RESEARCH PAPER

Investigation of the Nephroprotective Potential of Crataeva nurvala through In-Vivo Pharmacological Studies and HPTLC Characterization

Dr Vishal Shrivastava[1], Rajeev Sharma[2]

[1]Professor, School of Pharmacy, Email: shrivastava.vishal16@gmail.com, ORCID ID: 0009-0007-5184-5459
[2]PhD Research Scholar, Department of Pharmacology ,LNCT University, Email: rsrajeev21@gmail.com, ORCID ID: 0009-0003-8772-3577

ABSTRACT

Background: Crataeva nurvala, traditionally utilized as its antidiabetic, antihyperlipidemic, diuretic, antimicrobial, anticancer, and many more but still, no strong biomedical evidence was reported on the nephroprotective potential of C. nurvala.

Aim: The present study was designed to investigate the nephroprotective effects of a polyphenol-enriched Crataeva nurvala extract (CNE) against cisplatin-induced renal toxicity in Wistar albino rats.

Methdology: Charactetisation of herbal crude done by HPTLC methods, polyphenolic compounds were determined. Biochemical estimation were done to assure nephroprotective. To strength the role of Crataeva nurvala extract (CNE) on proximal tubules and bowmans's capsules histopathological studies were performed.

Results: Results of the serum biochemical indicators and antioxidant enzymes significantly improved against cisplatin-induced nephrotoxicity. Inflammatory cytokines including TNF-α and IL-6 were considerably reduced by CNE. Additionally, CNE restores kidney tissue damage and reduces interstitial hemorrhage, capillary congestion, inflammatory cell infiltration, vacuolated cytoplasm, and tubular epithelial injury with enlarged Bowman's gap. HPTLC examination also showed that CNE was enriched with polyphenols such as quercetin and gallic acid.

Conclusion: Conclusively, CNE demonstrated nephroprotective potential by modifying the expression of oxidative stress, inflammation, and kidney tissue histology.

Keywords: Crataeva nurvala, polyphenol, nephroprotective, nephrotoxicity, cisplatin , chromatography.

How to cite this article: Dr Vishal Shrivastava, Rajeev Sharma (2026 Investigation of the Nephroprotective Potential of Crataeva nurvala through In-Vivo Pharmacological Studies and HPTLC Characterization International Journal of Drug Delivery Technology; 2026;16(69s):180-189. DOI: 10.25258/ijddt.16.69s.20

INTRODUCTION

Kidney dysfunction caused by direct or indirect exposure to chemicals or drugs is known as nephrotoxicity, and it is one of the most common kidney disorders. The kidney is the principal osmoregulatory organ that supports the body's physiological functions by regulating blood filtration and removing waste metabolites from the body to maintain proper tonicity, fluid volume, pH balance, and electrolyte homeostasis [1]. Chronic kidney disease (CKD) develops over time as a result of several pathogenic events, including oxidative stress, inflammatory cytokines, and detrimental antioxidant imbalances, as well as gradual renal failure [2]. CKD develops over time as a result of several pathogenic events, including oxidative stress, inflammatory cytokines, and detrimental antioxidant imbalances, as well as gradual renal failure. With a frequency of 13.4% worldwide, it is one of the most significant public health issues.Cardiovascular disease, hypertension, diabetes, dyslipidemia, obesity, and aging are among the conditions that contribute to chronic kidney disease [3][4].

Cisplatin is frequently used to treat solid cancers, including stomach cancer, lung cancer, and ovarian cancer. However, it has several negative side effects, including neurotoxicity, nephrotoxicity, and bone marrow suppression. 25-30% of cisplatin users experience nephrotoxicity [5] [6]. Thus, the development of nephrotoxicity by cisplatin is associated with major

aggression factors such as transporter-mediated cisplatin accumulation, transformation into nephrotoxins, formation of DNA adducts, mitochondrial dysfunction due to oxidative and nitrosative stress (OS) and inflammation, signal transducers, and activation of apoptosis. Nevertheless, the scant evidence indicates that OS and inflammation are crucial in cisplatin toxicity [7]. According to various research, herbal medicines are rich in bioactive chemicals with range of bioactivities, including anti-autoimmune, inflammatory, antidiabetic, anticancer, and antioxidant properties. The trend of choosing herbal medicines instead of synthetic ones to treat ailments suggests a return to nature [8] [9]. In recent decades, the use of herbal therapy has increased dramatically and gained acceptance in both industrialized and developing nations. Furthermore, because of its natural origins, accessibility, and lack of adverse effects, herbal therapy has been utilized for millennia and is considered globally as a treatment regimen for illness prevention. We have all seen that there is currently no viable treatment to stop cisplatin-induced nephrotoxicity. To prevent nephrotoxicity, a number of effective and less harmful plant-based medications have been created recently [10].

Crataeva nurvala was widely utilized as a medicinal and nutraceutical in various parts of the world. One of the most well-known medicinal herbs, it is commonly used in the Ayurvedic medical system for the management of various disease ad disorders such as ringworm infections, diarrhea, gastroenteritis, diabetes, hyperlipidemia, cancer, and skin inflammations. According to cited research, Crataeva nurvala is rich in alkaloids, polyphenols, glycosides, and many other substances that are primarily in charge of a variety of biological functions [11]. Additionally, by enhancing kidney function parameters and having antioxidant and anti-inflammatory qualities, the polyphenolic components in C. nurvala are intended to stop the deterioration of kidney function and restore the cellular structure and physiology of renal-challenged patients. Furthermore, evidence-based research showed that C. nurvala still lacks nephroprotective effect [12]. Therefore, the current investigation uses a mouse model of nephrotoxicity to assess the nephroprotective impact of a polyphenolic enriched extract of Crataeva nurvala.

