same when observed in plant extract treated groups induced with gentamycin **Fig. 10** and paracetamol **Fig. 11**, the kidneys had been protected from the damage.

DISCUSSION: Instead, Gentamycin is an effective antibiotic in treating gram-negative bacterial infections, it accounts for nearly 25% of acute renal injury and renal failure. As it is positively charged, it binds to the anionically charged cell membrane of glomerulus, Bowman's capsule and brush border (PCT) of nephron and causes oxidation of the membrane [5, 6]. This ultimately causes cell injury and cell death as oxidation is one of the causes of reversible and irreversible cell injury. As well the ions get accumulated in the cell of nephron. So, with this, lysosomes are activated to perform their function of pinocytosis, disturbing the entire renal function causing renal dysfunction and renal failure.

Paracetamol, a common over-the-counter drug used as an NSAID and also antipyretic, is commonly used by many people. Paracetamol overdoses will cause nephrotoxicity along with hepatotoxicity [7]. Hepatotoxicity is well reported than nephrotoxicity. But in some cases, nephrotoxicity is reported without causing damage to the hepatic texture and normal physiology of it [8]. An increase in serum creatinine, urea, BUN mainly represents the renal injury [9]. It is also evidenced by a decrease in urine creatinine, uric acid, alterations in electrolytes in AKI [10].

In the study, there was a marked surge in the levels of serum creatinine, Blood urea nitrogen and urea in the gentamycin and paracetamol-induced nephrotoxic rats when compared to that in positive control group rats (untreated group). This indicated the reduced rate of glomerular filtration, which is indicative of renal failure. After supplementation of CEAP in gentamycin and paracetamol-induced nephrotoxic rats, the levels were decreased indicating the protecting activity of *Abrus precatorious*. Even there is a decline in urine creatinine and uric acid levels in Gentamycin and paracetamol control groups, and after supplementation with CEAP there is significant and marked amelioration in their levels when compared to that in nephrotoxic rats. This was also evidenced by histopathology studies of renal tissues. The decrease in the congestion in glomerulus, intratubular hemorrhage, and protection from damage shown by reduced tissue/cellular damage to the cells of nephron was seen in animals treated with CEAP when compared to that in disease control group animals, where there is damage to nephrons was observed in those animals when compared to that in the positive control group [11].

It was previously evidenced that the presence of polyphenols and flavonoids in the plant extract will protect the tissues from being oxidised and prevent injury [12]. In *Abrus precatorious* chloroform extract also after performing phytochemical screening, the results evidenced the presence of polyphenols and flavonoids. So presence of these substances may be responsible for protecting the nephrons and kidney internal structure from being oxidised and injured.

By considering this, oxidative stress is mainly responsible for the toxic effects of many drugs [8]. The intake of antioxidants like vitamin E, phospholipid-rich diet (ex.: Egg) is referred along with gentamycin to reduce the injury to the kidneys by physicians. This has reduced the AKI in many patients[2].

CONCLUSION: As a conclusion, from our study, we are reporting that *Abrus precatorious* has nephroprotective activity. However, still, studies are needed to characterize and evaluate the phytochemical constituents which are responsible for antioxidant and nephroprotective effect in *Abrus precatorious*.

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CONFLICTS OF INTEREST: The authors declare no conflicts of interest.

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