An Investigation of Nephroprotective Activity of Abrus precatorius Leaves in Experimental Rats

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ABSTRACT
The nephroprotective activity of Abrus precatorius leaves extract against Gentamicin and Cisplatin induced nephrotoxicity in rats was performed. The acute toxicity studies conducted on ethanolic extract of Abrus precatorius was found to be non-toxic at a dose of 2000mg/kg. Two doses 200 mg/kg and 400 mg/kg b.w p.o. of the extract were subjected for the evaluation of nephroprotective activity against the nephrotoxicity induced by Gentamicin (100mg/kg, i.p) and Cisplatin (5mg/kg, i.p) in rats. Selenium (6mg/kg, p.o.) was served as standard in both the models. Urinary and serum biochemical parameters, assessment of oxidative stress, kidney weight and histopathology were evaluated in the study. Both the low (200mg/kg) and high dose (400mg/kg) of Abrus precatorius extract showed dose dependent significant decrease in serum creatinine, urea, BUN and cholesterol levels and increase in urea creatinine, urea, sodium and potassium levels when compared with toxic control. Both the doses showed decrease in LPO and increase in GSH, SOD and CAT levels. Histopathological analysis of kidney showed less necrosis in extract treated rats, thus confirming the nephroprotective effect. The result obtained was comparable with that of the standard drug Selenium. The finding of the present study provides the evidence that, the ethanolic extract of Abrus precatorius is beneficial against Gentamycin and Cisplatin induced nephrotoxicity, this might be due to the presence of array of phytoconstituents.

Keywords: Abrus precatorius, Cisplatin, Gentamycin, Nephroprotective activity.

INTRODUCTION
The kidneys are a pair of beans shaped, reddish brown organs located just above the waist between the peritoneum and the posterior wall of the abdomen and are protected by the ribcage. They play an important part in the maintenance of our endocrine and acid base balance, blood pressure, erythropoiesis etc. Kidneys have some delicate tasks especially when they have to deal with unwanted substances, which they have to clear from the system, especially toxins. Therefore, it becomes critical when kidney function declines, induced by diseases which seem to have no direct relation to renal pathophysiology. Humans are exposed intentionally or unintentionally to a variety of diverse chemicals that harm the kidney.

Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin. One of the causes of renal injury is by a pharmacologic agent used to diagnose or treat a medical disorder. Many drugs are nephrotoxic because they are excreted from the blood flow, glomerular filtration or tubular function. Most nephrotoxic drugs cause proximal renal tubular necrosis. If renal injury is severe, acute renal failure develops. When kidney damage occurs, body becomes unable to get rid of excess urine & wastes from the body. Blood electrolytes such as potassium and sodium become elevated. Aminoglycosides have long been one of the common causes of drugs induced nephrotoxicity.

Gentamicin is a very effective antibiotic in treating gram negative bacterial infection in human and animals. It causes renal failure in 10-20% of therapeutics course. Gentamicin nephrotoxicity occurs in about 15-30% of treated subjects, is manifested clinically as non-oliguric renal failure, with a slow rise in serum creatinine and hypo-osmolar urinary output developing after several days of treatment. It has been demonstrated that gentamicin-induced nephrotoxicity is a complex phenomenon characterized by severe proximal tubular necrosis, followed by deterioration and renal failure due to direct tubular necrosis, which is localized mainly in the proximal tubules.

Cisplatin (cis-diamino dichloro-platinum II) is currently one of the most important chemotherapeutic agents used intensively in humans, being effective in ovarian & bladder carcinoma, neuroblastoma, head and neck carcinoma, and lymphoma as well as thyroid, endometrial neoplasm and the most significant activity, in testicular cancer. However, the clinical usefulness of this drug is limited due to nephrotoxicity.

In the recent year many researchers have examined the effects of plants used traditionally by the indigenous healers and herbalists to support kidney function and to treat the diseases of the kidney. In most cases, research has confirmed traditional experience and wisdom by...
discoversing the mechanism and mode of action of these plants as well as reaffirming the therapeutic effectiveness of certain plants or plant extracts in clinical studies. Several hundred plants have been examined for use in a wide variety of kidney disorders.