MATERIALS AND METHODS

Preparation of extract

A conical flask containing 500 ml of methanol was filled with 50 g of dried Crataeva nurvala, which were then macerated for three days at 25°C while being constantly stirred. Filter the extract using Whatman No. 1 filter paper once the maceration had finished. Ultimately, vacuum evaporation was used to dry the extracted material, which was then kept in an airtight container for further research. 12.16% was the extraction percentage yield.

Total polyphenolic content (phenol and flavonoid)

The total phenol concentration in Crataeva nurvala extract (CNE) was estimated using a modified version of the Folin Ciocalteu technique. To put it briefly, HPLC-grade methanol was used to prepare stock solution (10 mg/mL) of the test sample. Folin Ciocalteu reagent (5.0 mL; 1:10, v/v) was mixed with 1000 mL of the test samples from the stock solution. After that, 5.0 mL of sodium bicarbonate solution was added, and it was shaken occasionally for half an hour. At 765 nm, the absorbance was finally measured [13].

With some limitation, the aluminum chloride technique was used to assess the total flavonoid content of Crataeva nurvala extract (CNE). 3.0 mL of methanol and 1000 µL of extract solution from the aforementioned stock solution were mixed, and the mixture was incubated for five minutes. This misxture was then left for another 40 minutes after adding distilled water (3.6 mL), sodium acetate (0.2 mL; 1M), and aluminum chloride (0.2 mL 10%). Finally, the absorbance was measured at 415 nm. The results were represented as mg gallic acid/quercetin equivalent/gm extract (mg gallic acid/quercetin/gm extract), respectively [13].

DPPH inhibition activity

A standard method with certain adjustments was used to assess C. nurvala extract (CNE) antioxidant activity. In short, 180 µL of DPPH solution was combined with 20 µL of the test sample (25-500 µg/mL). Further, the sample was kept ate RT for 30 minuts in a dark room, and then the measured the absorbance at 517 nm [14]. Ascorbic acid served as the standard. The following formula was used to assess the DPPH scavenging activity:

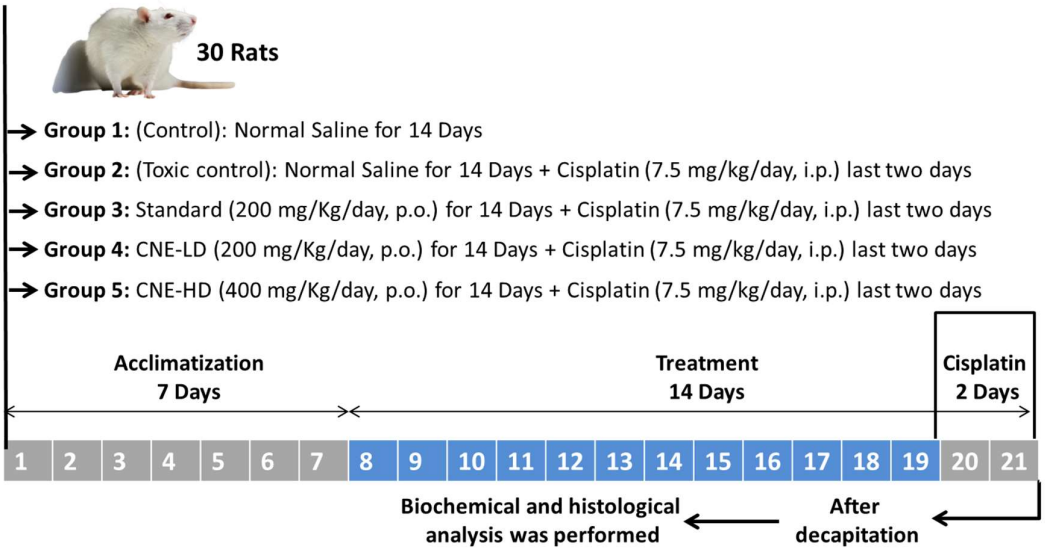
HPTLC determination

The test sample was dissolved in UPLC-grade methanol to create the solvate (50 mg/mL of extract and 0.5 mg/mL of standards). The test sample and standard (gallic acid and quercetin) were applied to TLC plates using CAMAG-Linomat 5 with the following parameters: The application rate was 150 nL/s, the band length was 6 mm, the track margin was 4 mm, and the side edge and bottom were 1.5 and 2 cm apart, respectively [15]. The TLC plate was then placed in a pre-saturated TLC chamber with mobile phases such as formic acid, toluene, and ethyl acetate (5.5: 4.0: 0.5 v/v/v/). Following full development, the plate was

allowed to air dry, scanned at 254 and 366 nm, respectively, and subjected to Wincats1.2 analysis.

Experimental animal models

Wistar albino rats weighing 200-225 g were used for the in vivo nephroprotective activities, which were carried out using a modified version of the technique. Throughout the experiment, all of the animals were kept in regular laboratory settings and provided a standard food. Figure 1 showed the animal study's experimental setup. For comparative analysis, amino acid (AA) was utilized as a standard medication. Every week, the animals' body weights were recorded. Blood samples were drawn on the eleventh day, allowed to clot for 20 minutes, centrifuged for 10 minutes at 1350 rpm, and the serum was carefully separated before being stored at -4°C for additional examination. Additionally, the animals were put to death and killed in order to get kidney tissue for histological and antioxidant research [16].



Estimation of serum biochemical markers

The biochemical markers were used to evaluate the kidney's biochemical changes. The kidney markers analysis included measurements of blood urea (BU), uric acid (UA), creatinine (Cr), total bilirubin (TB), total protein (TP), direct bilirubin (DB), albumin (Alb), globulin (Glb), calcium (Ca), sodium (Na), phosphorus (P), and potassium (K) [16] [17].

