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PHARMACOLOGICAL INVESTIGATION OF THE METHANOLIC EXTRACT OF *COCCINIA GRANDIS* LEAVES FOR NEPHROPROTECTIVE ACTIVITY

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ABSTRACT: The nephroprotective activity of the methanolic extract of *Coccinia grandis* (MECG) leaves was evaluated against acetaminophen-induced nephrotoxicity in Wistar albino rats. Wistar albino rats (150–200 g) were divided into six groups, and nephrotoxicity was induced using acetaminophen (750 mg/kg) administered on alternate days for 10 days. MECG was administered at doses of 125, 250, and 500 mg/kg, while N-acetylcysteine (140 mg/kg) served as the reference standard. Biochemical parameters including serum urea, creatinine, uric acid and antioxidant activity were assessed, along with histopathological examination. All treatment groups showed significant improvement in urine volume and body weight compared to the toxic control. The MECG-500 mg/kg group demonstrated the most pronounced effect ($p < 0.001$), restoring urine volume to approximately 9.70 mL, close to the normal baseline of 10.85 mL, while the reference group reached 10.81 mL. Lower MECG doses produced dose-dependent improvements. Histopathological analysis further confirmed reduced kidney damage in MECG-treated groups. Overall, MECG, particularly at 500 mg/kg, exhibited strong nephroprotective activity against acetaminophen-induced kidney injury.

INTRODUCTION: The kidneys play a crucial role in maintaining homeostasis by filtering metabolic waste, regulating electrolytes, and balancing fluid levels [1]. Exposure to toxins, drugs, or metabolic disturbances can impair renal function, leading to structural and biochemical alterations. Experimental models, including *in-vitro* antioxidant assays and *in-vivo* nephrotoxic models, are widely used to evaluate the protective effects of medicinal plant extracts [2, 3]. Acetaminophen (N-acetyl-p-aminophenol; APAP) is a commonly used and generally safe analgesic and antipyretic drug, but overdose is a major cause of drug-induced toxicity.

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At high doses, APAP is metabolized into the reactive compound N-acetyl-p-benzoquinone imine (NAPQI) [4]. Normally, NAPQI is detoxified by glutathione (GSH), but excessive intake depletes GSH, allowing NAPQI to bind cellular proteins and trigger lipid peroxidation. This results in oxidative stress, inflammation, and cellular injury [5]. Although less frequent than liver injury, N-acetyl-p-aminophenol overdose can still cause nephrotoxicity, including tubular necrosis, elevated creatinine, reduced glomerular filtration, & acute renal failure [6, 7].

Coccinia grandis, commonly known as ivy gourd, is a widely used medicinal plant in traditional systems of medicine across Asia. Its leaves are rich in bioactive compounds such as flavonoids, alkaloids, tannins, and phenolic constituents, which are known for their strong antioxidant and anti-inflammatory properties [8]. Oxidative stress and inflammation are major contributors to kidney damage, leading to conditions such as acute kidney injury and chronic nephrotoxicity [9]. Because of this, natural plant-derived agents with potent antioxidant capacity have gained significant interest as potential nephroprotective candidates. Exploring the pharmacological potential of *C. grandis* leaves may therefore provide valuable insights into their therapeutic benefits and their possible role in safeguarding renal function [10, 11, 12].

This study aims to investigate the nephroprotective potential of *Coccinia grandis* leaves extract through comprehensive *in-vivo* assessments, focusing on their nephroprotective activity, biochemical responses, and histopathological improvements. The findings may contribute to the development of safer, plant-based therapeutic agents for the prevention and management of kidney disorders.

MATERIALS AND METHODS:

Collection and Authentication of Plant: The *Coccinia grandis* plant was collected from the medicinal garden of Rohilkhand Medical College, Bareilly, during the month of January- 2023. The collected leaves were dried under shade and crushed to coarse powder with mechanical grinder.

