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Research

Evaluation of Nephroprotective Effect of Ethanolic Extract (Leaves) of *Neolamarckia cadamba* Against Folic Acid-Induced Nephrotoxicity in Wistar Rats

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Abstract

Nephrotoxicity, a key trigger of kidney failure (AKI), often arises from therapeutic agents, metabolic disturbances, or toxic metabolites, leading to tubular necrosis, oxidative stress, and impaired renal function. Folic acid–induced nephrotoxicity is a firm experimental typical for studying renal damage. *Neolamarckia cadamba* (Rubiaceae), commonly known as Kadamba, has long been utilized in Ayurvedic medicine for treating inflammation, fever, and hepatic disorders. Its leaves are rich in bioactive phytochemicals comprising bioactive constituents like alkaloids, terpenoids, flavonoids, and phenolic compounds that possess significant antioxidant and protective effects against cellular damage.The purpose of the learning was to assess the kidney-protective potential of the ethanolic leaf extract of Neolamarckia cadamba (EENC) against folic acid–induced renal injury in Wistar rats. Five groups of 6 rats each were randomly selected from among the animals (n = 6). Group II was given folic acid (250 mg/kg), while Group I was certain saline (1 mL, p.o.) as the standard reference, Group III received folic acid along with ascorbic acid (250 mg/kg), while Folic acid and EENC were administered to Groups IV and V at doses of 200 mg per kg and 400 mg per kg, respectively.

All treatments were given orally for 14 consecutive days. Renal function was evaluated by determining blood urea nitrogen (BUN) & serum creatinine levels to evaluate the protective effect of the extract, urine volume, and creatinine clearance. Antioxidant markers, including glutathione (GSH) and glutathione peroxidase (GPx), were evaluated, and histopathological

examinations were conducted to assess renal tissue integrity.Folic acid administration resulted in significant nephrotoxicity, evidenced by increased creatinine and BUN with reduced clearance. Oral administration of EENC at both 200 and 400 mg/kg markedly restored renal biochemical parameters, enhanced antioxidant enzyme activities, and preserved renal histoarchitecture in a dose-related way. The results designate that the ethanolic leaf extract of Neolamarckia cadamba exhibits strong kidney-protective effects, likely due to its antioxidant and membrane-stabilizing potential. These results provide scientific validation for the customary application of N. cadamba as a natural remedy for renal protection.

Keywords: Nephroprotection, *Neolamarckia cadamba*, Folic acid, Antioxidant enzymes, Acute kidney injury, Ethanolic extract, Wistar rats.

1. INTRODUCTION

Kidneys are essential organs that perform vital excretory and regulatory roles in the body. They are involved in sustaining physiological stability by controlling fluid and electrolyte levels, maintaining normal blood pressure, promoting red blood cell production, balancing the body's acid–base status, and clearing toxic substances originating from internal metabolism or external sources. Functioning as key organs for metabolic regulation, they filter roughly 180 liters of plasma daily and eliminate waste products, including urea, creatinine, and uric acid, to preserve overall homeostasis while conserving essential nutrients and electrolytes. Any impairment in renal function can interrupt this delicate stability, important to the accumulation of toxic metabolites and subsequent systemic complications.

Nephrotoxicity, defined as the structural and functional deterioration of renal tissue caused by exposure to toxic agents, remains a major concern in modern clinical practice [1]. It is a common adverse effect associated with various pharmacological agents, environmental toxins, heavy metals, and chemotherapeutic drugs. Drug-induced nephrotoxicity alone contributes to approximately 20–30% of all hospitalized cases of acute renal injury, frequently progressing to chronic renal disease if left untreated [2]. The underlying mechanisms of nephrotoxicity often involve oxidative stress, mitochondrial dysfunction, inflammation, and apoptosis of tubular epithelial cells, which together impair the glomerular filtration rate (GFR) and renal excretory capacity.