Antioxidant status

Kidney tissues were homogenized (10% w/v) in sterile phosphate buffer (50 mM, pH 7.4) and centrifuged at 1300 rpm for 10 minutes at 4°C. By identifying the expression of superoxide dismutase (SOD), catalase (CAT), glutathione (GPx), and malondialdehyde in the supernatant, the antioxidant state of the kidney was evaluated spectrophotometrically [17] [18].

Assessment of inflammatory biomarkers

Following the manufacturer's instructions, the expression of inflammatory biomarkers such as TNF-, and IL-6 was evaluated sequentially using an ELISA reader.

Histopathology

The tiny kidney specimen was embedded in paraffin blocks after being fixed in a 10% formalin solution for the entire night. Additionally, tissue samples were cut with a rotatory microtome to a thickness of 5 m, stained with hematoxylin and eosin, dried, and photographed using a microscope (Motic).

Statistical analysis

The data was statistically represented as mean standard deviation using the Tukey test and One Way ANOVA. P values were deemed statistically significant if they were less than 0.05. The toxic group was contrasted with the treatment and control groups.

RESULTS

Total phenolic and flavonoids content in Crataeva nurvala extract (CNE)

Total phenols and flavonoids were evaluated in this investigation. The results show that CNE's total phenolic content was 59.32 ± 2.08 mg equivalent to GAE/gm

extract, and its flavonoid content was 27.65 ± 1.93 mg equivalent to rutin/gm extract. The findings show that CNE has a higher concentration of polyphenols.

Determination of antioxidant potential of Crataeva nurvala extract (CNE)

The antioxidant activity of individual substances and extracts is frequently assessed using biochemical tests. Antioxidant compounds in the test samples Crataeva nurvala extract (CNE) react with DPPH, a purple solution, to create a light yellow hue. The study's findings showed that, at a tested concentration (25-500 µg/mL), Crataeva nurvala extract (CNE) exhibits strong inhibitory capacity in graded dose-response on DPPH free radicals. The test sample and standard were found to have IC50 values of 79.65 ± 5.76 and 72.32 ± 4.06 µg/mL, respectively.

Identification of polyphenols in Crataeva nurvala extract (CNE)

HPTLC was used in this work to determine conventional bioactive indicators. We employed a variety of solvent solutions with varying compositions to achieve better separation in order to determine the aforementioned bioactive markers. The optimal mobile phase for all the bioactive indicators was determined to be toluene: ethyl acetate: formic acid (5.5: 4.0: 0.5 v/v/v/). Compared to the previously published approach, this mobile phase provides good results. According to the chromatographic separation of the extract, all of the polyphenolic components were well resolved and separated on TLC plates, and their fluorescence bands were all visible at 254 nm. Polyphenols (gallic acid and quercetin) were identified as the Crataeva nurvala extract (CNE) spots with Rf values of 0.17 and 0.38, respectively (Figure 2). In terms of percentage area, the polyphenolic content in Crataeva nurvala extract (CNE) displayed the following order 13.70% and 12.12%. Furthermore, there was no tailing at 254 nm, and the peaks were symmetrical.

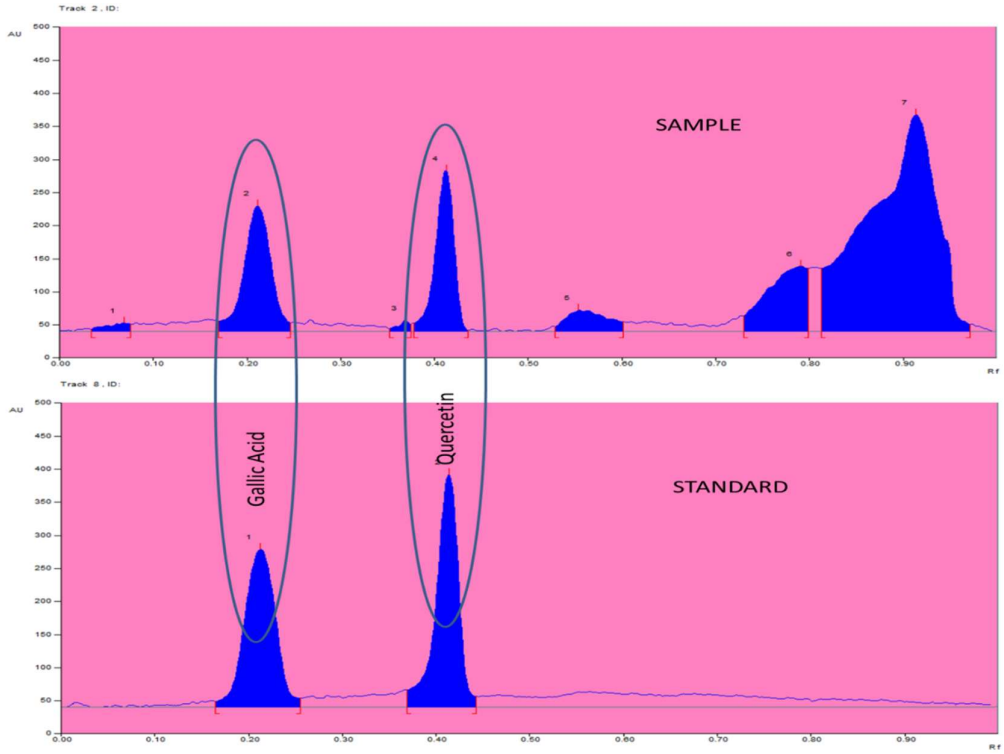


Figure 2: Representing the typical HPTLC chromatograms of Crataeva nurvala extract (CNE) (above) and standards (below).