The aim of the present study was to find out new nephroprotective drugs from indigenous plant Abrus precatorius using Gentamicin and Cisplatin induced nephrotoxicity.

**MATERIALS AND METHODS**

**Collection and Authentication of Plant Material**

The fresh plants of *Abrus precatorius* were collected in the month of July-august from the forest of Mangalore district, Karnataka state, India and authenticated by Botanist.

**Preparation of Ethanolic Extract**

The powdered material (150g) of *Abrus precatorius* leaves was packed in Soxhlet extractor and extracted using ethanol as solvent for 12 cycles. The temperature was maintained on an electric heating mantle with thermostat control. Appearance of colorless solvent in the siphon tube was taken as the termination of extraction. The extract was concentrated by using rotary flash evaporator. The concentrated extract was then air dried at room temperature, weighed and percentage yield was calculated. The color and consistency of the extract were noted.

**Experimental animals**

Wistar albino rats (150–200g) of either sex were used for the experiment were procured from the animal house of Srinivas College of Pharmacy, Mangalore. They were maintained under standard conditions (temperature 22° ± 2°C, relative humidity 60±5% and 12-hour light/dark cycle). The animals were housed in sanitized polypropylene cages containing sterile paddy husk as bedding. They had free access to standard pellet diet and water ad libitum. All the experimental protocols were reviewed and approved by the institutional animal ethical committee (Approval no SCP/CPCSEA/P13/F150/2012) prior to the initiation of the experiment and the care of the laboratory animals were taken as per the CPCSEA regulations. The animals were acclimatized for one week before use.

**Preliminary Qualitative Phytochemical Analysis**

The preparation of ethanolic extract of *Abrus precatorius* leaves was subjected to preliminary phytochemical screening for the detection of chemical constituents.

**Determination of Acute toxicity (LD₅₀)**

Acute toxicity test was conducted to determine the median lethal dose (LD₅₀) of the ethanolic extract of *Abrus precatorius* leaves. The toxicity studies were carried out according to OECD guidelines-425.

Nephroprotective Activity of *Abrus precatorius* in Gentamicin Induced Nephrotoxicity in Rats

**Experimental Design**

The Wistar rats of either sex weighing between 150-200g were randomly divided into five groups of six animals each. Group I served as a normal control and received regular rat food and drinking water *ad libitum*. Group II served as Gentamicin control. All the animals except group I, received 100mg/kg/day gentamicin i.p. for 8 days. Group III animals were treated with Selenium 6mg/kg p.o. Group IV and V were treated with *A. precatorius* extract 200mg/kg and 400mg/kg respectively started 3 days prior to the gentamicin injection and continued for the next 8 days. After dosing on the day 8, individual rats were placed in separate metabolic cages for urine collection. On 9th day, animals were sacrificed after being anaesthetized with ketamine (75mg/kg i.p.), blood samples were collected via cardiac puncture and analyzed for various biochemical parameters. Kidneys were dissected out and used for histopathological studies.

**Nephroprotective Activity of *Abrus precatorius* in Cisplatin Induced Nephrotoxicity in Rats**

**Experimental Design**

Wistar rats of either sex weighing between 150-200g were divided into five groups of six animals each. Group I served as a normal control and received regular rat food and drinking water *ad libitum*. Group II served as Cisplatin control. All the animals except Group I were intoxicated by the administration of cisplatin (5mg/kg) on 1st and 2nd day of treatment 30 mins after respective administration. Group III animals with Selenium 6mg/kg and group IV and V were treated with *A. precatorius* leaf extract 200mg/kg and 400mg/kg respectively for eight days. After dosing on the day 8, individual rats were placed in separate cages for urine collection. On the 9th day, animals were sacrificed after being anaesthetized with ketamine (75mg/kg i.p.), blood samples were collected via cardiac puncture and analyzed for various biochemical parameters. Kidneys were dissected out and used for histopathological studies.

**Biochemical parameters estimated includes**

The biochemical parameters such as serum creatinine, serum urea, serum cholesterol, blood urea nitrogen (BUN), urinary creatinine, urinary sodium and potassium were estimated by using standard procedure.

**Physical parameter**

**Kidney weight**

Kidneys were mopped with filter paper and weighed. Weight is expressed in grams.

