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NEPHROPROTECTIVE POTENTIAL OF THE LEAVES OF *URENA LOBATA* LINN. IN CISPLATIN INDUCED NEPHROTOXICITY IN ALBINO RATS

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ABSTRACT

The nephroprotective effect of the methanolic extract of the leaves of *Urena lobata* was evaluated in cisplatin induced nephrotoxicity in albino rats. The methanolic extract at both the doses (200 and 400mg/kg) reduced the elevated blood urea, serum creatinine and normalised the decreased body weight, which indicates the nephroprotective claim of the leaves of *Urena lobata* in the curative regimen.

KEYWORDS: *Urena lobata*, cisplatin, nephroprotection.

INTRODUCTION

Nature always stands as a golden mark which exemplifies the outstanding phenomenon of symbiosis. The biotic and abiotic elements of nature are all interdependent. Plants are indispensible to man. Nature has provided a complete storehouse of remedies to cure all ailments of mankind. The knowledge of drugs has accumulated over thousands of years as a result of mans inquisitive nature. So that today we possess many effective means of ensuring health care.[1]

Nephrotoxicity is a poisonous effect of some substances, both toxic chemicals and medication on the kidneys.[2] It is the 9th leading cause of death in United States. There are various forms and some drug may affect renal function in more than one way.[3]

Fig. 1: *Urena lobata.*

Urena lobata Linn. (Malvaceae) is an annual or perennial erect under shrub, found in most of the states of India. It is commonly known as aramina fibre, caeser weed or congo jute. The ethnopharmacological usages of the parts of this plant are antique for the treatment of various diseases. The plant has been used as a traditional medicinal plant in India and China. Various extracts of leaf and roots are used by the traditional practitioners in herbal medicine to treat other ailments, including malaria, gonorrhoea, leucorrhoea, trauma, bleeding, cold, fever, pain, numbness caused by rheumatism, wounds, toothache and inflammation. The plant is also evident to use traditionally as an antibacterial and amoebicidal, in bronchitis, diarrhoea, dysentery, edema, gastritis, cough, nephritis, pneumonia, etc. Moreover, it has emollient and diuretic effects. The plant contains carbohydrates, proteins, fat, fiber, moisture and ash. Alkaloids, flavonoids, saponins and tannins are commonly found secondary metabolites in leaves and roots of this plant.[4] The plant is traditionally used in treating various diseases associated with kidney by the Kurumas, Paniyas, Kattunaikas, Adiyas and Kurichyas tribes of Wayanad region of Kerala state. This was the rationale in selecting the particular species of the medicinal plant for evaluating the nephroprotective activity.[5]

MATERIALS AND METHODS

Source of plant

The leaves of *Urena lobata* Linn were collected from the campus of Government Medical College, Kannur, Kerala. It was then dried and its botanical identity was

confirmed by Dr. Abdhul Jaleel, Professor, (Department of PG studies and Research in Botany, Sir Syed College, Taliparamba, Kannur, Kerala) and a voucher specimen has been deposited in the Department of Pharmacognosy, College of Pharmaceutical Sciences, Government Medical College, Kannur district, Kerala state, South India.

Preparation of methanolic extract

One kilogram dried leaves of *Urena lobata* was extracted with 95% methanol in a soxhlet apparatus for 6-8 hours. The methanolic extract was then concentrated to a syrupy consistency and dried in vacuum desiccator.

Nephroprotective studies Animals

Healthy adult male albino rats of Wistar strain weighing between 150 – 250 g aged 60 - 90 days were used for the study. The rats were housed, two in a cage and maintained in a temperature regulated and humidity controlled environment. The rats were fed with standard food pellets and water.