Measurement of body weight

All of the animals' body weights were recorded both before and after the experiment. When compared to other treated groups, the data showed a considerable decline in the body in the disease groups. When compared to toxic, the greater dose of Crataeva nurvala extract (CNE) and standard exhibit a comparable body weight pattern and considerably improve to normal (Figure 3). Cisplatin nephrotoxicity was demonstrated by decreased body weight.

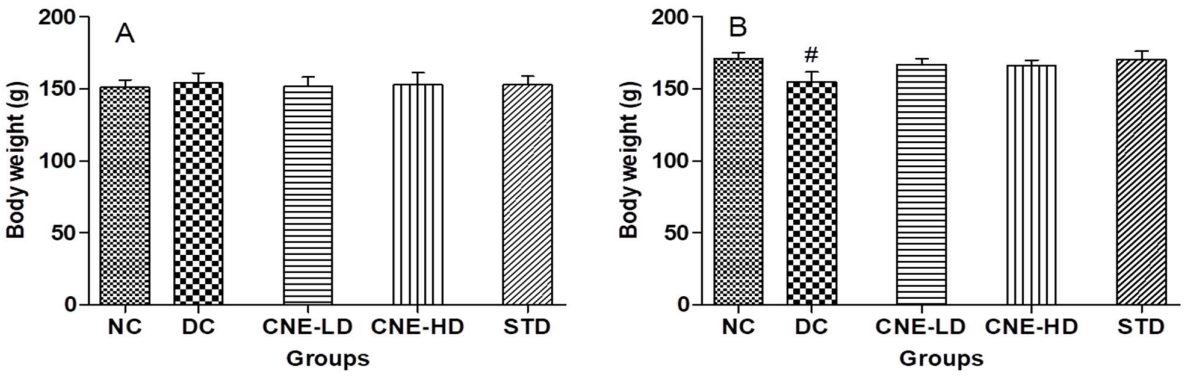


Figure 3: Evaluation of bodyweight of each group prior and post-treatment groups. The statistical representation was made as Mean ± SD (n=6). The comparisons were made to control and disease control (#), toxic to drug-treated groups (*). The significance level was observed at #/*p < 0.05.

Keys: NC:Normal control; DC:Disease Control ; CNE-LD: *Crataeva nurvala* extract low dose ;CNE-HD *Crataeva nurvala* extract high dose; STD:Ascorbic acid

Estimation of biochemical markers in blood serum

The biochemical indicators of blood were markedly altered in experimental rats that received cisplatin in succession. The toxic group had higher levels of electrolyte sodium and biochemical indicators such as urea, uric acid, creatinine, total protein, albumin, globulin, and total bilirubin. Conversely, there was a significant ($p \leq 0.05$) decrease in calcium, phosphorus, and potassium levels. Nephrotoxicity's typical distinctive trait is depicted in the above description. It's interesting to note that the therapy groups preserve and preserve biochemical levels close to normal. Results from higher Crataeva nurvala extract (CNE) dosages were similar to those from AA. Table 1 showed the overall results.

Table 1: Estimation of biochemical markers of blood in experimental groups

Parameters	Control	Toxicant	CNE-LD	CNE-HD	AA
Urine urea (mg/dl)	20.21 ± 2.08	56.34 ± 3.49###	46.24 ± 3.38**	36.49 ± 3.91***	31.08 ± 2.67***
Uric Acid (mg/dl)	2.41 ± 0.21	4.08 ± 0.26###	3.15 ± 0.22**	2.63 ± 0.29***	3.06 ± 0.19**
Creatinine (mg/dl)	0.57 ± 0.05	1.68 ± 0.92###	0.76 ± 0.07***	0.65 ± 0.08***	0.66 ± 0.09***
Total Protein (gm/dl)	7.43 ± 0.14	10.26 ± 0.35###	8.67 ± 0.41**	7.98 ± 0.38***	8.28 ± 0.34***
Albumin (gm/dl)	2.71 ± 0.09	5.04 ± 0.16###	4.07 ± 0.32**	4.9 ± 0.17***	4.785 ± 0.18***
Globulin (gm/dl)	3.37 ± 0.31	5.86 ± 0.23###	5.09 ± 0.18**	4.69 ± 0.18***	4.57 ± 0.20***
Total Bilirubin (mg/dl)	0.17 ± 0.05	0.23 ± 0.21#	0.21 ± 0.04	0.17 ± 0.03*	0.16 ± 0.04*
Calcium (mg/dl)	12.68 ± 0.42	9.19 ± 0.32###	10.44 ± 0.35**	11.86 ± 0.27***	11.16 ± 0.24***
Phosphorus (mg/dl)	5.97 ± 0.34	4.36 ± 0.30###	4.88 ± 0.32	5.78 ± 0.23***	6.03 ± 0.39***
Sodium (mmol/l)	139.24 ± 6.56	160.33 ± 7.18###	156.66 ± 5.64*	153.44 ± 5.15**	142.04 ± 5.07***
Potassium (mmol/l)	4.98 ± 0.11	4.17 ± 0.16###	4.64 ± 0.09**	4.51 ± 0.12***	4.83 ± 0.17***

Biochemical analysis of biomarkers in blood was estimated and statistical representation was made between control to disease control (#p<0.05, ##p<0.01, ###p<0.001) and disease control to treatment (*p<0.05, **p<0.01, ***p<0.001).