Plant authentication is the process of identifying a plant species. The plant was authenticated by Dr. Alok Srivastav, Associate Professor, Department of Plant Science, MJP Rohilkhand University, Bareilly (U.P.), India. The voucher specimen of plant was DPS/MJPRU/04.

Soxhlet Extraction Procedures: The fresh leaves were wash and dry at room temperature. All leaves dry (after two weeks) & crushed with the help of in mortars & pestles. The powdered material was extracted by Soxhlet apparatus using the solvents for petroleum ether, ethanol and methanol.

The extraction process was done at temperature (40-60 °C) for 6 hours. The concentrated product was collected and stored in refrigerator for further experimental analysis [13].

Investigation of Preliminary Phytochemical Studies: The various extracts of *Coccinia grandis* (Methanol, ethanol and petroleum ether) obtained were subjected to qualitative analysis to test the presence of various phytochemical constituents like alkaloids, carbohydrates, glycosides, flavonoids, steroids, aminoacid, phenols, proteins, tannins *etc* [14].

Pharmacological Activity

Experimental Animals: According to CPCSEA, male and female Wistar Albino rats weighing 150–200 grammes were purchased from an authorized breeder. With six rats per cage, the animals were kept in polypropylene cages with conventional settings, which included a 12 hour light and 12-hour dark cycle, 23 ± 5° C, and 40–60% humidity.

Ad libitum water and the usual rat food were given. The animals in each group are distributed randomly, and the CPCSEA criteria are also adhered to. The Institutional Animal Ethical Committee of Deshpande Laboratory in Bhopal, Madhya Pradesh, gave its approval to the experimental protocol (CPCSEA No. 1582/PO/Re/ S/11/CPCSEA).

Acute Toxicity Studies (Safety Evaluation) of CG Extract: The acute oral toxicity was carried out as per the OECD guidelines no. 423. For acute toxicity studies, 3 animals of a single sex had been selected for acute toxicity and the dose 5, 50, 300 and 2000mg/kg body weight of extract was selected.

Methanolic extract of *Coccinia grandis* was found to be safe to dose levels of 2000mg/kg per oral. The LD_{50} calculation was done as per Karber's method and 1/4, 1/8 and 1/16 dose was selected for animal study [15].

Experimental Induction of Nephrotoxicity: The rats were given dosages of 125, 250, and 500 mg/kg b.w. Oral gavage is used to administer them orally. Animals were randomly divided into six groups of which six animals in each group [16]. Group II, III, IV V and VI were administered with acetaminophen (APAP) suspension (750 mg/kg, p.o) for three alternative days for 10 days.

TABLE 1: EXPERIMENTAL INDUCTION OF NEPHROTOXICITY [17]

Animal group	Treatment
Group I	Normal saline 0.9% NaCl (control) daily for 10 days
Group II	Toxic and treated with acetaminophen (APAP) (750 mg/kg, p.o) suspended in 1% CMC three alternative

	days for 10 days.
Group III	Served as standard group and was treated as 140 mg/kg of N-acetyl cysteine orally for 10 days + acetaminophen (APAP) 750 mg/kg
Group IV	*Coccinia grandis* methanol extract (125 mg/kg, p.o) +Acetaminophen (APAP) 750 mg/kg
Group V	*Coccinia grandis* methanol extract (250 mg/kg, p.o) + Acetaminophen (APAP) 750 mg/kg
Group VI	*Coccinia grandis* methanol extract (500 mg/kg, p.o) + Acetaminophen (APAP) 750 mg/kg

Collection and Analysis of Urine: To avoid infection, metabolic cages were cleaned. Following the final day of dosing, the experimental animals were moved to different metabolic cages.

Urine samples were taken every twenty-four hours. Urine samples were collected, moved to sanitized containers, and combined with an appropriate amount of purified water [18].

The collected urine was mixed with a drop of HCl. Both microbial growth and metal hydrolysis are inhibited by this. After being measured, the collected urine was moved to a sterile, airtight container for the urine analysis.

Using autoanalyzer's and diagnostic kits, the levels of urine glucose, urine creatinine, and urine urea were calculated from the rat urine samples that were obtained.

