



## Ameliorative Effect of *Lagenaria siceraria* on Cisplatin-Induced Kidney Injury in Wistar Rats

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### Abstract

The objective of the present study was conducted to investigate the nephroprotective activity of hydroalcoholic extract of *Lagenaria siceraria* against cisplatin-induced nephrotoxicity in Albino Wistar rats. Cisplatin (6mg/kg.b.w.t, i.p.) used as nephrotoxicant. The oral administration of hydroalcoholic extract at two different doses (200mg/kg.b.w.t and 400mg/kg.b.w.t) of *Lagenaria siceraria* were used to examine the Nephroprotection using Urinary and serum biomarkers, as well as renal oxidative stress biomarkers, histological and immunohistological studies. Enhanced levels of Urinary, serum biomarkers, total protein and lipid peroxidation and decreased urinary creatinine and anti-oxidant enzymes observed after cisplatin induction. Treatment with Hydroalcoholic extract alters the Cisplatin induced nephrotoxic effects. Histopathological studies and immunohistochemical observations provided evidence consistent with the biochemical findings. Thus, the current study reveals the advantageous use of *Lagenaria siceraria* in renal toxicity.

**Keywords:** *Lagenaria siceraria*, Nephroprotective activity, Cisplatin, Hydro-alcoholic extract.

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### INTRODUCTION

In recent years, the global incidence of kidney diseases has been a notable rise, due to drug-induced nephrotoxicity emerging as a significant contributor to acute kidney injury (AKI) [1]. Among the commonly implicated pharmacological agents are aminoglycosides (e.g., gentamicin), anthracyclines (e.g., doxorubicin), non-steroidal anti-inflammatory agents (NSAIDs), and platinum-based chemotherapeutic agents such as cisplatin [2]. Cisplatin [cis-diamminedichloroplatinum(II)] is widely employed in the management of various solid tumors, namely bladder, cervix, ovaries, and testes. In spite of its clinical efficacy, the therapeutic use of cisplatin is severely limited by its dose-dependent toxicities [3]. Rising evidence specifies that Oxidative stress is a major contributor to kidney damage caused by cisplatin, revealed through Enhanced generation of reactive oxygen species (ROS) and, improved lipid peroxidation, and impaired mitochondrial function [4].

This has prompted growing interest in the development of adjunct therapies aimed at modifying oxidative damage and protective renal function during cisplatin chemotherapy [5]. Although researchers have investigated multiple approaches in conventional medicine, nephrotoxicity management is still based on empirical practices [6]. As a result of the limitations of Modern pharmacotherapy agents, Research is ongoing into the therapeutic practices of traditional medicine [7]. Various herbal agents have both been claimed and experimentally proven to offer nephroprotection [8]. *Lagenaria siceraria* (bottle guard) is a nutritious vegetable that has been used for food and medicine since ancient times [9]. It contains dietary fiber, protein, carbohydrates, and essential fatty acids. It is also a Abundant source of essential minerals such as potassium and calcium as well as vitamin C [10]. The seeds, peel, and leaves of bottle gourd are plentiful in bioactive compounds, including phenolic acid, saponins, flavonoids, lignans, glycosides, cucurbitacins, and triterpenoids [11]. These natural compounds are linked to several health benefits, particularly anti-oxidant, anti-inflammatory, anti-diabetic, and antimicrobial effects [12]. Till today the *Lagenaria siceraria* was not scientifically explored for its nephroprotective activity Hence the current study is designed to evaluate the nephroprotective capacity of

hydroalcoholic extract of *Lagenaria siceraria* against cisplatin-induced nephrotoxicity in rats.

## MATERIALS AND METHODS

### Chemicals

Cisplatin was procured from American oncology Hospitals, NRI medical College, Mangalagiri, Guntur, India. Blood Urea Nitrogen (BUN) and serum creatinine assay kits (SC) were obtained from Diagnostics, Bangalore, India. All the reagents and chemicals used were of analytical grade and supplied by Empire Scientific Company, Andhra Pradesh, India.

### Collection of *Lagenaria siceraria*

*Lagenaria siceraria* were purchased from local market Bapatla, Andhra Pradesh. The plant material was authenticated by a qualified botanist Dr. Raju, Herbarium keeper, Department of botany, Acharya Nagarjuna University, Guntur, India.

