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Research Article

NEPHROPROTECTIVE ACTIVITY OF AERIAL PARTS OF *URARIA PICTA* AGAINST DRUG-INDUCED NEPHROTOXICITY IN RATS

NITESH KUMAR RAJAK*, SUNIL SHAH, DUBEY BK, DEEPAK BASEDIA

Department of Pharmacology, TIT College of Pharmacy, Bhopal, Madhya Pradesh, India. E-mail: niteshkumarrajak19@gmail.com

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ABSTRACT

Objectives: The present study aimed to investigate the nephroprotective potential of the ethanolic extract of the aerial parts of *Uraria picta* against gentamicin (GM)-induced nephrotoxicity in Wistar rats. In addition, the study evaluated the phytochemical composition, total phenolic content (TPC), and total flavonoid content (TFC) of the extract to understand its role in renal protection.

Methods: Preliminary phytochemical screening was conducted, followed by estimation of TPC and TFC. Nephrotoxicity was induced in rats using GM (100 mg/kg, i.p.) for 8 consecutive days. The extract was administered orally at doses of 100 mg/kg and 200 mg/kg. Renal function was evaluated by estimating serum creatinine (Cr), blood urea nitrogen (BUN), urea, total protein (TP), and albumin levels.

Results: The aerial parts of *U. picta* were extracted using ethanol, yielding 9.25% (w/w). Phytochemical analysis confirmed the presence of alkaloids, flavonoids, phenols, saponins, and proteins. The TPC and TFC were found to be 0.578 mg/100 mg and 0.624 mg/100 mg, respectively. GM administration caused a significant elevation in serum Cr, BUN, and urea, along with a reduction in TP and albumin levels, confirming renal damage. Treatment with *U. picta* extract resulted in a dose-dependent improvement in all biochemical parameters, with the 200 mg/kg dose showing highly significant ($p<0.001$) protection, restoring values toward normal.

Conclusion: The ethanolic extract of *U. picta* demonstrated significant nephroprotective activity against GM-induced renal toxicity in rats. The protective effects may be attributed to its antioxidant, anti-inflammatory, and membrane-stabilizing properties linked to its phytochemical constituents. These findings support the therapeutic potential of *U. picta* in managing drug-induced nephrotoxicity.

Keywords: *Uraria picta*, Nephroprotective activity, Gentamicin, Drug-induced nephrotoxicity, Antioxidant, Renal protection, Flavonoids, Phenolic compounds.

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INTRODUCTION

Acute kidney injury (AKI) and chronic kidney disease are major global health concerns and are often triggered or exacerbated by therapeutic agents with nephrotoxic potential. The kidneys' high perfusion rate, concentrating ability for xenobiotics, and active tubular transport make them particularly vulnerable to toxic damage, which may lead to acute tubular necrosis, interstitial nephritis, or progressive renal fibrosis [1].

Drug-induced nephrotoxicity involves multiple mechanisms, including oxidative stress, mitochondrial dysfunction, inflammation, and apoptosis of renal tubular epithelial cells. Gentamicin (GM) and cisplatin are the most commonly used experimental nephrotoxins because they reliably induce renal tubular injury through reactive oxygen species generation and inflammatory signaling, closely reflecting clinical drug-induced AKI [2].

Uraria picta (Prishniparni), an important component of the Ayurvedic Dashamoola group, contains phenolics, flavonoids, tannins, terpenoids, and other antioxidant-rich phytoconstituents. Aerial-part extracts of *U. picta* have demonstrated significant radical-scavenging, anti-inflammatory, and anticancer activities in preliminary studies [3,4], suggesting that the plant may modulate oxidative and inflammatory pathways involved in nephrotoxicity.

Considering that oxidative stress and inflammation are major mediators of GM- and cisplatin-induced nephrotoxicity, an antioxidant-rich plant, such as *U. picta* may offer significant renoprotection. Therefore, the present investigation evaluates the nephroprotective potential of the methanolic extract of *U. picta* aerial parts in drug-induced nephrotoxicity in rats, using biochemical, oxidative stress, and histopathological markers to elucidate its protective mechanisms [5].