The study was conducted after obtaining ethical committee clearance from the Institutional Animal Ethics Committee of College of Pharmaceutical Sciences, Pariyaram No (1097/PO/Re/S/07/CPCSEA)

Drugs and chemicals: Cisplatin Injection (Biochem Pharmaceutical industries, Mumbai), Urea estimation kit (Agappe diagnostics, Maharashtra), Creatinine estimation kit (Agappe diagnostics, Maharashtra)

Acute toxicity studies

8-12 week old male albino rats were selected. Temperature: 22±3^{o}c, Relative humidity: 30%- 70% and 12 hour light and dark cycle was maintained. Volume of test substance taken was 1ml/100g body weight. Food was be withheld overnight prior to dosing. The test substance (1ml/100g) was administered in a single dose by gavage using stomach tube or suitable intubation cannula. After the substance had been administered food was withheld for further 3-4 hours.[96]. Animals were observed individually after dosing at least once during the first 30 minutes, periodically during first 24 hours, with special attention given during the first 4 hours, and daily for a period of 14 days. All observations were systemically recorded. Additional observations would be necessary if the animals continue to display signs of toxicity. Observation should include changes in skin and fur, eyes and mucous membrane, and also respiratory, circulatory, autonomic and central nervous system, and behavior pattern.[6]

***In vivo* pharmacological screening of Nephroprotective activity**

Treatment Schedule for cisplatin induced renal damage in curative regimen

Six groups of six rats in each group were used in this model. The first group was administered with equivalent volumes of 2% gum acacia for 15 days. The second group was treated with the higher dose of leaf extract of *Urena lobata* L for 15days. On the 16th day the blood was withdrawn from the retro orbital vein for renal function tests. The remaining groups were treated with cisplatin 5mg/kg body weight, single dose, intra peritonially.[7] The blood was withdrawn from the animals through retro orbital vein on the 6th day in 3rdgroup and on the 16th day in 4th group to assess the renal functions.

Curative group: The 5th group of animals was treated with cisplatin 5mg/kg body weight, single dose intra peritonially and with lower dose of alcoholic extract of the leaves of *Urena lobata* L from 6th day to 15th day orally and the blood was withdrawn on 16th day to assess the renal functions. The 6th group of animals were treated with cisplatin 5mg/kg body weight, single dose intra peritonially and with higher dose of alcoholic extract of the leaves of *Urena lobata* L from 6th day to 15th day orally and the blood was withdrawn on 16th day to assess the renal functions.

Parameters assessed for renal function

1. Body weight: The weight (in grams) of the animals were noted on the first and last day of treatment and the percentage change in body weight was calculated.
2. Blood urea: The estimation had been conducted by Modified Berthelot method .Urea concentration in the blood was estimated by enzymatic method using Urease enzyme kit.[8]
3. Serum creatinine: Creatinine level in serum was estimated by alkaline picrate method using creatinine kit.[8]

Table 1: Curative effect of the alcoholic extract of the leaves of *Urena lobata* in various parameters in cisplatin induced renal damage.

Group N=6/group	Treatment Regimen	Mean±SE		
		%change in body weight	Blood urea mg/dl	Serum Creatinine Mg/dl
1	Control	19.36±1.19	35.70±3.51	0.85±0.09
2	Alc.Ext.400mg/kg	26.11±4.39	29.12±2.70	0.79±0.02
3	Cisplatin 6th day	-18.91±3.45 ^{a}	76.39±3.47 ^{a}	3.93±0.07 ^{a}
4	Cisplatin 16th day	-33.35±2.79 ^{a}	88.11±1.35 ^{a}	5.20±0.06 ^{a}
5	Cisplatin + Alc.Ext.200mg/kg	-8.92±4.65^{b}	51.23±2.25^{b}	3.30±0.01
6	Cisplatin + Alc.Ext.400mg/kg	-5.10±1.14^{b}	40.14±7.65^{b}	1.10±0.05^{b}

a $p< 0.05$ vs control (group 1), b $p< 0.05$ vs Cisplatin 16^{h} day (group 4) One way ANOVA followed by Sheffe's test