### Preparation of hydroalcoholic extract of *Lagenaria siceraria*

*Lagenaria siceraria* were thoroughly washed with distilled water, cut into small pieces and shade dried. The dried material was powdered using mixer. The obtained powder was air dried and defatted with pet ether (60-80°C). The defatted marc air dried and subjected to soxhlet extraction with hydro alcoholic solvent (ethanol, water 1:1 v/v) for 72 hrs. The resulting hydroalcoholic extract was filtered, concentrated under reduced pressure and stored in desiccators until further use. This extract characterised using Preliminary phytochemical screening standard procedures to identify the presence of various phytoconstituents and LC-MS study.

### Animals

Wistar albino rats of either sex, weighing between 150–200 g, were procured from Mahaveer Enterprises, Hyderabad, India. The animals were housed in the institutional animal facility under standard laboratory conditions with a 12-hour light/dark cycle, temperature of  $25 \pm 2$  °C and relative humidity of 50–60%, with free access to a standard rat diet and water ad libitum. All experimental procedures were carried out with the prior approval of the committee of Institutional Animal Ethics Committee (IAEC), in accordance with CPCSEA guidelines (IAEC/XVI/04/BCOP/2023).

### Experimental Plan

#### Evaluation of nephroprotective activity

The Five group of animals were formed using random allocation, (n = 6). Nephrotoxicity was experimentally induced by administering single intraperitoneal dose of Cisplatin (6 mg/kg body weight) on the fifth day of the study protocol. The detailed treatment schedule for each group does exist in table 01. The treatment schedule for assessing the hydro alcoholic extract of *Lagenaria siceraria* was followed:

**Table 01: Treatment schedule**

S. No	Group	Treatment	Dose
1	Group-I	Normal Saline	0.9%v/w
2	Group-II	Cisplatin	6 mg/kg b.w.
3	Group-III	Extract –Low dose	200 mg/kg b.w
4	Group-IV	Extract –High dose	400 mg/kg b.w
5	Group-V	Only Extract	400 mg/kg b.w

On day 9, urine samples were collected using metabolic cages and analyzed for urinary functional parameters. Blood samples were obtained via cardiac puncture, and serum was separated by centrifugation at 3000 rpm for 10 minutes at 4 °C. The serum was subsequently used for the estimation of biochemical markers.

Biochemical parameters were measured using standard commercial kits. Blood urea nitrogen (BUN) was measured by the DAM method, serum creatinine (SC) by Jaffe's alkaline picrate method, urinary total protein (UTP) by the turbidity method, and urinary creatinine (UCr) by the alkaline picrate method. The animals were sacrificed by cervical decapitation. The kidneys were excised and two kidneys were isolated, one for processed for antioxidant assay and another kidney was preserved for histopathological and Immunohistological examination [13].

### Anti-oxidant studies

The excised Kidneys were homogenized in ice-cold 0.05 M phosphate buffer (pH 7.8) to obtain a 20% (w/v) tissue homogenate. The homogenate was centrifuged at 10,000 rpm for 15 minutes at 4 °C, and the clear supernatant was immediately used for the estimation of antioxidant enzymes. The antioxidant parameters assessed included reduced glutathione (GSH), catalase (CAT), superoxide dismutase (SOD), and lipid peroxidation (LPO) [14, 15].

### Histological studies

Kidneys from each experimental group were used for histological studies. The isolated kidneys were fixed in 10% neutral buffered formalin and processed for paraffin embedding. Tissue sections of 5 µm thickness were prepared stained with hematoxylin and eosin (H&E), and examined under a light microscope at 10× magnification [16]

### Immuno-histochemical studies

Formalin-fixed, paraffin-embedded kidney sections were mounted on poly-L-lysine-coated slides, deparaffinized in xylene, and rehydrated through graded alcohols. Antigen retrieval was performed in citrate buffer (10 mM, pH 6.0) at 95 °C for 20 min, followed by blocking of endogenous peroxidase with 3% H<sub>2</sub>O<sub>2</sub>. Sections were incubated overnight at 4 °C with antibody, washed with Tris buffer, and incubated with a biotinylated secondary antibody and Streptavidin Peroxidase (Thermo Fisher Scientific,

USA). The reaction was developed with 3,3'-Diaminobenzidine (DAB) substrate, counterstained with Harris hematoxylin, dehydrated, and mounted with Distrene, Plasticizer, and Xylene (DPX). Slides were examined under a light microscope at 40× magnification [17].