MATERIALS AND METHODS

Materials

The materials used in the present study included various analytical-grade chemicals and reagents procured from reputed suppliers. Potassium mercuric iodide and picric acid were obtained from Thomas Baker, Mumbai, while iodine, potassium iodide, sodium nitroprusside, sodium hydroxide, lead acetate, and Folin-Ciocalteu reagent were purchased from Loba Chemie Pvt. Ltd., Mumbai. Potassium bismuth iodide, pyridine, gelatin, nitric acid, copper acetate, and sodium chloride were supplied by S. D. Fine Chem. Ltd., Mumbai. Methanol, ethanol, and chloroform were procured from Qualigens Fine Chemicals, Mumbai. Fehling's solution was obtained from Central Drug House Ltd., New Delhi. All chemicals used were of analytical grade and used without further purification.

Methods

Collection and authentication of plant materials

Aerial parts of *U. picta* free from diseases were collected from Shubham nursery of Bhopal (M.P.) in the month of March, 2025. The aerial parts of *U. picta* were authenticated by J. Mehta, Career College, Bhopal (M.P.).

Extraction by soxhlet extraction process

Fifty grams of aerial parts of *U. picta* was extracted with Ethanol solvent by soxhlet extraction method. The extract was evaporated above their

boiling point. Finally, the percentage yields were calculated of the dried extracts [6].

Determination of percentage yield

The extraction yield is evaluate of the solvent's efficiency to extract bioactive components from the selected natural plant samples and it was defined as the quantity of plant extracts recovered in mass after solvent extraction compared with the initial quantity of plant samples. After extraction, the yield of the plant extracts obtained were calculated in grams and then converted it into a percentage. The percentage yield of the extract was calculated by using the following formula:

$$\text{Percentage Yield} = \frac{\textit{Weight of Extract}}{\textit{Weight of Powder drug taken}} \times 100$$

Phytochemical screening

Medicinal plants are resources of traditional medicines and many of the modern medicines are produced indirectly from plants. Phytochemical constituents are of two types: Primary bioactive constituents, including chlorophyll, proteins, amino acids, sugar, etc. and secondary bioactive constituents, including alkaloids, terpenoids, phenols, flavonoids, etc. Phytochemical examinations were carried out for all the extracts as per the standard methods [7].

Quantitative estimation of bioactive compounds

Estimation of total phenolic content (TPC)

The TPC of dry extract was performed with folin-ciocaltaeu assay [8]. 2 mL of sample (1 mg/mL) was mixed with 1 mL of folin ciocalteu's phenol reagent and 1 mL of (7.5 g/L) sodium carbonate solution was added and mixed thoroughly. The mixture was kept in the dark for 10 min at room temperature, after which the absorbance was read at 765 nm. The TPC was determined from the extrapolation of a calibration curve which was made by preparing Gallic acid solution. The estimation of the phenolic compounds was carried out in triplicate. The TPC was expressed as 100 milligrams of Gallic acid equivalents/100 mg of dried sample.

Total flavonoids content estimation

Determination of total flavonoids content was based on the aluminum chloride method [8]. 10 mg quercetin was dissolved in 10 mL methanol, and various aliquots of 5–25 µg/mL were prepared in methanol. 10 mg of dried extract was dissolved in 10 mL methanol and filter. Three mL (1 mg/mL) of this extract was for the estimation of flavonoids. 1 mL of 2% $AlCl_3$ solution was added to 3 mL of extract or each standard and allowed to stand for 15 min at room temperature; absorbance was measured at 420 nm.

***In vivo* nephroprotective activity of *U. picta* extract**

Animals

Wistar rats (150–200 g) were group-housed (n=6) under a standard 12 h light/dark cycle and controlled conditions of temperature and humidity (25±2°C, 55–65%). Rats received standard rodent chow and water *ad libitum*. Rats were acclimatized to laboratory conditions for 7 days before carrying out the experiments. All experiments were conducted in a noise-free room between 08:00 and 15:00 h. A separate group of rats (n=6) was used for each set of experiments. The animal studies were approved by the Institutional Animal Ethics Committee (IAEC), (Approval No. TIT/IAEC/2025/89) which was constituted by the Ministry of Environment and Forests, Government of India, New Delhi, India, for the purpose of controlling and supervising experimental animals.

Acute toxicity studies

Toxicity studies were conducted in accordance with OECD guidelines, including an acute oral toxicity study of the *U. picta* extract. An acute toxicity study was performed based on OECD guideline no. 423. The mice were assessed for signs of toxicity throughout the next 14 days. *U. picta* extract was given orally at a safe dose. Clinical symptoms, such as behavioral alterations, changes in the eyes, body weight, skin, and fur were noted.

Experimental protocol

The rats were randomly divided into four groups of six rats (n=6) [9].