**Preparation of kidney homogen**

The kidney was quickly removed and perfused immediately with ice-cold saline (0.9% NaCl). A portion of the kidney was homogenized in chilled Tris-HCl buffer (0.025 M pH 7.4) using a homogenizer. The homogeny
obtained was centrifuge at 5,000 rpm for 10 min, supernatant was collected and used for analysis.

**Estimation of renal antioxidants**

Superoxide dismutase (SOD) was measured in tissue supernatant by inhibiting the production of nicotinamide adenine dinucleotide-phenazine methosulfate-nitro blue tetrazolium formazani. Catalase (CAT) action in tissue supernatant was measured spectrophotometrically at 620 nm by calculating the rate of debasement of hydrogen peroxide, the substrate of the protein. Diminished glutathione (GSH) substance in tissue supernatant was measured spectrophotometrically by using Ellman’s reagent (Dinitro thiobenzoic corrosive) as a coloring reagent.

**Estimation of renal lipid peroxidation**

Estimation of malonaldehyde as an index for lipid peroxidation (LPO) was done utilizing thiobarbituric acid assay.

**Histopathological studies**

The kidney was preserved in 10% neutral buffered formalin. A 5µm thickness of tissue sections were stained with hematoxylin and eosin stain (H and E stain) for routine histopathological examination.

**Statistical Analysis**

All data were expressed as Mean ± SEM. The statistical significance between groups were compared using one way ANOVA, followed by Dunnett’s using students t test.

**RESULTS**

**Preliminary phytochemical screening**

The preliminary phytochemical investigation of ethanolic extract of *Abrus precatorius* showed the presence of carbohydrates, flavonoids, glycosides, steroids, tannins, proteins and volatile oil.

**Determination of nephroprotective activity Gentamicin induced nephrotoxicity**

**Effect on serum creatinine, urea, BUN and cholesterol in Gentamicin induced nephrotoxicity**

Serum levels of enzymes like creatinine and urea were elevated in gentamicin treated animals when compared to normal control. The prophylactic treatment with Standard (Selenium) showed extremely significant (P<0.001) reduction in marker enzymes such as creatinine and urea and moderately significant reduction (P<0.01) in cholesterol levels. The animals pre-treated with higher dose of *A. precatorius* leaf extract (400mg/kg) showed extremely significant (P<0.001) reduction in marker enzymes such as creatinine, urea and BUN levels, and less significant (P<0.05) reduction in cholesterol level where as lower dose of *A. precatorius* leaf extract (200mg/kg) treated animals showed moderately significant (P<0.01) in creatinine, urea and BUN levels and no significant (P>0.05) reduction in cholesterol levels when compared to positive control group.

**Effect on Urinary Creatinine, Urea, Sodium and Potassium levels in Gentamicin induced nephrotoxicity**

Decreased level of creatinine, urea, sodium and potassium were observed in gentamicin treated animals when compared to normal control. Standard (selenium) treated animals showed extremely significant (P<0.001) elevated in creatinine, urea, sodium and potassium levels. *Abrus precatorius* extract low dose (200mg/kg) treated animals showed moderately significant (P<0.01) increase in creatinine, urea and sodium level, and less significant (P<0.05) increase in potassium level. Whereas, higher dose (400mg/kg) showed extremely significant (P<0.001) increase in creatinine and urea levels, moderately significant (P<0.01) increase in sodium and potassium levels, compared to positive control group.

**Effect on kidney weight**

Kidney weight was considerably increased in gentamicin treated animals compared to normal control. There was extremely significant (P<0.001) reduction in elevated kidney weight in Standard (Selenium) treated animals. The animal pretreated with *A. precatorius* extract low dose (200mg/kg) showed moderately significant (P<0.01) decrease in kidney weight whereas higher dose of the extract (400 mg/kg) showed extremely significant (P<0.001) reduction compared to positive control group.