### Statistical analysis

All data were presented as mean ± standard error of the mean (SEM). Statistical comparisons among groups were performed using one-way analysis of variance (ANOVA), p-value of <0.05 was considered statistically significant.

## RESULTS

### Preliminary Phytochemical studies

The hydroalcoholic extract of *Lagenaria siceraria* yielded 8.4% (w/w). Preliminary phytochemical screening identified the presence of carbohydrates, proteins, sterols, terpenoids, flavonoids, fiber, and saponins.

### Assessment of nephroprotective activity

Table 02: Effect of hydroalcoholic extract of *Lagenaria siceraria* on serum and urinary markers on Cisplatin produced nephrotoxicity.

Group	BUN (mg/dl)	SC (mg/dl)	UTP (mg/24hrs)	UCr (mg/24hr)
Group-I-Normal Saline	14.41±0.91	0.69±0.04	2.15±0.11	19.97±0.49
Group-II Cisplatin	38.43±0.32 <sup>a</sup>	3.18±0.07 <sup>a</sup>	6.70±0.29 <sup>a</sup>	5.91±0.32 <sup>a</sup>
Group-III Extract –Low dose	26.67±1.52 <sup>b</sup>	0.80±0.12 <sup>b</sup>	4.64±0.26 <sup>*b</sup>	10.84±0.52 <sup>b</sup>
Group-IV Extract –High dose	20.01±1.39 <sup>b</sup>	0.52±0.04 <sup>b</sup>	2.32±0.14 <sup>b</sup>	15.33±0.51 <sup>b</sup>
Group-V Only Extract	13.41±0.71	0.61±0.04	1.05±0.51	18.57±0.89

Each value represents the mean ± SEM (n = 6). p < 0.05; a: Group II compared with Group I; b: Groups III and IV compared with Group II.

Table 03: Effect of hydroalcoholic extract of *Lagenaria siceraria* on Liver parameters on Cisplatin- produced nephrotoxicity

Group	SGOT(U/L)	SGPT(U/L)	ALP(U/L)
Group-I-Normal Saline	33.83 ± 1.49	30.17 ± 1.70	42.33 ± 2.40
Group-II Cisplatin	119.01 ± 5.94 <sup>a</sup>	114.2 ± 3.83 <sup>a</sup>	220.8 ± 4.27 <sup>a</sup>
Group-III Extract –Low dose	98.01 ± 7.07 <sup>b</sup>	96.80 ± 7.41 <sup>b</sup>	165.5 ± 1.45 <sup>b</sup>
Group-IV Extract –High dose	69.00 ± 3.37 <sup>b</sup>	64.47 ± 3.13 <sup>b</sup>	120.67 ± 2.33 <sup>b</sup>
Group-V Only Extract	31.83 ± 1.49	29.17 ± 1.70	50.33 ± 2.40

Each value represents the mean ± SEM (n = 6). p < 0.05; a: Group II compared with Group I; b: Groups III and IV compared with Group II

Table 04: Effect of hydroalcoholic extract of *Lagenaria siceraria* on antioxidant parameters on Cisplatin- produced nephrotoxicity.

Group	LPO (nmol/g of wet tissue)	GSH (µmol/g of wet tissue)	SOD (units/mg of tissue)	CAT (units/mg of tissue)
Group-I-Normal Saline	2.14±0.09	2.83±1.12	34.22±0.55	42.37±0.75
Group-II Cisplatin	7.32±0.25 <sup>a</sup>	0.83±0.42 <sup>a</sup>	11.87±0.46 <sup>a</sup>	15.68±0.92 <sup>a</sup>
Group-III Extract –Low dose	4.83±0.43 <sup>b</sup>	1.48±0.30 <sup>b</sup>	19.18±0.66 <sup>b</sup>	26.05±0.43 <sup>b</sup>
Group-IV Extract –High dose	2.82±0.14 <sup>b</sup>	2.02±0.57 <sup>b</sup>	26.71±2.14 <sup>b</sup>	36.01±1.19 <sup>b</sup>
Group-V Only Extract	1.68±0.07	2.33±1.16	30.12±0.55	40.17±0.75

Each value represents the mean ± SEM (n = 6). p < 0.05; a: Group II compared with Group I; b: Groups III and IV compared with Group II