Among several experimental models of AKI, folic acid–induced nephrotoxicity is one of the most widely accepted and reproducible models that closely mimics human tubular injury [3]. High doses of folic acid lead to the intratubular deposition of folate crystals, primarily within the proximal tubular segments, which induce mechanical obstruction, oxidative stress, and mitochondrial dysfunction [4]. This cascade results in cellular necrosis, apoptosis of renal epithelial cells, and disruption of tubular integrity. The resulting decline in renal filtration capacity is reflected by a decrease in creatinine clearance and an elevate in blood urea nitrogen (BUN) & serum creatinine concentrations, is widely recognized as a characteristic sign of kidney toxicity [5].

The development and advancement of nephrotoxicity are strongly influenced by oxidative damage. The body's natural antioxidant capacity is exceeded by an excess of reactive oxygen species (ROS) and reactive nitrogen species (RNS), which outcomes in oxidative damage to cellular constituents such lipids, proteins, and nucleic acids [6]. The imbalance between pro-oxidant and antioxidant systems damages renal cell membranes, mitochondrial structures, and enzymes essential for cellular homeostasis. Consequently, therapeutic interventions aimed at enhancing antioxidant capacity or scavenging free radicals have gained prominence as effective strategies for preventing or mitigating nephrotoxicity.

In this context, medicinal plants have attracted considerable scientific interest as potential nephroprotective agents. Their high content of polyphenolic compounds, flavonoids, alkaloids, terpenoids, and tannins contributes to their free radical–scavenging, anti-inflammatory, and cytoprotective effects [7]. Importantly, plant-based therapies offer a safer alternative to synthetic drugs, with minimal side effects and potential synergistic interactions between bioactive constituents.

One such promising plant is Neolamarckia cadamba (syn. Anthocephalus cadamba), a tropical tree a member of the Rubiaceae family, native to the Indian subcontinent, and commonly found throughout Southeast Asia and tropical regions of Africa [8]. In Ayurveda, N. cadamba holds significant medicinal importance and has long been utilized for its wide range of therapeutic benefits in managing ailments such as liver diseases, fever, inflammation, and dysentery ,urinary ailments [9]. Pharmacological investigations have demonstrated multiple biological activities of different plant parts—bark, leaves, and fruits—including hepatoprotective [10], anti-

inflammatory [11], antimicrobial [12], antioxidant [13], and diuretic properties [14], underscoring its broad therapeutic potential.

Phytochemical analyses of N. cadamba have identified several bioactive constituents such as cadambine, betulinic acid, chlorogenic acid, caffeic acid, and other polyphenolic compounds, which exhibit potent free radical–scavenging, anti-inflammatory, and cytoprotective effects [15]. These compounds are known to enhance cellular antioxidant defense systems, stabilize cell membranes, and inhibit lipid peroxidation—mechanisms that are particularly relevant to renal protection. Given this phytochemical richness and pharmacological profile, it is rational to hypothesize that the ethanolic extract of Neolamarckia cadamba leaves (EENC) may exert nephroprotective effects by counteracting oxidative stress and preserving renal cellular integrity in conditions of toxic insult.

Therefore, the current investigation was carried out to assess the kidney-protective potential of EENC in counteracting folic acid–induced renal toxicity in Wistar rats. The investigation involved a comprehensive assessment through biochemical parameters (serum creatinine, BUN, urine volume, creatinine clearance), antioxidant enzyme assays (glutathione [GSH], glutathione peroxidase [GPx]), and histopathological evaluation of renal tissues. The study aims to scientifically validate the traditional applications of N. cadamba and investigate its potential as a kidney-protective natural medicinal agent.

2. EXPERIMENTAL SECTION

2.1 Gathering and Confirming Plant Material

Fresh, mature green leaves of *Neolamarckia cadamba* (Family: Rubiaceae) were composed from the local botanical area of Haridwar, Uttarakhand, India, during July, when the plant is in its peak vegetative phase. To get rid of dust and dirt, the collected specimens were thoroughly cleansed with distilled water.. A qualified botanist at the Department of Botany, Motherhood University, Roorkee carried out taxonomic identification & authentication. A voucher specimen (Voucher No.: **MU/PHC/NC-07/2024**) was ready and placed in the department's herbarium for future reference and record verification.