- Group I: Normal control: Animals received saline orally for 8 days
- Group II: GM: Animals received GM (100 mg/kg), i.p., for 8 days
- Group III: Test-I (100 mg/kg): Animals received *U. picta* extract (100 mg/kg) orally, and 1 h later received GM (100 mg/kg) i.p., for 8 days
- Group IV: Test-II (200 mg/kg): Animals received *U. picta* extract (200 mg/kg) orally, and after 1 h, received GM (100 mg/kg) i.p., for 8 days.

On the 9th day, all the rats were anesthetized with diethyl ether. Blood was collected in tubes from the retro-orbital venous plexus and allowed to clot for 60 min at 25°C. The serum samples were obtained by centrifuging blood at 1000× *g* for 15 min using a cooling centrifuge and stored frozen for biochemical assays.

Assessment of serum biochemical parameters

The estimation of serum creatinine (Cr), blood urea nitrogen (BUN), total proteins (TP), albumin, and urea levels were carried out by using Tulip assay kits according to the manufacturer's instructions [10].

Table 1: Results of the percentage yield of the extract of *Uraria picta*

S. No.	Extract	Percentage yield (w/w) (%)
1.	Ethanolic	9.25

Table 2: Result of phytochemical screening of the extract of *Uraria picta*

S. No.	Constituents	Ethanolic extract
1.	Alkaloids	
	Hager's test	+Ve
2.	Glycosides	
	Legal's test	−Ve
3.	Flavonoids	
	Lead acetate test	+Ve
	Alkaline reagent test	+Ve
4.	Saponins	
	Froth test	+Ve
5.	Phenol	
	Ferric chloride test	+Ve
6.	Proteins	
	Xanthoproteic test	+Ve
7.	Carbohydrate	
	Fehling's test	−Ve
8.	Diterpenes	
	Copper acetate test	−Ve
9.	Tannins	
	Gelatin test	−Ve
10.	Sterols	
	Salkowski test	−Ve

+Ve: Positive; −Ve: Negative

Table 3: Estimation of total phenol and flavonoids content of *Uraria picta*

S. No.	Ethanolic extract	Total phenol content	Total flavonoids content
		mg/100 mg	
1.	*Uraria picta*	0.578	0.624

Table 4: Effect of *Uraria picta* extract on serum creatinine, blood urea nitrogen, total proteins, albumin, and urea levels in GM-induced renal damage in rats

Group	Treatment	Serum creatinine (mg/dL)	Blood urea nitrogen (mg/dL)	Serum albumin (g/dL)	Total protein (g/dL)	Urea (mg/dL)
Group I	Normal control (0.5% CMC)	0.65±0.03	18.4±0.72	4.5±0.12	6.9±0.18	29.6±0.81
Group II	Gentamicin (100 mg/kg)	2.18±0.09#	51.0±1.40#	2.2±0.09#	4.1±0.15#	66.1±1.20#
Group III	*Uraria picta* extract (100 mg/kg)+GM	1.62±0.06*	40.2±1.24*	3.5±0.10*	5.6±0.16*	53.4±1.05*
Group IV	*Uraria picta* extract (200 mg/kg)+GM	0.78±0.04***	22.9±0.85***	4.3±0.08**	6.6±0.11**	32.1±0.80***

GM: Gentamicin, CMC: Carboxymethylcellulose, SEM: Standard error of the mean. Results are expressed as mean±SEM (n=6). #p<0.001 as compared to normal control rats and **p<0.01, ***p<0.001 compared to gentamicin rats