**Histological Studies**

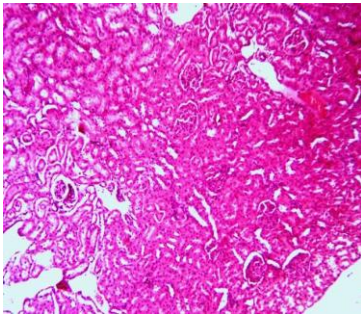


Fig. 1a: Group-I Normal (1\*10X)

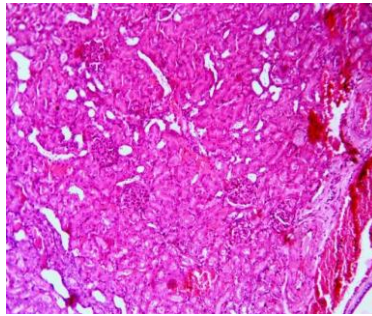


Fig. 1b: Group-II Cisplatin(1\*10X)

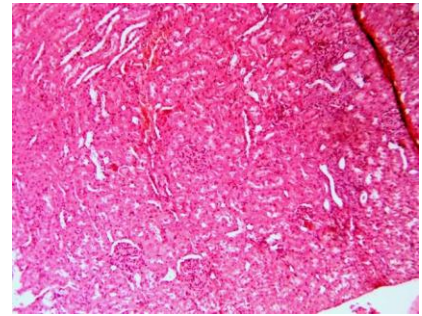


Fig.no.1c Group-III Extract (Low dose) (1\*10X)

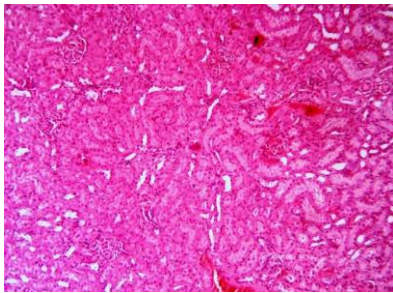


Fig.no.1d Group-IV Extract (High dose) (1\*10X)

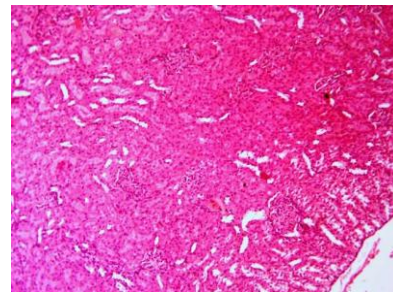


Fig.no.1e Group-V only Extract (1\*10X)

Fig 01: Assessment of Histopathological evaluation of the nephroprotective effect of *Lagenaria siceraria* against Cisplatin produced nephrotoxicity in Rats.

**Immuno-histochemical Studies**

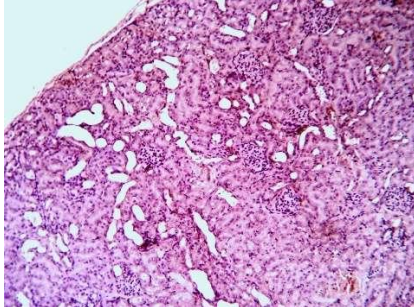


Fig 2.a: Group-I: Normal

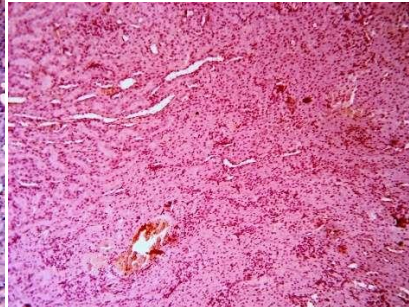


Fig 2.b: Group-II : Cisplatin



Fig 2.c Group-III: Extract Low dose

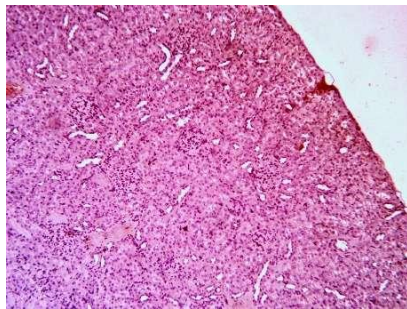


Fig 2.d Group-IV : Extract high dose

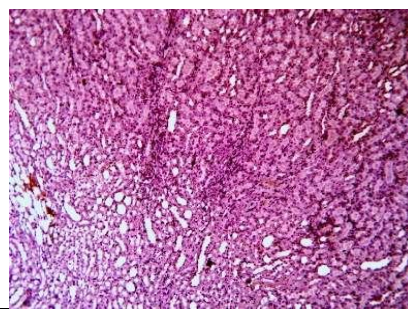


Fig 2.e Group-V: Only Extract

Fig 02: Assessment of Immuno Histochemical evaluation of the nephroprotective effect of *Lagenaria siceraria* against Cisplatin produced nephrotoxicity in Rats

Localization of KIM expression of the kidney tissue seen in the all groups Immunohistochemical studies: (a) Normal Kidney architecture showing No detectable KIM-I expression (Group I). (b) prominent KIM-I expression (Group II).