2.2 Making an Ethanolic Extract

To retain thermolabile phytoconstituents, the validated leaves were air-dried for roughly two weeks at room temperature (25 ± 2°C) in the shade. A mechanical grinder was then used to turn the dried material into a coarse powder. In order to fully dissolve the active ingredients, about 500 g of the powdered leaves were extracted by cold maceration with 95% ethanol (2.5 L) for 72 hours, with sporadic stirring. Whatman No. 1 filter paper was used after the mixture was initially filtered through muslin cloth. In order to produce a dark green semisolid residue, the filtrate was concentrated under decreased pressure using a rotary evaporator kept at 40–45°C. This was followed by further drying on a water bath. The extractive yield was found to be around 8.5% w/w relative to the dry weight of the plant material. The last excerpt was preserved in a tightly sealed glass container at 4°C to protect it from microbial contamination and oxidative degradation until use.

2.3 Initial Plant-based Chemical Evaluation

The ethanolic extract of *Neolamarckia cadamba* (EENC) stayed examined for the presence of different classes of phytochemicals using qualitative analytical methods. Standard procedures outlined by Harborne (1998) and Kokate (2005) [16] were followed to identify key secondary metabolites possessing biological significance. The conducted tests along with their respective findings are detailed in Table 1.

Table 1. Initial Ethanolic Extract Phytochemical Screening of *Neolamarckia cadamba* Leaves

Phytochemical Test	Observation	Inference
Dragendorff's and Mayer's Tests	Orange/Brown precipitate	Alkaloids present
Shinoda Test	Red coloration	Flavonoids present
Ferric Chloride Test	Bluish-black color	Phenols and Tannins present
Foam Test	Persistent froth	Saponins present
Liebermann–Burchard Test	Greenish coloration	Triterpenoids present
Molisch's Test	Violet ring at junction	Glycosides present

The phytochemical profiling demonstrated the occurrence of several major secondary metabolites, including alkaloids, flavonoids, phenolics, tannins, glycosides, saponins, and triterpenoids. The presence of these bioactive components indicates that the extract is rich in antioxidant and membrane-protective molecules, which are likely responsible for its kidney-protective effects.

2.4 Laboratory Animals

The Central Animal House Facility at Motherhood University in Roorkee provided adult Wistar albino rats of both sexes, weighing between 150 and 200 g. All animals were given a week to acclimate to well-

maintained laboratory settings prior to the experiment, which included a temperature of 25 ± 2°C, a relative humidity of 50–60%, and a 12-hour light/dark cycle. The rats were housed in sterile rice husk-lined, sterilized polypropylene cages with unlimited access to water and regular pellet meal. The Institutional Animal Ethics Committee (IAEC) of Motherhood University (Approval No.: MU/IAEC/PHC/2024/06) approved all animal handling and experimental procedures in accordance with the government's CPCSEA (Committee for the Purpose of Control and Supervision of Experiments on Animals) regulations.

2.5 Induction of Nephrotoxicity

Experimental nephrotoxicity was induced by the oral administration of **folic acid (250 mg kg^{-1} body weight)** suspended in 0.3% carboxymethyl cellulose (CMC) solution. This dose was selected based on previous studies reporting reliable induction of acute tubular necrosis and oxidative renal damage [17]. Folic acid was freshly prepared before each administration to ensure stability and uniform dispersion.

2.6 Design of Experiments

Five experimental sets, each with six rats (n = 6), were randomly assigned to the animals with specific treatments administered as follows:

Group No.	Experimental Design and Treatment Regimen
Group I	Served as the normal control and received saline solution (1 mL, orally)
Group II	Induced with folic acid at a dose of 250 mg/kg (administered orally)
Group III	Treated with folic acid (250 mg/kg, p.o.) along with ascorbic acid (250 mg/kg, p.o.)
Group IV	Received folic acid (250 mg/kg, p.o.) combined with ethanolic extract of *Neolamarckia cadamba* (EENC) at 200 mg/kg (p.o.)
Group V	Administered folic acid (250 mg/kg, p.o.) along with EENC at a higher dose of 400 mg/kg (p.o.)