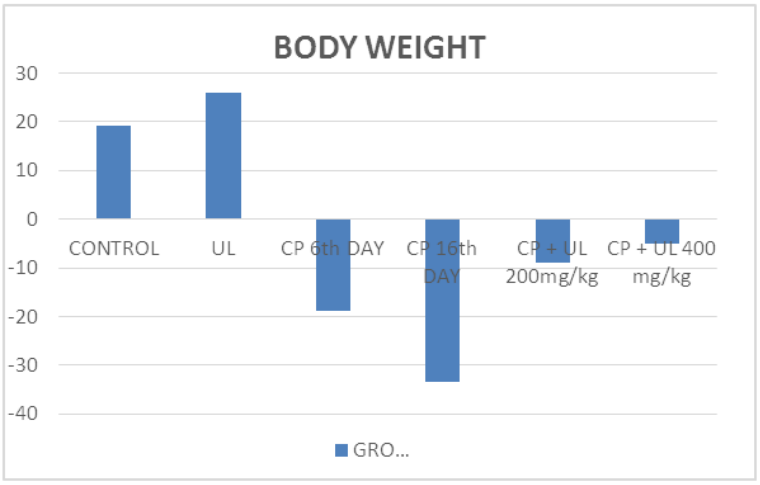

Fig. 2: Curative effect of *Urena lobata* on percentage change in body weight in Cisplatin nephrotoxic model (n=6/group, CP=Cispaltin, UL=*Urena lobata*).

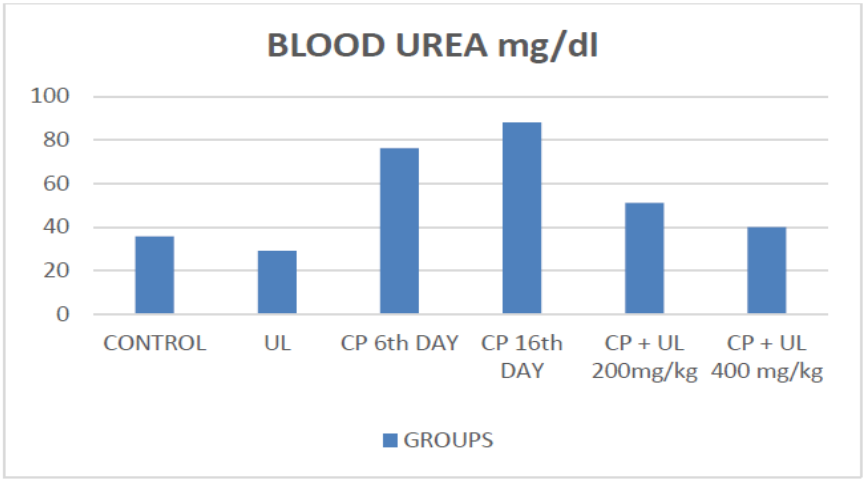

Fig. 3: Curative effect of *Urena lobata* on blood urea levels in cisplatin nephrotoxic model (n=6/group, CP=Cispaltin, UL=*Urena lobata*).

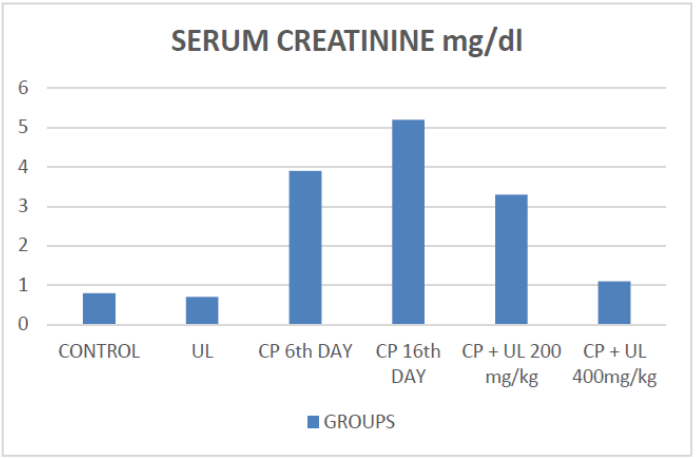

Fig. 4: Curative effect of *Urena lobata* on serum creatinine levels in cisplatin nephrotoxic model (n=6/group, CP=Cispaltin, UL=*Urena lobata*).

DISCUSSION AND CONCLUSION

The present study was undertaken to carry out the Nephroprotective studies of the indigenous medicinal plant, *Urena lobata* Linn. The plant has been well documented in literatures for various disorders associated with kidney. The leaf extract on preliminary phytochemical investigation revealed the presence of phytosterols, phenolic compounds, tannins, flavonoids, glycosides, proteins, amino acids and carbohydrates.

In our study, cisplatin induced renal injury was evidenced by a decrease in the renal function of experimental animals. Single dose administration of cisplatin (5 mg/kg body weight) produced significant nephrotoxicity as characterized by an increase in blood urea and serum creatinine levels accompanied by a significant loss in body weight of the experimental animals.

