ABSTRACT

The present study was undertaken to evaluate the nephro-protective potential of cardiospermum halicacabum, family sapindaceae. Aqueous extract of whole plant of cardiospermum halicacabum Linn were prepared by maceration. LD₅₀ studies for all the two extracts were carried by “up and down method” in albino mice following OCED guidelines No.425 of CPCSEA up to the dose limit of 2000 mg/kg. 1/5 of the maximum dose were tested. The extract was studied for nephroprotective activity. Preliminary photochemical studies revealed the presence of sterols, saponins, carbohydrates, tannins and flavanoids in aqueous extracts. Male wistar rats were divided into five groups and received saline orally (control group), vehicle control group received 2% Gum acacia orally, Rutin 20mg/kg, 200mg/kg & 400mg/kg aqueous extract was administered orally for 7 days pre-treatment. On the 7th day of experiment, each groups were kept fasted for 14 hrs and gentamycin in a dose of 100mg/kg body weight given to all rats. After 48 hrs animals were anesthetised by chloroform and blood samples were collected by retro-orbital method by using heparin coated capillaries and animals were sacrificed. The supernatant was used for estimation of various biochemical parameters by using semi auto-analyzer (MISPA EXCEL) and the kidney was isolated for histopathological studies. Nephrotoxicity produced by the significant increase in serum levels of ALP, Creatine, BUN, Uric acid, Cholesterol was reduced in Rutin, Aqueous extract pre-treated groups. Nephroprotective effect of Rutin & cardiospermum halicacabum likely results from suppression of oxidative stress.

Keywords: Rutin, cardiospermum halicacabum, Nephroprotective and Gentamycin.

INTRODUCTION

Acute renal failure (ARF) is one of the commonest life threatening condition [1]. Toxic effects of kidney related to medications are common and expected, gives the kidneys roles in plasma filtration and maintenance of metabolic homeostasis. The renal vascular bed is exposed to a
quarter of resting cardiac output. As glomerular, tubular and renal interstitial cells frequently encounter significant concentrations of medications and their metabolites, which can induce changes in kidney function and structure. Urinary obstruction due to stone or tumour, or glomerular disease are common cause of acute glomerular disease known as acute tubular necrosis [2]. Etiology varies in different parts of the world.

Traditionally gastroenteritis and infections are common causes in developing countries while major surgery and hemolytic uremic syndrome (HUS) are important causes of ARF in developed countries [1]. Nowadays, causes for ARF were 45% acute tubular necrosis, 21% prerenal, 12.7% acute onset chronic renal failure and 10% obstructive ARF [3]. Most of ARF are secondary to acute tubular necrosis occurring because of a multi-organ dysfunction syndrome. Factors most often associated with acute renal damage are: advanced age, volume depletion, arterial hypotension, massive bleeding and sepsis [4]. ARF often leads to complications like liver disease, pancreatitis, pre-existing renal dysfunction, great burns, and cardiosurgery [5]. Mortality is low for the isolated forms of ARF, where as it peaks to 0-80% in multi organ failure. Although pharmacological supports and dialysis instruments have improved, the mortality is higher among elderly patients [6]. Hence, search for clinically superior medicine for renal failure is warranted. The present investigation is undertaken to study the nephroprotective activity of *cardiospermum helicacabum linn* against gentamycin induced toxicity using Rutin as standard.

**MATERIALS AND METHODS**

**Plant material:**
*cardiospermum helicacabum linn* plant was collected from local fields of Kurnool, Andhra Pradesh, India. This plant material was taxonomically identified and authenticated by approved Botanist Dr. K.Madhava chetty, Sri Venkateswara university, Tirupathi.

**Preparation of extract:**
The freshly collected whole plant were dried at room temperature and powdered. Briefly 20g of powder was soaked in500ml distilled water for 24 h with constant stirring. The suspension was further filtered through Whatman filter paper. The filtrate was concentrated in vacuo using a rotary evaporator to obtain the aqueous extract [7].

**Drugs and chemicals:**
Standard drug Rutin and gentamicin are obtained from Sigma- Aldrich chemicals Ltd, Bangalore and gentamicin are obtained from glan pharma Hyderbad respectively as gift sample. All the estimation kits are purchased from agape chemicals kerala.

**Experimental Procedure:**
Albino rats of either sex weighing between 150-200 g were used for the study. Animals were kept relative temperature (25±2°C) and relative humidity 44–56%, light and dark cycles of 10 and 14 h, respectively during the experiments. Animals were provided with standard rodent pellet diet. Rats were fasted 14 h before the experiment though water was allowed *ad libitum*. All animal procedures have been approved and prior permission from the Institutional Animal Ethical Committee (No. 557/02/c/CPCSEA) was obtained as per the prescribed guidelines.
Study procedure:
In the present study albino Wister rats weighing about 150-200 gms were selected and divided into 5 groups containing 6 animals in each group. Group-I animals served as untreated control and was fed with normal saline 5ml/kg body weight daily for 7 days. Group-II animals were treated with 2% gum acacia orally for 7 days. Group-III animals were treated with Rutin 20mg/kg for 7 days. Similarly Group-IV and Group-V animals were treated with 200 mg and 400mg of AECH for 7 days respectively. Following termination of experiment on 7th day rats were fasted overnight for 14 hrs and gentamycin was given by intra peritoneal route in a dose of 100 mg/kg body weight to all rats except group-I animals. After 48 hrs blood samples were collected by retro-orbital method by using heparin coated capillaries and then go for the centrifugation, the supernatant was used for estimation of various biochemical parameters and the animals were scarified, kidney was isolated for histopathological studies [8].