This experimental grouping was designed to compare the protective efficacy of *Neolamarckia cadamba* leaf extract at two different concentrations against folic acid–induced nephrotoxicity [18].

2.7 Biochemical Analysis

To enable 24-hour urine collection, each animal was placed in a metabolic cage at the end of the dosing period, and the total amount of pee produced was precisely quantified and recorded. Using sterile capillary tubes, blood samples were drawn from the retro-orbital plexus while under mild ketamine anesthesia. The serum was separated from the collected blood by centrifuging it at 3000 rpm for 10 minutes. It was then stored at -20°C for further biochemical analysis.

Standardized commercial diagnostic kits (Span Diagnostics Pvt. Ltd., India) were used to assess renal functional indices, such as serum creatinine, blood urea nitrogen (BUN), and creatinine clearance, in compliance with the manufacturer's suggested procedures.

2.8 Determination of Antioxidant Parameters

Kidney tissues were rapidly removed following animal sacrifice, rinsed thoroughly with chilled saline to eliminate traces of blood, and homogenized to create 10% (w/v) tissue homogenates in ice-cold phosphate buffer (pH 7.4). Antioxidant enzyme analysis was performed on the supernatants obtained from centrifuging the homogenates at 10,000 rpm for 15 minutes at 4°C.

Ellman's reagent (DTNB, 5,5'-dithiobis-2-nitrobenzoic acid) is used to quantify reduced glutathione (GSH), which forms a yellow chromophore that may be measured at 412 nm, according to Ellman [19].

Glutathione Peroxidase (GPx): Calculated using the Paglia and Valentine method, which gauges the oxidation of reduced glutathione while hydrogen peroxide is present [20].

All enzyme activities were standardized based on protein content and expressed as units per milligram of protein.

2.9 Microscopic Evaluation of Kidney Tissue

For histological analysis, kidney tissues were kept in 10% neutral buffered formalin for a full day. The fixed samples were dehydrated using different concentrations of ethanol after being cleaned in xylene and embedded in paraffin wax. Hematoxylin and eosin (H&E) staining was applied after thin tissue slices (5 µm) were divided using a rotary microtome. The stained sections were examined under a light microscope at 40× magnification to assess glomerular integrity, tubular degeneration or necrosis, inflammatory infiltration, and interstitial alterations.

2.10 Information and Statistical Analysis

Mean ± SEM (n = 6) was used to display all experimental data. Using GraphPad Prism software (version 9.0), one-way ANOVA and Tukey's multiple comparison post hoc test were used to assess statistical differences between groups. A p-value of less than 0.05 ($p < 0.05$) was considered statistically significant.

3. OUTCOMES

3.1 Impact on the Volume of Urine

Administration of folic acid When equated to the normal control group, the 24-hour urine volume significantly decreased (p less than 0.05) at a dose of 250 mg/kg, showing disrupted kidney excretory capacity and possible tubular blockage. Oral supplementation with the ethanolic extract derived from Neolamarckia cadamba leaves (EENC) at concentrations of 200 and 400 mg per kg significantly enhanced urine production in a dose-dependent pattern. The improvement was more evident at the higher concentration, demonstrating better recovery of renal filtration efficiency and osmotic balance, comparable to that observed in the group treated with ascorbic acid (Table 2).

Table 2. EENC effect on Urine Volume in Folic Acid–Induced Nephrotoxicity

Group	Treatment	Urine Volume (mL/24 h)
I	Normal Control (Saline)	8.23 ± 0.15
II	Folic Acid (250 mg/kg)	4.92 ± 0.22*
III	Folic Acid + Ascorbic Acid (250 mg/kg)	7.01 ± 0.19#
IV	Folic Acid + EENC (200 mg/kg)	6.88 ± 0.16#
V	Folic Acid + EENC (400 mg/kg)	7.93 ± 0.17#

*Values are Mean ± SEM (n is equal to 6); *p less than 0.05 vs. control, *p less than 0.05 vs. folic acid group.*

3.2 Effect on Body Weight

Rats given folic acid showed a notable reduction in body weight, indicating systemic toxicity and reduced renal performance. Oral administration of EENC significantly increased body weight in a way that was dose-dependent, suggesting attenuation of folic acid–induced systemic toxicity and restoration of physiological balance. The 400 mg/kg EENC group showed body weight recovery nearly equivalent to the ascorbic acid group (Table 3).