(c) moderate expression of KIM-1 (Group III). (d) mild expression of KIM-1 (Group IV). (e) profound expression of KIM-1 (Group V).

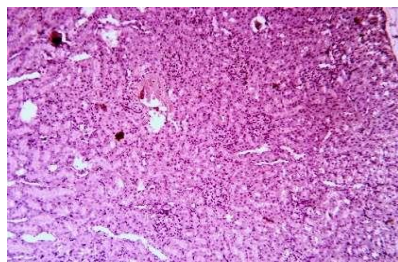


Fig 3a Group-I: Normal

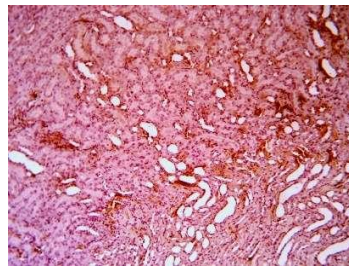


Fig 3 b Group-II : Cisplatin

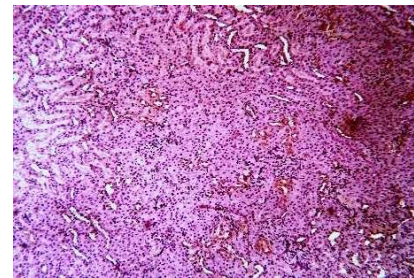


Fig 3 c Group-III: Extract Low dose

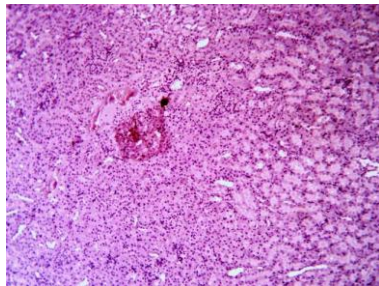


Fig 3 d Group-IV: Extract high dose

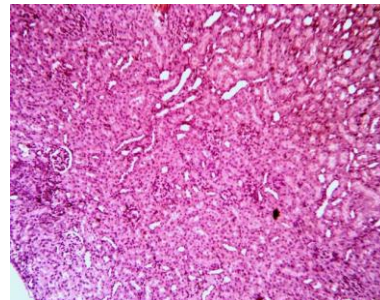


Fig 3 e Group-V: Only Extract

Fig. 03” Immuno histochemical Localization of TNF- $\alpha$  in Kidney Tissue

3a) No detectable TNF- $\alpha$  expression.; 3b) (Cisplatin control): Pronounced TNF- $\alpha$  expression; 3c) (Standard treatment): Moderate TNF- $\alpha$  expression; 3d) (Low-dose *Lagenaria siceraria*): Mild TNF- $\alpha$  expression; 3e) (High-dose *Lagenaria siceraria*): Minimal TNF- $\alpha$  expression.

## DISCUSSION

Drug-induced nephrotoxicity is often linked to drug accumulation in the renal cortex, depending on kidney affinity and drug-trapping kinetics [18]. Cisplatin, a generally used anticancer drug, has been demonstrated to exert nephrotoxic effects, with even a minimum dose of 6 mg/kg reported to induce renal damage in rats [19]. Oxidative stress, inflammation, and apoptosis are key mechanisms underlying cisplatin-induced nephrotoxicity. Although cisplatin has significant therapeutic potential, its clinical application is limited due to adverse nephrotoxicity [20]. Hence, there is a pressing need to develop effective and safer drugs for the treatment of nephrotoxicity. Several studies have demonstrated that numerous medicinal plants possess significant nephroprotective activity against renal toxicity produced by various nephrotoxics [21]. *Lagenaria siceraria* is an example of such a plant used as indigenous medicine, where its seeds are employed in the treatment of various kidney ailments [22]. Based on this, the current study was planned to estimate the nephroprotective effect of the hydro alcoholic extract of *Lagenaria siceraria*. Hydroalcoholic extracts were selected for this study because they reported to be rich in antioxidant compounds including flavonoid glycosides and phenolics, and they are widely preferred in Ayurvedic preparations.