**Effect on anti-oxidant parameters GSH, LPO, SOD and CAT in Gentamicin induced nephrotoxicity**

Gentamicin treated animals developed with kidney damage observed as an increase in LPO and decrease in GSH, CAT & SOD when compared to normal control. Animals treated with standard (Selenium) showed extremely significant (P<0.001) increase in GSH, CAT & SOD and decrease in LPO. Animals pretreated with low dose of extract (350 mg/hg) showed extremely significant (P < 0.001) increase in SOD, moderately significant (P<0.01) increase in GSH, less significant increase in CAT & moderately significant decrease in IPO. Whereas higher dose (700 mg/kg) treated animals showed extremely significant (P<0.001) increase in GSH and SOD, decrease in IPO & moderately significant (P<0.01) increase in CAT compared to positive control.
Table 1: Nephroprotective effect of *A. precatorius* extract on Urine parameters In Gentamicin induced nephrotoxicity

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Creatinine (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Sodium (mmol/l)</th>
<th>Potassium (mmol/l)</th>
<th>Kidney weight (in g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Saline</td>
<td>97.62 ± 3.28</td>
<td>20.78 ± 1.36</td>
<td>134.9 ± 4.79</td>
<td>3.87 ± 0.81</td>
<td>0.55 ± 0.02</td>
</tr>
<tr>
<td>Toxic control</td>
<td>Gentamicin (100mg/kg)</td>
<td>45.45 ± 1.27</td>
<td>12.18 ± 2.06</td>
<td>88.41 ± 0.942</td>
<td>2.64 ± 0.12</td>
<td>0.75 ± 0.02</td>
</tr>
<tr>
<td>Standard</td>
<td>Selenium (6mg/kg)</td>
<td>83.40 ± 2.71</td>
<td>18.342 ± 0.08</td>
<td>128.11 ± 3.59***</td>
<td>3.55 ± 0.11***</td>
<td>0.58 ± 0.001***</td>
</tr>
<tr>
<td>Low dose</td>
<td><em>A. precatorius</em> (200mg/kg)</td>
<td>55.67 ± 1.03</td>
<td>14.45 ± 1.11</td>
<td>109.8 ± 1.99**</td>
<td>3.11 ± 0.09*</td>
<td>0.6 ± 0.01**</td>
</tr>
<tr>
<td>High dose</td>
<td><em>A. precatorius</em> (400mg/kg)</td>
<td>78.51 ± 4.07</td>
<td>17.32 ± 0.82***</td>
<td>114.12 ± 5.16**</td>
<td>3.48 ± 0.07**</td>
<td>0.62 ± 0.01***</td>
</tr>
</tbody>
</table>

All the values were Mean ± SEM, n=6. One way ANOVA followed by Dunnett’s t test. *p< 0.001 when compared with vehicle treated control group. *p<0.05, **p<0.01, ***p<0.001 when compared with toxic control.

Table 2: Effect of *A. precatorius* extracts on antioxidant parameters- GSH, LPO, SOD and CAT in Gentamicin induced nephrotoxicity

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>GSH (Abs at 412nm)</th>
<th>LPO (Abs at 535nm)</th>
<th>SOD (Abs at 560nm)</th>
<th>CAT (Abs at 620nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Saline</td>
<td>0.51±0.08</td>
<td>0.04 ± 0.02</td>
<td>0.69 ± 0.03</td>
<td>0.45 ± 0.04</td>
</tr>
<tr>
<td>Toxic control</td>
<td>Gentamicin (100mg/kg)</td>
<td>0.20 ± 0.03</td>
<td>0.09 ± 0.05</td>
<td>0.072 ± 0.06</td>
<td>0.24 ± 0.02</td>
</tr>
<tr>
<td>Standard</td>
<td>Selenium (6mg/kg)</td>
<td>0.482±0.03***</td>
<td>0.103±0.02***</td>
<td>0.58 ± 0.09***</td>
<td>0.38 ± 0.02***</td>
</tr>
<tr>
<td>Low dose</td>
<td><em>A. precatorius</em> (200mg/kg)</td>
<td>0.38±0.09</td>
<td>0.23 ± 0.02**</td>
<td>0.45±0.07***</td>
<td>0.29 ± 0.01*</td>
</tr>
<tr>
<td>High dose</td>
<td><em>A. precatorius</em> (400mg/kg)</td>
<td>0.42±0.02***</td>
<td>0.18 ± 0.04***</td>
<td>0.51±0.08***</td>
<td>0.32±0.03***</td>
</tr>
</tbody>
</table>

All the values were Mean ± SEM, n=6. One way ANOVA followed by Dunnett’s t test. *p< 0.001 when compared with vehicle treated control group. *p<0.05, **p<0.01, ***p<0.001 when compared with toxic control.