Estimation of Body Weight: Each animal group was housed in its own cage at the conclusion of the experiment. After removing the food and water, each animal is weighed separately, and the results were recorded [19].

Biochemical Estimation: Using a fine capillary, blood was drawn via retro-orbital vein puncture and placed in an anticoagulant tube, then allowed to stand at 37°C for 30 minutes before the serum was separated and centrifuged for biochemical analysis, including the assessment of Blood Urea Nitrogen (BUN), estimation of uric acid, and estimation of creatinine by kits methods [20].

$$\text{Creatinine clearance} = \text{Urinary creatinine} / \text{Serum creatinine} \times \text{vol. of urine ml/min} / 1.73\ m^2$$

$$\text{Urinary creatinine} = \text{Abs. of test} / \text{Abs. of standard} \times \text{Conc. of standard}$$

Kidney Homogenate Analysis: On 11th day, animals were sacrificed by chloroform entrapment. The abdomen was opened to remove both kidneys and washed in 0.9% cooled saline, kept on ice, one kidney stored in 10% formalin for histopathology study. Another one homogenized in cold phosphate buffer (0.1 M, pH 7.4).

The post-mitochondrial supernatant (PMS), which was produced after centrifuging the homogenates for 10 minutes at 4°C at 10,000 rpm, was used to quantify lipid peroxidation.

One additional quantity of the homogenized supernatant was centrifuged at 17,000 rpm for one hour at 4°C. The resulting supernatant was used to further quantify SOD, CAT, and GSH 21. SOD CAT, and GSH were measured in nmoles/mg of protein.

Histopathological Study: Kidneys had been eliminated and glued in 10% formalin for histopathological assessment. Then it is implanted in paraffin and sections were stained with hematoxylin and eosin (H&E) [22].

Statistical Analysis: Results were expressed as mean ± S.D. Total variation, present in a set of data were estimated by t-test. P-value lower than 0.05 was considered to be significant. MS excel 2016 was used for calculation of t-test [23].

RESULTS AND DISCUSSION:

Extraction of *Coccinia grandis* Leaves: The percentage yields of different extracts of *Coccinia grandis* leaves were determined to evaluate the efficiency of the extraction process.

The methanolic extract showed the highest yield at 9.87% w/w, followed by the ethanolic extract at 7.11% w/w. The petroleum ether extract yielded the lowest amount, at 5.62% w/w.

These results indicate that methanol was the most effective solvent for extracting phytoconstituents from *C. grandis* leaves, while petroleum ether extracted comparatively fewer components.

FIG. 1: EXTRACTION OF *COCCINIA GRANDIS* IN DIFFERENT SOLVENTS

Preliminary Phytochemical Study: Preliminary phytochemical screening of *Coccinia grandis*, revealed the presence of following phytoconstituents.

TABLE 2: PHYTO-CHEMICAL SCREENING OF DIFFERENT EXTRACTS OF *COCCINIA GRANDIS*

(A) Test for Carbohydrates			
Extract	**Pet. ether**	**Ethanol**	**Methanol**
Molisch's Test	_	+	+
Fehling's	+	+	+
Benedict's test	-	-	-
(B) Alkaloids			
Extract	Pet. ether	Ethanol	Methanol
Meyer's reagent	_	-	+
Dragendroff's reagent	+	+	+
Wagner's reagent		-	-
Hager's reagent	-	+	+
Muroxide test	-	-	-
(C)Test for Amino Acids			
Extract	Pet. ether	Ethanol	Methanol
Millon's Test	_	-	-
Ninhydrine Test	+	-	+
Biuret Test	+	+	+
Xanthoprotein Test	+	-	+
(D) Test for Anthraquinone Glycosides			
Extract	Pet. ether	Ethanol	Methanol
Baljet' s Test	_	+	+
Legal's Test	_	+	+
Borntrager's Test	+	-	+
(E) Test for Tests for Saponins			
Extract	Pet. ether	Ethanol	Methanol
Foam Test	_	+	+
Haemolysis Test	+	+	+
(F) Test for Flavonoids			
Extract	Pet. ether	Ethanol	Methanol
Shinoda test	+	+	+
II	_	-	+
(G) Test for Phytosterols			
Extract	Pet. ether	Ethanol	Methanol
Liebermann-burchard test	+	-	+
Salkowski reactions	_	-	+
(H) Test for Phenolic Compounds and Tannins			
Extract	Pet. ether	Ethanol	Methanol
I	_	+	+
II	_	+	+
III	-	+	+
IV	+	-	+

+ mean present, -mean absent.