Keys:NC:Normal control; DC:Disease Control ; CNE-LD: Crataeva nurvala extract low dose ;CNE-HD Crataeva nurvala extract high dose; STD:Ascorbic acid

4.6 Estimation of antioxidant status of kidney tissue in the experimental groups: One of the hallmarks of cisplatin-induced nephrotoxicity is oxidative stress (OS). As a result, kidney tissue homogenates were examined

for antioxidant status (SOD, CAT, GPx, and MDA). According to the study's findings, the hazardous group's MDA level was lower but SOD, CAT, and GPx levels were noticeably higher. When it comes to cisplatin-induced OS in kidney tissues, the above antioxidant status level considerably ($p \leq 0.05$) improves to normal in treatment groups. For SOD, CAT, and GPx, the increased treatment dose and standard showed nearly identical efficacy. Additionally, all of the antioxidant observations are shown in Table 2.

Table 2: Estimation of antioxidant status of kidney in experimental groups

Parameters	Control	Toxicant	CNE-LD	CNE-HD	Ascorbic Acid
SOD	20.24 ± 2.09	7.15 ± 0.46$^{###}$	12.26 ± 1.34**	18.48 ± 1.30***	18.11 ± 1.21***
CAT	53.59 ± 4.78	17.39 ± 1.59$^{###}$	37.96 ± 3.98***	53.12 ± 4.65***	55.94 ± 3.24***
GPx	31.56 ± 2.61	10.30 ± 1.64$^{###}$	25.98 ± 1.98**	29.68 ± 3.07***	28.66 ± 3.66***
MDA	2.85 ± 0.22	5.39 ± 1.08$^{###}$	4.85 ± 0.30^{ns}	2.83 ± 0.30**	2.41 ± 0.31***

Antioxidant status of the kidney was estimated and statistical representation was made between control to disease control (#p<0.05, ##p<0.01, ###p<0.001) and disease control to treatment (*p<0.05, **p<0.01, ***p<0.001).

Keys: Superoxide Dismutase (SOD), Catalase (CAT), Glutathione Peroxidase (GPx), Malondialdehyde (MDA)

Estimation of inflammatory markers in the experimental groups

We looked at TNF-α, and IL-6 expression in each of the experimental groups. All of the indicators' expression increased simultaneously in the hazardous group. All of the inflammatory cytokines' expression, however, was considerably recovered to almost normal in the therapy groups. When compared to a lower dose, a higher dose of Crataeva nurvala extract (CNE) demonstrated superior protective activity. Remarkably, a high dosage of Crataeva nurvala extract (CNE) had an impact that was similar to that of regular ascorbic acid **(Figure 4).** Therefore, it can be concluded that Crataeva nurvala extract (CNE) prevents cisplatin-induced nephrotoxicity.

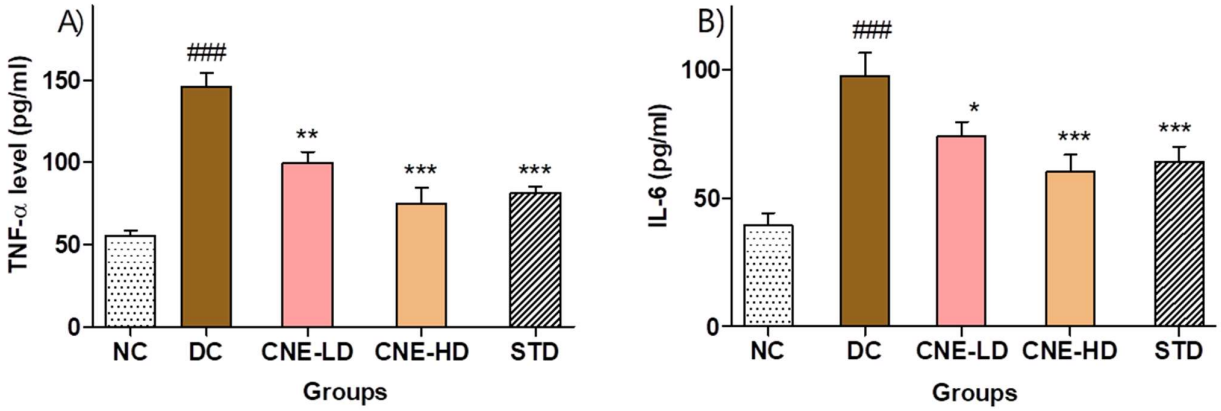


Figure 4: Effectiveness of CNE on IL-6, IL-1β, and TNF-α in each group. The final data was statistically represented as Mean ± SD (n=6). Control to illness control (#) and toxic to drug-treated group (*) were compared. #/*p < 0.05 was found to be the significant level.

Keys:NC:Normal control; DC:Disease Control ; CNE-LD: Crataeva nurvala extract low dose ;CNE-HD Crataeva nurvala extract high dose; STD:Ascorbic acid

Histological observations of the kidney

The histopathological observations of renal tissues was observed normal in the control group. Incase of disease control group, renal morphology was observed with significant changes such as inflammatory cell infiltration, interstitial hemorrhage, irregular dilated lumina, vacuolated cytoplasm, damaged brush border cell atrophy, increased Bowman's gap, and congestion in glomerular capillaries.. Significant outcomes were seen in the Crataeva nurvala extract (CNE) and conventional therapy groups, and the kidney tissue's cellular architecture was shown to be normal **(Figure 5).**

Therefore, it can be concluded that Crataeva nurvala extract (CNE) is effective in preventing kidney injury.