Figure 1: Haematoxylin and eosin (H&E) stained section of kidney in Gentamicin induced nephrotoxicity

(a) Normal

(b) Gentamicin

(c) Selenium

(d) *A. precatorius* (200 mg/kg)

(e) *A. precatorius* (400 mg/kg)
(a) Control group showed a normal histology of kidney tissue (b) The kidney section from animal treated with Gentamicin control has been shown tubular necrosis. (c) The selenium treated group revealed an almost complete prevention of histopathological alterations. (d) The animal treated with *A. precatorius* (200mg/kg) shown slight necrotic change. (e) The animal treated with *A. precatorius* (400mg/kg) shown regeneration in tubular epithelial cells.

**Cisplatin induced Nephrotoxicity**

**Effect on Serum Creatinine, Urea, BUN and Cholesterol in Cisplatin induced nephrotoxicity**

Animals treated with cisplatin developed a significant renal damage as elevated serum levels of renal specific enzymes like creatinine & compared to normal control. There was an extremely significant (*P<0.001*) reduction in creatine, Urea, BUN and cholesterol levels in animals treated with Standard (Selenium) when compared to positive control group. The animals pretreated with ethanolic extract of *A. precatorius* 200mg/kg (low dose) showed extremely significant (*P<0.001*) decrease in creatinine level, moderately significant (*P<0.001*) decrease in urea and BUN level and less significant (*P>0.05*) decrease in cholesterol level where as high dose (400mg/kg) treated animals showed extremely significant (*P<0.001*) decrease in creatinine, urea & BUN level and moderately significant (*P<0.01*) decrease in cholesterol level compared to the positive control group.

**Effect on Kidney weight**

Kidney weight was increased in cisplatin treated animals when compared to normal control. There was extremely significant (*P<0.001*) decrease in kidney weight in Standard (Selenium) treated animals. The animals pretreated with low dose of extract showed moderately significant (*P<0.01*) reduction in increased kidney weight, whereas higher dose treated animals showed extremely significant (*P<0.001*) decrease in kidney weight compared to positive control group.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Treatment</th>
<th>Creatinine (mg/dl)</th>
<th>Urea (mg/dl)</th>
<th>Sodium (mmol/l)</th>
<th>Potassium (mmol/l)</th>
<th>Kidney weight (in g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Saline</td>
<td>95.64 ±3.812</td>
<td>20.65 ±1.251</td>
<td>133.9 ±4.898</td>
<td>3.96 ±0.674</td>
<td>0.534 ±0.02</td>
</tr>
<tr>
<td>Toxic control</td>
<td>Cisplatin (5mg/kg)</td>
<td>38.62 ±0.35⁴</td>
<td>11.77 ±0.052²</td>
<td>98.46 ±0.57⁴</td>
<td>2.739 ±0.107⁴</td>
<td>0.78 ±0.105⁴</td>
</tr>
<tr>
<td>Standard</td>
<td>Selenium (6mg/kg)</td>
<td>80.11 ±0.579***</td>
<td>19.60 ±0.12***</td>
<td>121.56 ±0.167**</td>
<td>0.588 ±0.29***</td>
<td>0.588 ±0.27***</td>
</tr>
<tr>
<td>Low dose</td>
<td><em>A. precatorius</em> (200mg/kg)</td>
<td>45.482 ±1.06***</td>
<td>15.60 ±1.83**</td>
<td>106.2 ±1.52*</td>
<td>2.942 ±0.0329ns</td>
<td>0.642 ±0.012**</td>
</tr>
<tr>
<td>High dose</td>
<td><em>A. precatorius</em> (400mg/kg)</td>
<td>59.45 ±0.55***</td>
<td>17.21 ±1.56***</td>
<td>112.4 ±2.63**</td>
<td>3.264 ±0.094⁴</td>
<td>0.61 ±0.082***</td>
</tr>
</tbody>
</table>

All the values were Mean ± SEM, n=6. One way ANOVA followed by Dunnett’s t test. *p<0.001 when compared with vehicle treated control group. *p<0.05, **p<0.01, ***p<0.001 when compared with toxic control.