Overall, methanol proved to be the most effective extractant for a wide range of phytochemicals, followed by ethanol, while petroleum ether extracted mainly non-polar constituents such as phytosterols and certain alkaloids. These findings support the traditional use of *Coccinia grandis* and highlight the plant's rich phytochemical profile, which may contribute to its pharmacological potential.

Nephroprotective Activity:

Assessment of Urine Volume and Body Weight: The administration of varying doses of the methanolic extract of *Coccinia grandis* produced dose-dependent effects on urine volume and body weight in the experimental subjects.

TABLE 3: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON URINE VOLUME AND BODY WEIGHT

Groups	Drug Treatment	Urine Volume (ml)	Body Weight (gm)
I	Normal Control	10.85±0.223	190.6±3.462
II	Toxic Control	5.90±0.762	123.6±3.688
III	Reference Control	10.81±0.24	182.2±3.131
IV	MECG (125mg/kg)	7.89±0.345	150.6±3.688
V	MECG (250mg/kg)	9.17±0.40	168.6±2.86
VI	MECG(500mg/kg	9.70±0.28	174.8±3.181

TABLE 3A: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON URINE VOLUME

Group's Comparison	t (Urine Volume)	p-value	Significant?
Normal control vs. Toxic control	15.272	0.0001	Yes
Reference control vs. Toxic Control	6.15	0.0001	Yes
MECG (125mg/kg) vs. Toxic Control	2.38	0.0387	Yes
MECG (250 mg/kg) vs. Toxic Control	3.80	0.0035	Yes
MECG (500 mg/kg) vs. Toxic Control	4.68	0.0009	Yes

TABLE 3B: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON BODY WEIGHT

Group	t (Body Weight)	p-value	Significant?
Normal control vs. Toxic control	32.445	0.0001	Yes
Reference control vs. Toxic Control	12.11	<0.0001	Yes
MECG (125mg/kg) vs. Toxic Control	5.18	0.0004	Yes
MECG (250 mg/kg) vs. Toxic Control	9.64	<0.0001	Yes
MECG (500 mg/kg) vs. Toxic Control	10.51	<0.0001	Yes

All treatment groups, including the reference control, MECG-125 mg/kg, MECG-250 mg/kg, and MECG-500 mg/kg, showed statistically significant improvements in both urine volume and body weight when compared to the toxic control group.

The MECG-500 mg/kg group exhibited highly significant improvement ($p < 0.001$) in both parameters, indicating strong nephroprotective efficacy. Urine volume in the normal control group was approximately 10.85 mL, representing a healthy baseline, while the toxic control group showed a marked reduction to about 5.90 mL due to APAP-induced kidney damage. The reference control group restored urine volume to around 10.81 mL, demonstrating complete protection. The MECG-125 mg/kg and MECG-250 mg/kg groups showed dose-dependent increases toward normal values, whereas the MECG-500 mg/kg group achieved an almost complete restoration, with urine volume reaching approximately 9.70 mL. Together, these findings indicate that the reference control and MECG-500 mg/kg treatments were the most effective in normalizing renal function.

Assessment of Serum Biochemical Parameters: In evaluating the nephroprotectiveactivity of the methanolic extract of *Coccinia grandis,* serum biochemical parameters serve as vital indicators of renal function and damage.

Key markers such as serum creatinine, blood urea nitrogen (BUN), and uric acid were routinely measured to assess kidney function, as their elevated levels typically reflect impaired renal clearance and nephrotoxicity.