"Nephrotoxicity is a quick process resulting from the response of cisplatin with proteins in the kidney

tubules, resulting kidney damage within one hour of following administration [23]. Therefore, the existence of a protective agent in kidney tissues may mitigate the toxic effects produced by cisplatin, which forms the scientific basis for the prophylactic regimen. In the current study, cisplatin administered at a dose of 6 mg/kg b.w. produced nephrotoxicity in albino wister rats, evidenced by elevated plasma creatinine and BUN levels, increased urinary total protein, and reduced creatinine clearance. These findings are in accordance with previously published data [24]. Similar to the protective effects reported with *Hygrophila spinosa*, *Bassia malabarica*, and *Berberis aristata*, management with *Lagenaria siceraria* restored the nephrotoxic alterations. Cisplatin-induced nephrotoxicity occurs in a dose related fashion under both curative and prophylactic regimens. Reactive oxygen species (ROS), normally produced through cellular processes, are efficiently scavenged by cellular antioxidants, such as GSH, catalase, and SOD. However, elevated ROS accumulation caused by cisplatin, disrupt the antioxidant defense system, resulting in imbalance between reactive oxygen species and endogenous antioxidants [25]. According to Kim et al., increased ROS attacks membrane lipids, increased tissue lipid peroxides, as indicated by improved MDA levels. This augmented levels of lipid peroxides further depletes GSH and inhibits antioxidant enzymes. Consistent with earlier reports, the current study also confirmed that

cisplatin administration decreased the activities of SOD and CAT, depleted GSH levels, and enhanced MDA production in renal tissues, thereby elevating lipid peroxidation. The hydroalcoholic extract of *Lagenaria siceraria* showed a pronounced protective action against the cisplatin produced impairment of antioxidant status. The nephroprotective activity of hydroalcoholic extract of *Lagenaria siceraria* was further supported by histological and immunohistochemical findings.

The hydroalcoholic extract of *Lagenaria siceraria* (HALC) mitigates cisplatin-induced renal injury through restoration of antioxidant defenses, suppression of inflammatory markers (KIM-1, TNF- $\alpha$ ), and preservation of histological integrity aligns closely with mechanisms attributed to polyphenols in other nephroprotective models. Flavonoid, prevented cisplatin-produced acute kidney damage in mice through activating the Nrf2/HO-1 signaling axis, suppressing oxidative stress and inflammation, attenuating apoptosis by down regulation of Bax and caspase-3 while upregulating Bcl-2 expression.

EGCG (epigallocatechin-3-gallate), the predominant catechin in green tea, enhanced renal mitochondrial function by preserving electron transport chain activities, boosting mitochondrial antioxidant enzymes, and attenuating NF- $\kappa$ B-mediated inflammation and apoptotic cell death in cisplatin-treated models [26]. Another polyphenol, epicatechin, has been shown to protect against mitochondrial dysfunction-specifically by preventing mitochondrial protein loss, cytochrome-c release, and membrane potential collapse in tubular cells-thereby preserving mitochondrial integrity and renal function post-cisplatin. Furthermore, epicatechin gallate (ECG) also demonstrated anti-inflammatory and anti-apoptotic actions by scavenging ROS, inhibiting NF- $\kappa$ B and MAPK signaling, and modulating Bax/Bcl-2 balance [27]. Together, these mechanistic equivalents suggest that hydroalcoholic extract of *Lagenaria siceraria* likely exerts its nephroprotective effects via a multifaceted pathway-activating antioxidant transcriptional programs (Nrf2/HO-1), suppressing NF- $\kappa$ B-driven inflammatory cascades, and preserving mitochondrial function to prevent apoptosis.

Treatment with the hydroalcoholic extract of *Lagenaria siceraria* for 10 days alone did not cause any adverse effects on the kidney, supporting the safety profile of the extract.

## CONCLUSION

*Lagenaria siceraria* showed a good kidney protective activity supported by urinary, serum biomarkers and histopathology, immunohistopathological studies. Anyway, further experimentation also needed for mechanism-based studies.