**Effect on Urinary Creatinine, Urea, Sodium and Potassium levels in Cisplatin induced nephrotoxicity**

A significant renal damage was observed as decreased creatinine, urea, sodium and potassium levels in cisplatin treated animals when compared to normal control. The prophylactic treatment with Standard (Selenium) showed extremely significant (*P<0.001*) increase in creatinine & urea levels and moderate significant (*P<0.001*) increase in sodium and potassium levels compared to positive control group. Treatment with low dose of *A. precatorius* extract (200mg/kg) showed extremely significant (*P<0.001*) elevation in creatinine and urea, less significant (*P<0.05*) increase in sodium and no significant (*P>0.05*) increase in potassium level whereas high dose of extract (400mg/kg) treated animal showed extremely significant (*P<0.001*) increase in Creatinine and Urea. Moderately significant (*P<0.01*) increase in sodium level and less significant (*P<0.05*) increase in potassium levels compared to positive control.

**Effect on antioxidant parameters like GSH, LPO, SOD and CAT in Cisplatin induced nephrotoxicity**

The Cisplatin induced kidney damage was shown by increase in LPO and decrease in GSH, SOD & CAT when compared to normal control. Treatment with standard (Selenium) showed extremely significant (*P<0.001*) increase in GSH, CAT & SOD and decrease in LPO. Animals Pretreated with *A. precatorius* low dose (200 mg/kg) showed extremely significant (*P<0.001*) increase in GSH and SOD, less significant (*P<0.05*) increase in CAT & moderately significant (*P<0.01*) decrease in LPO whereas extremely significant (*P<0.001*) increase in GSH &SOD, moderately significant (*P<0.01*) decrease in LPO and increase in CAT was observed in *A. precatorius* high dose (400 mg/kg) treated animals compared to toxic control.
**Table No 4:** Effect of *A. precatorius* extracts on antioxidant parameters- GSH, LPO, SOD and CAT in Gentamicin induced nephrotoxicity

<table>
<thead>
<tr>
<th>Group</th>
<th>Treatment</th>
<th>GSH (Abs at 412nm)</th>
<th>LPO (Abs at 535 nm)</th>
<th>SOD (Abs at 560nm)</th>
<th>CAT (Abs at 620nm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Saline</td>
<td>0.51±0.07</td>
<td>0.05 ±0.02</td>
<td>0.68±0.03</td>
<td>0.45±0.05</td>
</tr>
<tr>
<td>Toxic control</td>
<td>Cisplatin (5mg/kg)</td>
<td>0.18±0.001</td>
<td>0.31±0.08</td>
<td>0.10±0.07</td>
<td>0.29±0.02</td>
</tr>
<tr>
<td>Standard</td>
<td>Selenium (6mg/kg)</td>
<td>0.462±0.09***</td>
<td>0.16±0.053***</td>
<td>0.63±0.022***</td>
<td>0.38±0.02**</td>
</tr>
<tr>
<td>Low dose</td>
<td><em>A. precatorius</em> (200mg/kg)</td>
<td>0.40±0.06***</td>
<td>0.26±0.049**</td>
<td>0.51±0.011***</td>
<td>0.33±0.01*</td>
</tr>
<tr>
<td>High dose</td>
<td><em>A. precatorius</em> (400mg/kg)</td>
<td>0.44±0.01***</td>
<td>0.24±0.003**</td>
<td>0.55±0.98***</td>
<td>0.35±0.03**</td>
</tr>
</tbody>
</table>

All the values were Mean ± SEM, n=6. One way ANOVA followed by Dunnett’s t test. *p< 0.001 when compared with vehicle treated control group. *p<0.05, **p<0.01, ***p<0.001 when compared with toxic control.

**Figure 2:** Histopathological view of renal section from different groups stained with hematoxylin and eosin

(a) Control group showed normal structure of glomerulus, renal cortex, and interstitium with no evidence of acute cell necrosis. (b) The animal treated with Cisplatin showed marked vacuolization, necrosis of tubular cells. (c) The animal treated with selenium revealed an almost complete prevention of histopathological alterations. (d) The animal treated with *A. precatorius* (200mg/kg) shown slight changes in renal tissue injury. (e) The animal treated with *A. precatorius* (400mg/kg) shown remarkably attenuated renal tissue injury.