Nephroprotective activity:
Determination of nephroprotective activity in gentamicin induced nephrotoxicity. Wistar albino rats weighing between 150-200 g and each group containing 6 animals will be divided into 5 groups.
Group 1: Normal control group animals treated 1 ml saline orally.
Group 2: Vehicle control group animals treated 1 ml of 2% Gum acacia orally.
Group 3: Test group animals treated with Rutin with 20 mg/kg.
Group 4: Test group animals treated with AECH 200 mg/kg.
Group 5: Test group animals treated AECH 400 mg/kg.

RESULTS
The preliminary phytochemical investigation report indicates that the aqueous extract of *Cardiospermum Halicacabum* (Linn) found to contains alkaloids, carbohydrates, flavonoids, phenolic compounds, proteins, glycosides and tannins. The experimental results of the effect of aqueous extract of *Cardiospermum Halicacabum* (Linn) in nephroprotective effect in rats (Table 1) showed that reduced blood Alkaline Phosphatase, Creatine, Blood urea nitrogen, Uric acid, Total protein, Cholesterol, Albumin significantly.

Table: 1 Consolidated Table Showing the Effect of Rutin & AECH in Albino rats showing Nephroprotective activity

<table>
<thead>
<tr>
<th>Group</th>
<th>Alkaline phosphate</th>
<th>Creatinin</th>
<th>BUN</th>
<th>Uric acid</th>
<th>Total proteins</th>
<th>Cholesterol</th>
<th>Albumin</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>260.3±4.84</td>
<td>1.4 ±0.37</td>
<td>15.9 ± 0.73</td>
<td>7.23 ± 0.86</td>
<td>7.01 ± 0.32</td>
<td>199.5 ±2.1</td>
<td>5.19 ±0.57</td>
</tr>
<tr>
<td>Control</td>
<td>873±5.57</td>
<td>17.5 ±1.6</td>
<td>37.2 ± 1.7</td>
<td>16.6 ± 1.09</td>
<td>5.36 ± 0.63</td>
<td>291.9 ±4.25</td>
<td>1.61 ±0.26</td>
</tr>
<tr>
<td>Vehicle Control</td>
<td>858.8±4.47</td>
<td>16.1 ± 1.58</td>
<td>35.0 ± 1.9</td>
<td>14.9±1.13</td>
<td>5.8±0.59</td>
<td>292.2±4.07</td>
<td>1.69 ±0.20</td>
</tr>
<tr>
<td>Rutin 20mg/kg</td>
<td>297±5.4***</td>
<td>8.28±0.62***</td>
<td>17.5±0.78***</td>
<td>7.15±0.81***</td>
<td>10.2±0.75***</td>
<td>211.5±1.87***</td>
<td>4.06±0.23***</td>
</tr>
<tr>
<td>AECH 400mg/kg</td>
<td>314.4±5.4***</td>
<td>11.45±0.68***</td>
<td>21.3±0.88***</td>
<td>9.35±0.8***</td>
<td>7.93±0.76***</td>
<td>242.9±3.9***</td>
<td>3.92±0.42***</td>
</tr>
<tr>
<td>AECH 200mg/kg</td>
<td>409.4±4.47***</td>
<td>12.8±0.72***</td>
<td>25.1±1.3***</td>
<td>12.3±0.91***</td>
<td>6.31±0.68</td>
<td>264±4.6***</td>
<td>2.74±0.30***</td>
</tr>
</tbody>
</table>
Figure: 1 Graph Showing the Effect of Rutin & AECH in Alkaline Phosphatase

Figure: 2 Graph Showing the Effect of Rutin & AECH in Creatinine

Figure: 3 Graph Showing the Effect of Rutin & AECH in Blood Urea Nitrogen
Figure: 4 Graph Showing the Effect of Rutin & AECH in Uric Acid

Figure: 5 Graph Showing the Effect of Rutin & AECH in Total Proteins

Figure: 6 Graph Showing the Effect of Rutin & AECH in Cholesterol

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Treatment of rats with gentamicin produced an increase blood Alkaline Phosphatase, Creatine, Blood urea nitrogen, Uric acid, Total protein, Cholesterol.in normal control group. Rats treated with rutin, AECH and AECH showed significant decrease blood Alkaline Phosphatase, Creatine, Blood urea nitrogen, Uric acid, Total protein, Cholesterol compared to toxicant control group.

DISCUSSION

It has been found that the gentamycin treatment increases $H_2O_2$ (guidet and shah,1989;walker and shah,1987;yang et al.,1995) and $O_2^-$ (Cuzzocrea et al.,2002)Production,and it is known  that $H_2O_2$ (Duque et al.,1992) and $O_2^-$ (Martinez-salgado et al.,2002)induce mesangial cells contraction, altering the filtration surface area and modifying the ultra filtration coefficient factor, that decrease the glomerular filtration rate (GFR). It has been suggested that the oxidative stress induces tubular damage [9].

Most chemotherapy drugs targets pathways that are essential to dividing cells (Hanigan and Devarajan, 2003). Several studies have now documented the importance of reactive oxygen metabolites (ROM) in cisplatin and gentamycin induced renal damage (Ueda et al., 2000). Nephrotoxicity of the drugs is usually associated with their accumulation in renal cortex, dependent upon their affinity to kidneys and on kinetics of drug trapping process [8].

The protective effects of Aqueous extract of AECH and Rutin against gentamycin induced toxicity in experimental rats that can cause reduced blood Alkaline Phosphatase, Creatine, Blood urea nitrogen, Uric acid, Total protein, Cholesterol, Albumin, which is significantly. Compared with that of normal control group.

CONCLUSION

Based on the above findings it could conclude that nephroprotective acitivity of *cardiospernum Halicacabum* against gentamycin induced toxicity the particular active constituents like flavanoids responsible for the protective activity could be isolated and investigates for further studies.
REFERENCES