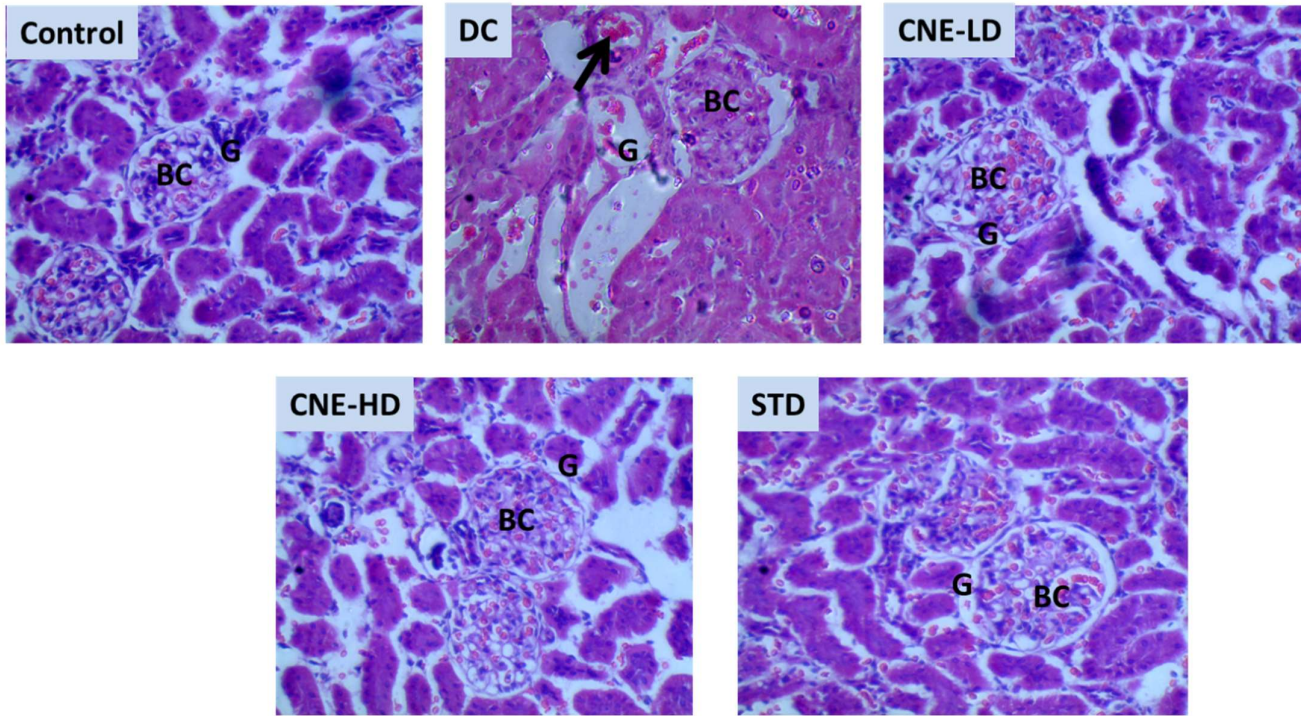


Figure 5: Histopathological examination shows treatment groups ameliorated the destruction of kidney tissue damage towards normal (Keys:NC:Normal control; DC:Disease Control ; CNE-LD: Crataeva nurvala extract low dose ;CNE-HD Crataeva nurvala extract high dose; STD)

DISCUSSION

The main disadvantage of cisplatin, a well-known anticancer medication that is often used to treat a variety of cancer types, including lung, testis, neck, brain, ovarian, and breast cancer, is that it can cause severe nephrotoxicity. Cellular stress, inflammation, and ROS-induced apoptosis result in cisplatin-induced nephrotoxicity, which lowers blood urea and serum creatinine levels and results in renal failure [5]. Therefore, multimechanistic strategies are used to battle nephrotoxicity by defeating oxidative stress, inflammation, and kidney apoptosis in order to prevent the pathological processes. There is a substantial correlation between this discovery and previous published research. Prior to Crataeva nurvala extract (CNE) 's in vivo nephroprotective potential, its phytochemistry, in vitro cytotoxicity, and protective impact must be understood. The polyphenolic phytoconstituents found in Crataeva nurvala extract (CNE) were analyzed using HPTLC. Crataeva nurvala extract (CNE) was shown to be enriched with polyphenols such as galloc acid and quercetin, according to the observed HPTLC study.

Nephrotoxicity was evaluated in this study following treatment with cisplatin and Crataeva nurvala extract (CNE) alone. Rats given cisplatin showed common clinical and pathological symptoms, such as decreased body weight and notable alterations in kidney function parameters, including creatinine, urea, uric acid, total protein, albumin, and electrolytes. However, a decrease in glomerular filtration rate suggested that cisplatin caused nephrotoxicity [17] [5]. Our results on cisplatin-induced nephrotoxicity are fairly similar to those of other research. It's interesting to note that serum levels of urea, creatinine, and uric acid are thought to be significant indicators of nephrotoxicity in renal diseases. According to earlier research, creatinine is the most accurate indicator of renal damage. According to Daenen et al. (2019), renal malfunction is indicated by elevated creatinine levels in the serum, which are maintained by the kidneys through excretion from the body. Concurrently, another significant indicator that can increase renal damage is urea [19]. Additionally, referenced research showed that renal physiology has a

major role in the excretion of water, urine, and electrolytes (Na+, K+, Ca2+, and phosphate) Crataeva nurvala extract (CNE) restores normal electrolyte levels in the serum, hence reducing cisplatin-induced nephrotoxicity [20].