**DISCUSSION**

Nephrotoxicity is a poisonous effect of some substances, both toxic chemicals and medication on the kidneys out of which the drugs are the most common source. A number of therapeutic agents like aminoglycosides, chemotherapeutic agents and NSAIDS can adversely affect the kidney resulting in acute renal failure, chronic interstitial nephritis and nephritis syndrome. Acute renal failure refers to the sudden and usually reversible loss of renal function which develops over a period of days or weeks. Among the causes of acute renal failure and acute tubular necrosis, nephrotoxins like cisplatin and gentamicin is most common and accounts for 85% of the incidence. Biochemical parameters such as blood urea, serum creatinine and creatinine clearance have been used for investigation of drug induced nephrotoxicity in animals and man as the rate of production of these parameters exceeds the rate of clearance in renal disease.\(^1^9\)

Gentamicin induces nephrotoxicity by the generation of superoxide, hydroxyl radical and hydrogen peroxide free radicals which results in cell death by causing oxidative stress. A severe reduction in glomerular filtration rate leads to a substantial elevation of serum creatinine, urea, cholesterol and BUN levels accompanied by a substantial reduction in the urinary creatinine, urea, sodium and potassium levels.\(^2^0\) This indicates a poor clearance capacity of the kidneys. Thus, abnormally high levels in serum as well as low levels in urine warn of possible malfunction or failure of the kidneys. Gentamicin decreased the level of catalase, glutathione peroxidase, superoxide dismutase and the level of reduced glutathione. Treatment with *Abrus precatorius* by both doses reversed the above condition by its antioxidant activity. The result suggests
that both extract of *Abrus precatorius* showed dose dependent significant action against renal damage. Antioxidant potential is believed that it may be due to presence of flavonoids.

Cisplatin gets accumulated in the renal proximal tubules characterized by morphological destruction of intra cellular organelles and cellular necrosis followed by function alterations including inhibition of protein synthesis and mitochondrial damage. It is toxified to form a reactive oxygen species intra cellulary by hydration and induce GSH depletion, lipid peroxidation, reduction in superoxide dismutase and catalase levels and direct DNA damage. Elevated levels of cholesterol are due to impaired lipid metabolism. Cisplatin treated rats also showed a marked decreased in GSH, SOD and CAT stores and increase in lipid peroxidation which indicates the oxidative stress induced by Cisplatin.

Both the doses of *Abrus precatorius* leaf extract reversed the above condition by its antioxidant activity which elevated GSH, SOD and CAT and decreased the LPO levels, which was comparable to standard drug selenium. The nephroprotectivity showed by *Abrus precatorius* extract in cisplatin induced nephrotoxicity is mediated through its potent antioxidant effect. Protective effect in Gentamicin as well as Cisplatin induced nephrotoxicity was also proved by decreased in elevated kidney weight in animals pretreated with both lower and higher dose of *Abrus precatorius* extract. Further histopathological studies in both the models also supported the nephroprotective activity.

CONCLUSION

Nephrotoxicity is one of the side effects which limit the use of gentamicin and cisplatin during treatments. The investigation undertaken was aimed to study nephroprotective activity of ethanolic extract of *Abrus precatorius* leaves, demonstrated the usefulness and beneficial effects in the treatment of nephrotoxicity induced by gentamicin and cisplatin. Ethanolic extract of the plant leaves offered dose dependent decrease in kidney biomarkers in rats. The results of serum and urine biochemical parameters as well as the histopathological analysis of kidney exhibits, role of the extract in renal function. The nephroprotective activity was found to be more significant in high and low dose of *Abrus precatorius* in all the animal models and was compared to the standard selenium. The activity may be attributed to presence of antioxidant constituents namely flavonoids and other polyphenolic compounds in the plant. The treatment with *Abrus precatorius* could also restore the kidney weight which was elevated in nephrotoxic animals, hence proving nephroprotective activity. Histopathological observation revealed that treatment with *Abrus precatorius* extract has reversed the renal damage induced by Cisplatin and Gentamicin.

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