Table 3. EENC effect on Final Body Weight of Rats

Group	Treatment	Final Body Wt. (g)
I	Normal Control (Saline)	180.33 ± 3.56
II	Folic Acid (250 mg/kg)	142.66 ± 4.78*
III	Folic Acid + Ascorbic Acid (250 mg/kg)	165.28 ± 4.42#
IV	Folic Acid + EENC (200 mg/kg)	172.45 ± 3.97#
V	Folic Acid + EENC (400 mg/kg)	178.82 ± 3.75#

*Values are Mean ± SEM (n is equal to 6); *p less than 0.05 vs. control, *p is less than 0.05 vs. folic acid group.*

3.3 Effect on Serum Creatinine

Serum creatinine levels, a key indicator of glomerular filtration efficiency, were markedly elevated (p less than 0.05) in Rats treated with folic acid were shown to have renal impairment when equated to the normal control. In a dose-dependent way, co-treatment with EENC dramatically decreased creatinine levels. The 400 mg/kg doses restored creatinine concentration close to normal values, demonstrating effective nephroprotection (Table 4).

Table 4. EENC effect on Serum Creatinine Levels

Group	Treatment	Serum Creatinine (mg/dL)
I	Normal Control (Saline)	0.78 ± 0.03
II	Folic Acid (250 mg/kg)	2.65 ± 0.12*
III	Folic Acid + Ascorbic Acid (250 mg per kg)	1.15 ± 0.07#
IV	Folic Acid + EENC (200 mg/kg)	1.23 ± 0.06#
V	Folic Acid + EENC (400 mg/kg)	0.92 ± 0.04#

*Values are Mean ± SEM (n equal to 6); *p less than 0.05 vs. control, #p less than 0.05 vs. folic acid group.*

3

.4 Effect on Blood Urea Nitrogen (BN)

As shown in Table 5, BUN levels were markedly elevated in rats administered folic acid, reflecting reduced glomerular filtration and nitrogenous waste accumulation. EENC administration significantly attenuated

this increase in a dose-dependent fashion. The 400 mg per kg EENC group demonstrated BUN values closely approaching those of the control, indicating improved nitrogen excretion and renal function.

Table 5. Effect of EENC on Blood Urea Nitrogen (BUN)

Group	Treatment	BUN (mg/dL)
I	Normal Control (Saline)	16.75 ± 0.65
II	Folic Acid (250 mg/kg)	49.32 ± 1.87*
III	Folic Acid + Ascorbic Acid (250 mg/kg)	23.89 ± 0.92#
IV	Folic Acid + EENC (200 mg/kg)	25.43 ± 1.02#
V	Folic Acid + EENC (400 mg/kg)	18.77 ± 0.84#

*Value are Mean ± SEM (n equal to 6); **p less than 0.05 vs. control, #p less than 0.05 vs. folic acid group.*

3.5 Effect on Creatinine Clearance

Creatinine clearance, a key marker reflecting glomerular filtration efficiency (GFR), exhibited a pronounced decrease in rats administered folic acid, demonstrating significant disruption of normal renal performance. Treatment with the ethanolic extract of Neolamarckia cadamba (EENC) led to a progressive, dose-related enhancement in clearance values, implying restoration of filtration capacity and functional recovery of the nephron (Table 6).

