



109/A

Dose response study of *Gmelina arborea* Roxb. (Verbenaceae) bark extract against adriamycin induced nephrotoxicity in Wistar rats

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Gmelina arborea (common name: *Et-demata*; Family: Verbenaceae) is a medicinal plant widely used in the management of renal insufficiency and chronic renal failure, by traditional Ayurvedic practitioners in Sri Lanka. The aim of the present study was to investigate the acute nephroprotective activity of the aqueous bark extract of *G. arborea* in adriamycin (ADR) induced nephrotoxic Wistar rats. The adult male Wistar rats were randomly divided into six groups (n=6). All the groups of rats except group one were administered with a single dose of ADR (20 mg/kg body wt., ip) for the induction of nephrotoxicity. The treatments were started 24 hours after induction of nephrotoxicity and continued for three days. Group one and two rats, serving as healthy and nephrotoxic control groups, were administered with equivalent volumes of normal saline. The rats of group three, four and five were administered orally with the lyophilized powder of the aqueous refluxed bark extract of *G. arborea* at three doses; 100, 300 and 500 mg/kg body wt. respectively. Rats of group six were administered orally with the standard drug, foscipril sodium (0.09 mg/kg). Blood and urine samples collected at the end of the intervention were used for the estimation of selected biochemical parameters to assess the nephroprotective activity. H&E stained sections of the kidney tissues were used for the assessment of histopathological changes using a semi-quantitative score system developed based on early features of acute tubular necrosis. The biochemical results in test groups were compared with the nephrotoxic control group. Treatment with the plant extract at the doses of 100, 300 and 500 mg/kg decreased the elevation of concentrations of serum creatinine (18%, 33% and 39%) and β_2 -microglobulin (54%, 70% and 71%) in ADR induced nephrotoxic rats respectively ($p < 0.05$). Administration of the plant extract with the three doses reduced the decrease in serum concentration of albumin (1%, 5% and 10%) and total protein (0%, 17% and 31%) respectively ($p < 0.05$). The loss of urine total protein was significantly reduced (48%, 74% and 78%) with the increased dose of plant extract ($p < 0.05$). The highest nephroprotective effect was observed in the plant extract at the dose of 500 mg/kg in ADR induced rats. Similar changes were observed in the foscipril treated rats compared to the ADR induced nephrotoxic group. H&E stained sections of the kidney tissues showed an attenuation of pathological changes in the rats treated with the plant extract and foscipril. Male rats and foscipril were included in the investigation due to their wide applicability and usage in previous research. The results revealed that the selected doses of the aqueous bark extract of *G. arborea* possess significant nephroprotective activity against ADR induced acute nephrotoxicity.

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