In the curative study of cisplatin induced nephrotoxicity, the alcoholic extract of the leaves of *Urena lobata* at dose levels of 200 and 400 mg/kg were found to normalize the raised blood urea and serum creatinine levels. The animals showed signs of recovery and an increase in body weight was observed on the final day of observation. The leaf extract exhibited nephroprotective activity in a dose-dependent manner.

Various studies have been reported that cisplatin induces renal damage by free radical generation.[9] and altering the arginine metabolism including nitric oxide production.[10] Hence the natural and synthetic antioxidants and free radical scavengers are claimed to provide nephroprotection in cispaltin induced renal injury. Among the natural free radical scavengers, Vitamin C, Vitamin E, Selenium, Synthetic glycine and Probucol have been shown to possess partial protection against cisplatin induced oxidative damages.

The alcoholic extract of the leaves were found to be rich in phenolic and tannin content. Polyphenolics and tannins are proven good natural antioxidants.[11] They decrease the thiobarbituric acid reactive species, thus preventing tissues from lipid peroxidation and causing an increase in the antioxidant enzymes levels.

It is also reported that the leaves of *Urena lobata* are possess potent antioxidant effect in *in vitro* evaluation [12]. Our studies also revealed that the leaves of *Urena lobata* are endowed with flavonoids and phenolic compounds. According to Raj Narayanan et.al., 2001, flavonoids are well documented to have potent antioxidant and free radical scavenging effect.[13] Hence the probable mechanism of nephroprotection by *Urena lobata* could be due to its antioxidant property.

Our studies shown that the leaves of *Urena lobata* possess nephroprotective activity with minimal toxicity and thus have a promising role in the treatment of acute renal failure induced by nephrotoxin like cisplatin. Further studies on the isolation of its active components and its effect in chronic renal failure has to be evaluated.

CONFLICT OF INTEREST: NIL

REFERENCES

1. Dr. C. K Kokate, A P Purohit, S B Gokhale, Pharmacognosy; Nirali prakashan publishers, 1: 1.
2. Paoulomi Chatterjee et.al, review on nephroprotective activity study by different plant extract, Advanced Journal of Pharmacie and Life science Research, 2014; 2(2): 24-40.
3. https://en.m.wikipedia.org/wiki/Nephrotoxicity.
4. Muhammad Torequel Islam et. al, Arevision on urena lobata L; International journal of medicine, 2017; 5(1): 126-131.
5. Silja V P et al. Ethnomedicinal plant knowledge of the Mullu kuruma tribe of Wayanad district, kerala, 2008; 7(4): 604-612.
6. OECD Guidelines for testing of chemicals. Acute oral toxicity. Acute toxic class method (OECD Guidelines 423).
7. Greggi Antunes L.M, Darin J.D, Bianchi M.D., "Protective effects of Vit.C against cisplatin induced nephrotoxicity and lipid peroxidation in adult rats: a dose dependent study", Pharmacol. Res., 2000; 41(4): 405-411.
8. Varley H, Alan H.G. Text book of clinical biochemistry. Heinemann medical book Ltd, London, 1989; 5: 451-596.
9. Sdzuka Y, Shoji T, Takino Y. Effect of cisplatin on the activation of enzymes, which protects against lipid peroxidation. Biochemistry and Pharmacology, 1991; 43: 1872- 1875.
10. Srivastava R.C, Farookh A, Ahmad N, et.al. Evidence for the involvement of nitric oxide in Cisplatin induced toxicity in rats. Biometals, 1996; 139-142.
11. Rao M, Kumar M.M, Rao M.N.A. In vitro and in vivo effects of phenolic antioxidants against cisplatin-induced nephrotoxicity. J Biochem (Tokyo), 1999; 125: 383-390.
12. P. L. Rajagopal, K. R. Sreejith, K. T. Linsha, K. Premaletha, Meera B. Nair, S. Aneeshia. Antioxidant Activity of the Leaves of *Urena lobata* Linn. International Journal of Research and Review, 2019; 6(5): 82-84.
13. Rajnarayanan K et.al Bioflavonoids, classification, Pharmacological, Biochemical, effects and therapeutic potential, Indian Journal of Pharmacology, 2001; 33: 2-16.