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## AUTHOR CONTRIBUTIONS

Conceptualization & Design: Prof. KVSRR Prasad, Research Supervision of Project: Dr Sujatha, Experimentation work and writing: G.Swarupa Rani

## CONFLICT OF INTEREST

The authors declare no conflict of interest.

## FUNDING STATEMENT

This research received no external funding

## ETHICAL STATEMENT

The study was approved by a recognized ethics committee. (IAEC/XVI/04/BCOP/2023)

## INFORMED CONSENT

Not Applicable

## REFERENCES

1. Amina Džidić-Krivić, Emina K. Sher, Jasna Kusturica, Esmā K. Farhat, Asma Nawaz, Farooq Sher, unveiling drug induced nephrotoxicity using novel biomarkers and cutting-edge preventive strategies, *Chemico-Biological Interactions*, Volume 388, 2024, 110838.
2. Thiruchenthooran, V., Sánchez-López, E., & Gliszczynska, A. (2023). Perspectives of the Application of Non-Steroidal Anti-Inflammatory Drugs in Cancer Therapy: Attempts to Overcome Their Unfavorable Side Effects. *Cancers*, 15(2), 475.
3. Ranmali Ranasinghe, Michael L. Mathai, Anthony Zulli, Cisplatin for cancer therapy and overcoming chemoresistance, *Heliyon*, Volume 8, Issue 9, 2022, e10608.
4. Piko N, Bevc S, Hojs R, Ekart R. The Role of Oxidative Stress in Kidney Injury. *Antioxidants (Basel)*. 2023 Sep 16;12(9):1772.
5. Zhang J, Ye ZW, Tew KD, Townsend DM. Cisplatin chemotherapy and renal function. *Adv Cancer Res*. 2021; 152:305-327.
6. Tamargo, C., Hanouneh, M., & Cervantes, C. E. (2024). Treatment of Acute Kidney Injury: A Review of Current Approaches and Emerging Innovations. *Journal of Clinical Medicine*, 13(9), 2455.
7. Balkrishna A, Sharma N, Srivastava D, Kukreti A, Srivastava S, Arya V. Exploring the Safety, Efficacy, and Bioactivity of Herbal Medicines: Bridging Traditional Wisdom and Modern Science in Healthcare. *Future Integr Med*. 2024;3(1):35-49.
8. akshmi, S. & Thimmapuram, Usha & Rani, K.S (2012). A review on medicinal plants for nephroprotective activity. *Asian Journal of Pharmaceutical and Clinical Research*. 5. 8-14.
9. Mitali Bhutani, Supriya Singh Gaur, Rafeeya Shams, Kshirod Kumar Dash, Sustainable utilization of bottle gourd by-products: A nutritional and functional perspective, *Food Chemistry Advances*, Volume 8, 2025, 101073.