When cisplatin causes overwhelming renal toxicity, OS is essential. Cellular protein and lipid oxidation is closely linked to physiological and structural processes. According to cited research, cisplatin-induced free radicals inhibit the activity of antioxidant enzymes such as SOD, CAT, and GPx. In biological systems, antioxidants serve as the main cellular defense barrier grid against oxidative stress by neutralizing oxidative free radicals The investigation's findings showed that cisplatin injection considerably raised the level of MDA while drastically lowering the levels of SOD, CAT, and GPx in tissue homogenate [21] [22]. The administration of Crataeva nurvala extract (CNE) considerably decreased the level of MDA and increased the levels of SOD, CAT, and GPx. Higher doses of CNE demonstrated greater efficacies in antioxidant enzymes than did low doses. Crataeva nurvala extract (CNE) at higher doses demonstrated nearly identical efficacy to the standard. Therefore, the current study confirmed Crataeva nurvala extract (CNE) 's antioxidant efficacy while also observing its nephroprotective function.

Moreover, inflammatory cytokines like TNF, IL-6, and IL-1β are closely linked to the pathogenesis of nephrotoxicity and are important in cellular inflammation. According to earlier research, cisplatin causes phosphorylation and then transports the NF-κB transcription factor to the nucleus while degrading the inhibitory IκBα protein. NF-κB increases the transcription of inflammatory mediators and creates inflammatory, proliferative, anti-apoptotic, and immunological responses [23]. This episode calls for the administration of cisplatin to increase the amount of TNF-α in kidney cells, a crucial inflammatory cytokine in systemic inflammation and acute-phase response. A crucial part of kidney homeostasis is played by IL-6 and IL-1β, which are quickly released when cisplatin damages renal cells and trigger acute phase reactions. According to our findings, Crataeva nurvala extract (CNE) reduces all of the inflammatory cytokines under investigation to almost normal levels. This outcome comes after multiple published studies that shown Crataeva nurvala extract (CNE)'s anti-inflammatory properties in animals with cisplatin-induced nephrotoxicity [4]. These findings highlight Costus spicatus's polyphenol-enriched extract's potential for reducing inflammation. According to cited research, polyphenolic is a great medication option for avoiding nephrotoxicity caused by cisplatin. In line with earlier findings, we also discovered elevated levels of TNF-α, IL-6, and IL-1β in this investigation.

In this investigation, administering cisplatin decreased body weight and damaged the kidney tissues' histological architecture. According to histopathological analysis, cisplatin causes severe inflammatory cell infiltration, irregularly dilated lumina, interstitial hemorrhage, tubular epithelial injury with widened Bowman's space, atrophy, and destructured brush border cells. It also causes congestion in the glomerulus's capillaries. Clinical confirmation of these deformities includes increased serum creatinine, electrolyte imbalance, and severe renal failure. Additionally, a variety of interstitial congestion and inflammatory infiltration have been seen [24]. Assessments of the Crataeva nurvala extract (CNE) -treated group indicate that the polyphenol-enriched extract mitigates the harmful effects of cisplatin and returns the kidney's histological architecture to nearly normal. According to cited resrach, histopathological results are consistent with biochemical data and previous reports [25].

Polyphenolic substances such as gallic acid and quercetin are ideal candidates to prevent OS-induced inflammation in biological systems and to prevent the production of free radicals. It's interesting to note that oral consumption of quercetin, ferulic acid, and caffeic acid reduces elevated levels of creatinine, urea, uric acid, and MDA. It also improves the status of antioxidant enzymes such as SOD, CAT, and GPx and restores normal kidney histology in response to cisplatin-induced nephrotoxicity [26] [27] [28].

CONCLUSIONS

According to the results of the current study, Crataeva nurvala extract (CNE) improves creatinine, antioxidant, and anti-inflammatory status and restores the histological architecture of kidney tissues, hence exerting a nephroprotective effect against cisplatin-induced toxicity preclinical models. Therefore, we suggest that during cisplatin treatment, Crataeva nurvala extract (CNE) could be used as a nephroprotective drug. Furthermore, it is claimed that additional molecular and clinical analysis will validate these results.

REFERENCES

[1] M. Al-Naimi, H. Rasheed, N. Hussien, H. Al-Kuraishy, and A. Al-Gareeb, “Nephrotoxicity: Role and significance of renal biomarkers in the early detection of acute renal injury,” 2019. doi: 10.4103/japtr.JAPTR_336_18.