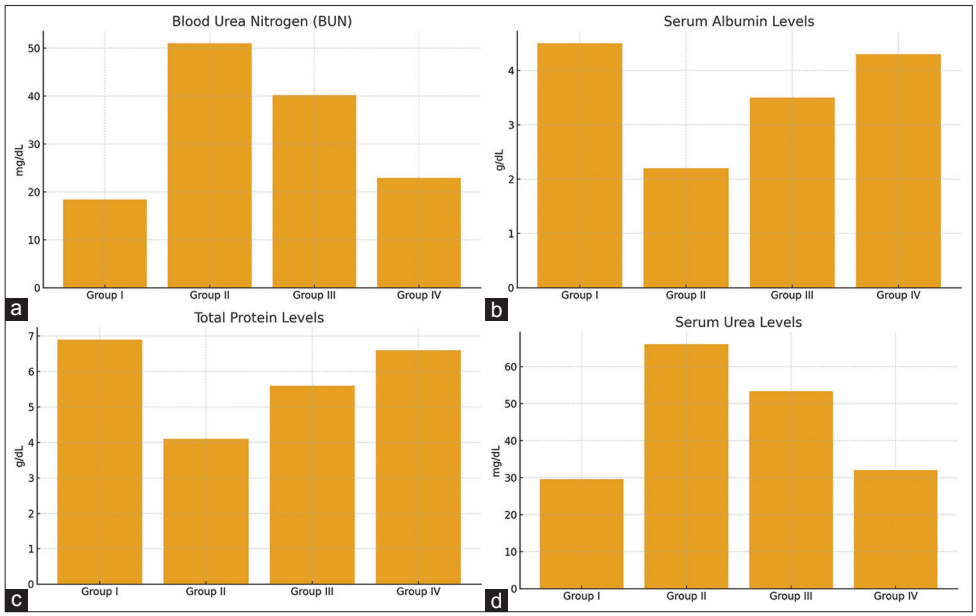

Fig. 1: Effect of *Uraria picta* extract in gentamicin-induced renal damage in rats. (a) Blood urea nitrogen. (b) Total protein levels. (c) Albumin levels (d) Urea levels

Statistical analysis

Data are expressed as mean±standard error of the mean, where n=number of rats. Statistical analysis was carried out using one-way analysis of variance followed by a Tukey multiple comparisons *post hoc* test. The level of significance was set at p<0.05. GraphPad Prism V 8.02 (GraphPad Software Inc., San Diego, California, USA) was used for statistical analysis.

RESULTS

None

DISCUSSION

The present study was undertaken to evaluate the nephroprotective potential of the ethanolic extract of *U. picta* against GM-induced nephrotoxicity in rats. The percentage yield of the ethanolic extract was found to be 9.25% (Table 1), indicating efficient extraction of phytoconstituents using ethanol as a solvent.

Preliminary phytochemical screening revealed the presence of alkaloids, flavonoids, phenols, saponins, and proteins, while glycosides, carbohydrates, diterpenes, tannins, and sterols were absent (Table 2). The detection of flavonoids and phenolic compounds, well-known for their antioxidant and free radical–scavenging activities, suggests that these constituents may play a major role in renal protection. The total phenolic and flavonoid contents of the ethanolic extract were found to be 0.578 mg/100 mg and 0.624 mg/100 mg, respectively (Table 3), confirming the rich presence of antioxidant compounds in *U. picta*.

GM administration (100 mg/kg) produced a marked increase in serum Cr, BUN, and urea levels, along with a significant reduction in serum albumin and TP levels, indicating nephrotoxicity due to renal tubular damage (Table 4). These findings are consistent with previous reports that GM induces oxidative stress–mediated renal injury through lipid peroxidation and inflammatory responses.

Co-administration of *U. picta* extract with GM produced a dose-dependent improvement in renal function parameters. The 200 mg/kg dose markedly reduced serum Cr, BUN, and urea levels while restoring TP and albumin concentrations toward normal values (Table 4). The graphical representation (Fig. 1) further demonstrates the significant nephroprotective effect of *U. picta* extract, particularly at the higher dose, against GM-induced biochemical alterations.

The protective action of *U. picta* may be attributed to its high phenolic and flavonoid content, which could neutralize reactive oxygen species, inhibit lipid peroxidation, and modulate inflammatory mediators. These findings corroborate earlier reports highlighting the antioxidant and cytoprotective roles of polyphenol-rich plant extracts in drug-induced nephrotoxicity.

Hence, the results clearly indicate that the ethanolic extract of *U. picta* possesses significant nephroprotective activity against GM-induced renal damage, likely due to its antioxidant, anti-inflammatory, and membrane-stabilizing properties.

CONCLUSION

The present study demonstrated that the hydroalcoholic extract of the aerial parts of U. picta exhibits significant nephroprotective activity against drug-induced nephrotoxicity in rats. The extract effectively restored biochemical parameters, such as serum Cr, urea, and uric

acid levels toward normal, suggesting improved renal function. The nephroprotective potential of U. picta may be attributed to its rich phytoconstituent content, including flavonoids, phenolics, and other antioxidants, which help mitigate oxidative stress and cellular damage in kidney tissues. Therefore, U. picta could serve as a promising natural therapeutic agent for preventing or managing nephrotoxicity induced by nephrotoxic drugs.

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AUTHOR' COTRIBUTIONS

All the authors have equally contributed to the manuscript.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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