Table 6. Effect of EENC on Creatinine Clearance

Group	Treatment	Creatinine Clearance (mL/min)
I	Normal Control (Saline)	0.88 ± 0.05
II	Folic Acid (250 mg/kg)	0.41 ± 0.02*
III	Folic Acid + Ascorbic Acid (250 mg/kg)	0.73 ± 0.04#
IV	Folic Acid + EENC (200 mg/kg)	0.68 ± 0.03#
V	Folic Acid + EENC (400 mg/kg)	0.82 ± 0.04#

*Values are Mean ± SEM (n = 6); *p less than 0.05 vs. control, #p less than 0.05 vs. folic acid group.*

3.6 Effect on Antioxidant Enzyme Level

(a) Glutathione Peroxidase (GPx) Activity

Folic acid administration led to a marked reduction in GPx activity, indicating oxidative stress–induced depletion of antioxidant enzymes. Treatment with EENC significantly restored GPx action in a dose-dependent manner, suggesting enhanced detoxification of hydrogen peroxide and lipid peroxides. The 400 mg/kg dose demonstrated near-normal enzymatic activity (Table 7a).

(b) Reduced Glutathione (GSH) Levels

Similarly, folic acid–The renal GSH concentration of treated rats significantly decreased in comparison to to the control group, reflecting compromised cellular redox balance. EENC administration dose-dependently restored GSH levels, with the 400 mg/kg group achieving values nearly equivalent to the normal control, indicating protection against oxidative damage (Table 7b).

Table 7a. Effect of EENC on Glutathione Peroxidase (GPx) Activity

Group	Treatment	GPx (U/mg protein)
I	Normal Control (Saline)	8.11 ± 0.21
II	Folic Acid (250 mg/kg)	4.09 ± 0.17*
III	Folic Acid + Ascorbic Acid (250 mg/kg)	7.45 ± 0.24#
IV	Folic Acid + EENC (200 mg/kg)	6.98 ± 0.19#
V	Folic Acid + EENC (400 mg/kg)	7.92 ± 0.16#

Table 7b. Effect of EENC on Reduced Glutathione (GSH) Levels

Group	Treatment	GSH (µmol/mg protein)
I	Normal Control (Saline)	12.55 ± 0.42
II	Folic Acid (250 mg/kg)	5.77 ± 0.31*
III	Folic Acid + Ascorbic Acid (250 mg/kg)	10.23 ± 0.37#
IV	Folic Acid + EENC (200 mg/kg)	9.76 ± 0.34#
V	Folic Acid + EENC (400 mg/kg)	11.98 ± 0.39#

*Values are Mean ± SEM (n = 6); *p less than 0.05 vs. control, #p less than 0.05 vs. folic acid group.*

3.7 Histopathological Observations

Histopathological analysis of renal tissues correlated well with the biochemical findings (Figure 1).

- **Group I (Normal Control):** Displayed normal renal histology with intact glomeruli, well-defined Bowman's capsules, and preserved tubular architecture.
- **Group II (Folic Acid):** Showed severe pathological alterations including tubular necrosis, epithelial desquamation, glomerular congestion, and interstitial inflammation.
- **Group III (FA + Ascorbic Acid):** Exhibited moderate recovery with partial regeneration of renal tubules and reduced inflammatory infiltration.
- **Group IV (FA + EENC 200 mg/kg):** Demonstrated mild tubular degeneration and noticeable restoration of epithelial integrity.
- **Group V (FA + EENC 400 mg/kg):** Displayed nearly normal histoarchitecture with well-preserved glomeruli and minimal pathological lesions, indicating substantial nephroprotective potential of EENC at higher doses.