[2] D. Formanowicz, “Chronic Kidney Disease as Oxidative Stress- and Inflammatory-Mediated Cardiovascular Disease,” 2020.
[3] M. S. Al Naimi, H. A. Rasheed, and N. R. Hussien, “Nephrotoxicity : Role and significance of renal biomarkers in the early detection of acute renal injury,” pp. 95–99, 2019, doi: 10.4103/japtr.JAPTR.
[4] S. Yaman, “Nephrology Renal Pathophysiology and Nephrotoxicity : Renal Biomarkers ’ Importance and F unction in the E arly Diagnosis of Acute Renal D amage,” vol. 5, no. 5, pp. 53–57, 2022, doi: 10.47532/oain.2022.5(5).53-57.
[5] S. Dasari and P. Bernard Tchounwou, “Cisplatin in cancer therapy: Molecular mechanisms of action,” 2014. doi: 10.1016/j.ejphar.2014.07.025.
[6] R. Z. Alicic, M. T. Rooney, and K. R. Tuttle, “Diabetic Kidney Disease,” vol. 12, no. 18, 2017, doi: 10.2215/CJN.11491116.
[7] S. Xavier et al., “Antioxidant and nephroprotective activities of the extract and fractions of Homonoia riparia Lour,” Pharmacogn. Mag., vol. 13, no. 49, pp. 25–30, 2017, doi: 10.4103/0973-1296.197647.
[8] G. E. S. Batiha et al., “Chemical constituents and pharmacological activities of garlic (Allium sativum L.): A review,” 2020. doi: 10.3390/nu12030872.
[9] R. C. Fierascu, I. Fierascu, A. Ortan, M. I. Georgiev, and E. Sieniawska, “Innovative approaches for recovery of phytoconstituents from medicinal/aromatic plants and biotechnological production,” 2020. doi: 10.3390/molecules25020309.
[10] F. Luan et al., “Traditional Uses , Phytochemical Constituents and Pharmacological Properties of Averrhoa carambola L .: A Review,” vol. 12, no. August, pp. 1–27, 2021, doi: 10.3389/fphar.2021.699899.
[11] A. Mannan, F. H. Khan, A. B. Abir, and M. Afroze, “The leaves of Crataeva nurvala Buch-Ham . modulate locomotor and anxiety behaviors possibly through GABAergic system,” pp. 1–12, 2018.
[12] X. Jiao, Q. Jin, P. Zhu, Z. Tan, L. Li, and L. Liu, “Clerodendranthus spicatus : a comprehensive review of the chemical constituents , pharmacology , quality control and clinical applications,” no. March, 2025, doi: 10.3389/fphar.2025.1452797.
[13] I. L. Lawag, E. S. Nolden, A. A. M. Schaper, L. Y. Lim, and C. Locher, “applied sciences A Modified Folin-Ciocalteu Assay for the Determination of Total Phenolics Content in Honey,” 2023.
[14] M. Ibrahim, G. R. Pawar, S. Khan, M. Mazhar, and S. Pathak, “Therapeutic Lead Identification from Ginkgo biloba against Enzyme Causing Alzheimer ’ s Disease Using in- vitro Studies Integrated Network Pharmacology and Molecular Docking,” vol. 12, no. 3, pp. 248–255, 2024, doi: 10.13189/app.2024.120309.
[15] V. Y. Thakker, V. N. Shah, U. D. Shah, M. P. Suthar, and V. V Nagar, “Simultaneous estimation of Gallic acid, Curcumin and Quercetin by HPTLC method,” vol. 80, pp. 70–80, 2011.
[16] A. Rezaee-Khorasany, B. M. Razavi, E. Taghiabadi, A. T. Yazdi, and H. Hosseinzadeh, “Effect of crocin, an active saffron constituent, on ethanol toxicity in the rat: Histopathological and biochemical studies,” Iran. J. Basic Med. Sci., 2020, doi: 10.22038/IJBMS.2019.37133.8845.
[17] S. Sultana, K. Verma, and R. Khan, “Nephroprotective efficacy of chrysin against cisplatin-induced toxicity via attenuation of oxidative stress,” J. Pharm. Pharmacol., 2012, doi: 10.1111/j.2042-7158.2012.01470.x.
[18] M. Kpemissi et al., “Nephroprotective activity of Combretum micranthum G. Don in cisplatin induced nephrotoxicity in rats: In-vitro, in-vivo and in-silico experiments,” Biomed. Pharmacother., 2019, doi: 10.1016/j.biopha.2019.108961.
[19] K. Daenen, A. Andries, D. Mekahli, A. Van Schepdael, F. Jouret, and B. Bammens, “Oxidative stress in chronic kidney disease,” 2019. doi: 10.1007/s00467-018-4005-4.
[20] K. G. Ingale, P. A. Thakurdesai, and N. S. Vyawahare, “Protective effect of Hygrophila spinosa against cisplatin induced nephrotoxicity in rats,” Indian J. Pharmacol., 2013, doi: 10.4103/0253-7613.111909.
[21] O. M. Ighodaro and O. A. Akinloye, “First line defence antioxidants-superoxide dismutase (SOD), catalase (CAT) and glutathione peroxidase (GPX): Their fundamental role in the entire antioxidant defence grid,” Alexandria J. Med., vol. 54, no. 4, pp. 287–293, 2018, doi: 10.1016/j.ajme.2017.09.001.
[22] C. Nephrotoxicity et al., “Review Article Protective Effect of Natural Antioxidants on Reducing,” vol. 2022, 2022.
[23] B. Humanes et al., “Cisplatin-induced renal inflammation is ameliorated by cilastatin nephroprotection,” Nephrol. Dial. Transplant., vol. 32, no. 10, pp. 1645–1655, 2017, doi: 10.1093/ndt/gfx005.
[24] M. G. Ewees, B. A. S. Messiha, A. A. Abo-Saif, A. M. A. Bayoumi, and M. S. Abdel-Bakky, “Erratum: Interference with Coagulation Cascade As a Novel Approach to Counteract Cisplatin-Induced Acute Tubular Necrosis; An Experimental Study in Rats ront (Frontiers in Pharmacology (2018) 9 (1155) DOI: 10.3389/fphar.2018.01155),” 2019. doi: 10.3389/fphar.2019.01259.
[25] T. E. J. Wang et al., “Honokiol, a polyphenol natural compound, attenuates cisplatin-induced acute

cytotoxicity in renal epithelial cells through cellular oxidative stress and cytoskeleton modulations," Front. Pharmacol., vol. 9, no. APR, 2018, doi: 10.3389/fphar.2018.00357.
[26] N. Tripathi and S. Devi, "Nephroprotective : A Comprehensive Review," vol. 3, no. 5, pp. 4409–4427, 2025, doi: 10.5281/zenodo.15528332.
[27] T. Mitochondria, F. Ashkar, K. S. Bhullar, and J. Wu, "The Effect of Polyphenols on Kidney Disease :," 2022.
[28] A. S. Fernandes and G. Costa, "Polyphenols and Their Metabolites in Renal Diseases : An Overview," pp. 1–22, 2022.

(1)