10. Begum Nabila, Khan Quadrat Ullah, Liu Leyna G., Li Wenwen, Liu Dahai, Haq Ijaz UI Nutritional composition, health benefits and bio-active compounds of chickpea *Frontiers in Nutrition* Volume 10 - 2023
11. R.V, Desai & A.K, Seth & B.N, Shah. (2010). Phytopharmacological Profile of *Lagenaria siceraria*: A Review. *Asian Journal of Plant Sciences*. 9. 10.3923/ajps.2010.152.157.
12. Hasin Hasnat, Suriya Akter Shompa, Md. Mirazul Islam, Safaet Alam, Fahmida Tasnim Richi, Nazim Uddin Emon, Sania Ashrafi, Nazim Uddin Ahmed, Md. Nafees Rahman Chowdhury, Nour Fatema, Md. Sakhawat Hossain, Avoy Ghosh, Firoj Ahmed, Flavonoids: A treasure house of prospective pharmacological potentials, *Heliyon*, Volume 10, Issue 6,2024, e27533.
13. Sinan Saral, Eda Dokumacioglu, Tolga Mercantepe, Mehtap Atak, Seda Cinar, Ozlem Saral, Lamiye Yildiz, Hatice Iskender, Levent Tumkaya, The effect of white tea on serum TNF- $\alpha$ /NF- $\kappa$ B and immunohistochemical parameters in cisplatin-related renal dysfunction in female rats, *Biomedicine & Pharmacotherapy*, Volume 112, 2019, 108604.
14. Sreedevi, Adikay; Saisruthi, Kaveripakam. Attenuation of Cisplatin-induced Nephrotoxicity by Ethanol Extract of Seeds of *Lens Culinaris* Medik. *Ancient Science of Life* 37(2):p 74-80, Oct-Dec 2017.
15. Spandana Uppuluri and Shaik Liakhat Ali and Thota Nirmala and Markapudi Shanthi and Babu Sipay and Kiran Babu Uppuluri Nephroprotective activity of hydro alcoholic extract of *Tinospora cordifolia* roots on cisplatin induced nephrotoxicity in rats *Drug Invention Today* volume (5) (4) 281-287, 2013.
16. YADAV, A. V., and C. D. UPASANI. "NEPHROPROTECTIVE ACTIVITY OF *PLUMERIA RUBRA* AGAINST CISPLATIN INDUCED NEPHROTOXICITY IN EXPERIMENTAL RATS". *International Journal of Pharmacy and Pharmaceutical Sciences*, vol. 11, no. 4, Apr. 2019, pp. 108-13.
17. Yıldırım, Ayşegül and DEĞER, Necla and SAYAN, Meryem and Akin, Ali and Ceylan, Tayfun and Kaymak, Emin and KARA, Mehmet and ÜNSAL, Murat and Karabulut, Derya , Investigation of the effect of thymoquinone on kidney damage in isoproterenol-induced myocardial infarction in rats and cardiorenal interactions *Experimental and Applied Medical Science* 4, 515-525, 2023.
18. Ghane Shahrabaf F, Assadi F. Drug-induced renal disorders. *J Renal Inj Prev*. 2015 Sep 1;4(3):57-60. doi: 10.12861/jrip.2015.12. PMID: 26468475; PMCID: PMC4594214.
19. Shraddha I. Khairnar and Yogesh A. Kulkarni and Kavita Singh Mitigation of cisplatin-induced nephrotoxicity by chelidonic acid in Wistar rats *Journal of Trace Elements in Medicine and Biology* (81),127321, 2024.
20. 20. Saraswati Patel and V. Sathyanathan and Samsi D. Salaman Molecular mechanisms underlying cisplatin-induced nephrotoxicity and the potential ameliorative effects of essential oils: A comprehensive review, *Tissue and Cell*, 88, 102377. 2024.
21. Al-Snafi, Ali and Talab, Tayseer A review of medicinal plants with nephroprotective effects *GSC Biological and Pharmaceutical Sciences* (8) 114-122:2019.
22. Buthelezi LG, Mavengahama S, Sibiya J, Mchunu CN, Ntuli NR. Phytochemical composition of *Lagenaria siceraria* fruits from KwaZulu-Natal and Limpopo, South Africa. *Food Chem X*. 2024 Mar 30; 22:101338.
23. Elsayed A. Elmorsy and Sameh Saber and Rabab S. Hamad and Mustafa Ahmed Abdel-Reheim and Attalla F. El-kott and Mohammed A. AIShehri and Kareem Morsy and Salama Advances in understanding cisplatin-induced toxicity: Molecular mechanisms and protective strategies, *European Journal of Pharmaceutical Sciences*, (203): 106939: 2024.
24. Adikay Sreedevi Nephroprotective Potential of *Lens Culinaris* Against Cisplatin-induced Nephrotoxicity *Indian journal of Physiology Pharmacology* 62 (1) 139-148: 2018.
25. Sreedevi, Adikay and Koganti, Bharathi and Prasad, Koganti, Effect of decoction of root bark of *berberis aristata* against cisplatin- induced nephrotoxicity in rats *International Journal of Pharmacy and Pharmaceutical Sciences* (2), 51-56:2010.
26. Alanezi AA, Almuqati AF, Alfwuaires MA, Alasmari F, Namazi NI, Althunibat OY, Mahmoud AM. Taxifolin Prevents Cisplatin Nephrotoxicity by Modulating Nrf2/HO-1 Pathway and Mitigating Oxidative Stress and Inflammation in Mice. *Pharmaceuticals (Basel)*. 2022 Oct 24;15(11):1310.
27. Tanabe K, Tamura Y, Lanaspa MA, Miyazaki M, Suzuki N, Sato W, Maeshima Y, Schreiner GF, Villarreal FJ, Johnson RJ, Nakagawa T. Epicatechin limits renal injury by mitochondrial protection in cisplatin nephropathy. *Am J Physiol Renal Physiol*. 2012 Nov 1;303(9): F1264-74.