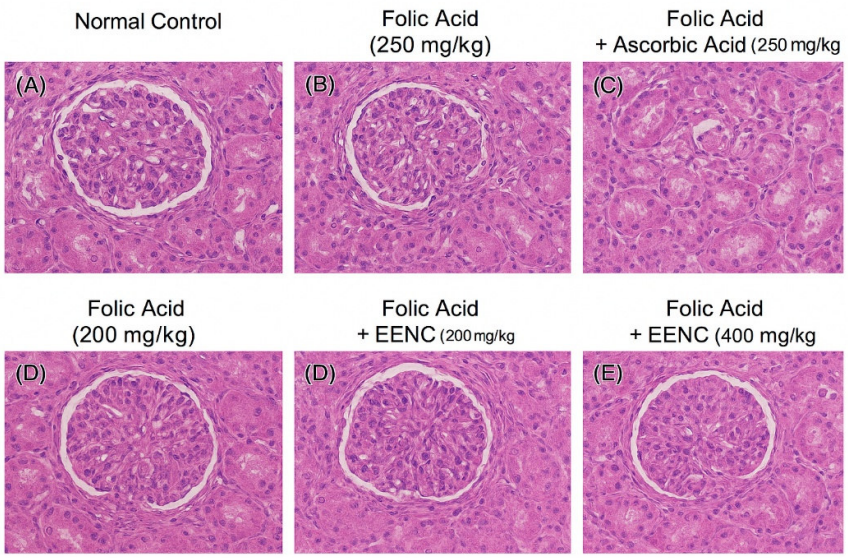

Figure 1. Representative histological sections of kidney tissues stained with H&E (40× magnification) showing protective effects of EENC against folic acid–induced renal damage.

4. DISCUSSION

The current study showed that the ethanolic extract of *Neolamarckia cadamba* leaves (EENC) provides significant protection against folic acid–induced nephrotoxicity in Wistar ratsRenal damage caused by folic acid is typically associated with the accumulation of folate crystals in the tubular structures of the kidney, which triggers oxidative stress, cell death, and inflammatory responses [21]. These pathological changes lead to elevated serum creatinine and BUN concentrations, reflecting reduced glomerular filtration efficiency and compromised kidney function [22].

Treatment with EENC significantly reversed these biochemical alterations. The extract's nephroprotective effects can be ascribed to its abundance of phenolic chemicals and flavonoids, which have potent

free-radical scavenging capabilities. Prior research has shown that flavonoids like quercetin and kaempferol mitigate oxidative injury by inhibiting lipid peroxidation and restoring antioxidant enzyme activities [23].
The observed improvement in antioxidant enzyme levels (GSH, GPx) confirms the role of oxidative stress modulation in nephroprotection. GSH acts as a primary intracellular antioxidant, while GPx catalyzes the reduction of hydrogen peroxide, protecting renal tissue from oxidative injury [24]. Restoration of these enzymes in EENC-treated groups suggests enhanced redox defense.

Histopathological analysis corroborated the biochemical findings, showing recovery of glomerular and tubular architecture in EENC-treated rats. The existence of bioactive metabolites such tannins, triterpenoids, and alkaloids could also contribute to membrane stabilization and anti-inflammatory effects [25].

The observed nephroprotective potential of *N. cadamba* aligns with previous studies reporting its antioxidant and hepatoprotective properties [10,13,14]. The dose-dependent efficacy observed in this study suggests that 400 mg/kg EENC provides optimal protection comparable to the reference standard ascorbic acid.
Mechanistically, the nephroprotection may involve:

1. **Antioxidant action:** Elimination of reactive oxygen species (ROS) coupled with activation of internal antioxidant mechanisms such as glutathione (GSH) and glutathione peroxidase (GPx).
2. **Anti-inflammatory effects:** Modulation of cytokine release and inhibition of renal tubular necrosis.
3. **Membrane stabilization:** Prevention of lipid peroxidation and preservation of cellular integrity.

Collectively, these mechanisms indicate that EENC mitigates folic acid–induced renal damage by restoring biochemical balance and cellular architecture.

5. CONCLUSION

The current investigation offers compelling experimental proof that the ethanolic extract of *Neolamarckia cadamba* leaves exerts significant nephroprotective effects against folic acid–induced nephrotoxicity in rats. The protective effect is associated with improved renal function markers, enhanced antioxidant enzyme activity, and histological recovery.

These findings scientifically validate the traditional use of *N. cadamba* in renal and oxidative disorders. Further studies aimed at isolating active constituents and elucidating molecular pathways are warranted to establish its potential as a natural nephroprotective agent.

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