TABLE 4: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON SERUM CREATININE LEVEL, SERUM BLOOD UREA NITROGEN (BUN) LEVEL AND URIC ACID

Groups	Drug Treatment	Serum Creatinine (mg/dl)	Serum Blood urea nitrogen (BUN) (mg/dl)	Uric acid (mg/dl)
I	Normal Control	0.65± 0.043	22.65±0.521	3.65±0.026
II	Toxic Control	5.12± 0.321	57.42±3.621	1.08±0.027
III	Reference Control	0.77± 0.011	23.45±0.65	2.64±0.028
IV	MECG (125mg/kg)	1.56±0.243	31.67±0.73	1.09±0.65
V	MECG (250mg/kg)	1.28±0.521	29.67±0.76	1.13±0.07
VI	MECG (500mg/kg)	0.86±0.065	24.55±0.55	1.25±0.01

TABLE 4A: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON SERUM CREATININE LEVEL

Group	t (Creatinine)	p-value	Significant
Normal control vs. Toxic control	−13.9	(p < 0.001)	Yes
Reference controlvs. Toxic Control	-13.54	0.00001	Yes
MECG (125mg/kg)vs. Toxic Control	-8.84	0.00001	Yes
MECG (250 mg/kg) vs. Toxic Control	-6.28	0.0001	Yes
MECG (500 mg/kg) vs. Toxic Control	-13.01	0.0000	Yes

TABLE 4B: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON SERUM BLOOD UREA NITROGEN (BUN) LEVEL

Group	t (BUN)	p-value	Significant
Normal control vs. Toxic control	−9.5	(p < 0.001)	Yes
Reference control vs. Toxic Control	-9.23	0.00001	Yes
MECG (125mg/kg) vs. Toxic Control	-6.97	0.00001	Yes
MECG (250 mg/kg)vs. Toxic Control	-7.50	0.00001	Yes
MECG (500 mg/kg) vs. Toxic Control	-8.97	0.00001	Yes

TABLE 4C: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON URIC ACID LEVEL

Group	t (Uric Acid)	p-value	Significant
Normal control vs. Toxic control	68.5	p ≪ 0.001)	Yes
Reference control vs. Toxic Control	40.11	0.00001	Yes
MECG (125mg/kg) vs. Toxic Control	0.02	0.9880	No
MECG (250 mg/kg) vs. Toxic Control	0.67	0.5202	No
MECG (500 mg/kg) vs. Toxic Control	5.90	0.0002	Yes

The methanolic extract of *Coccinia grandis* at 500 mg/kg (MECG-500) and the reference control group demonstrated significant protection across all kidney function parameters, showing marked improvement in serum creatinine, BUN, and uric acid levels. In contrast, the lower doses MECG-125 mg/kg and MECG-250 mg/kg were only partially effective, with reduced efficacy particularly in restoring uric acid levels. While all treated groups showed significant reductions in serum creatinine and BUN, indicating a reversal of renal toxicity, only the reference control and MECG-500 groups produced a statistically significant improvement in uric acid ($p < 0.05$). The MECG-125 and MECG-250 groups did not significantly restore uric acid levels compared to the toxic group, suggesting a dose-dependent nephroprotective effect.

Assessment of Urine Biochemical Parameters: The evaluation of urine biochemical parameters is essential for assessing kidney function and the nephroprotective efficacy of the methanolic extract of *Coccinia grandis*. Key urinary markers, which collectively reflect the kidney's ability to filter and reabsorb substances properly.

TABLE 5: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON CREATININE CLEARANCE (mL/min)

Groups	Drug Treatment	Creatinine Clearance
I	Normal Control	19.80±1.302
II	Toxic Control	5.05±0.445
III	Reference Control	18.265±0.512
IV	MECG (125mg/kg)	11.65±1.784

V	MECG (250mg/kg)	12.56±0.653
VI	MECG (500mg/kg)	17.20±1.146

TABLE 5A: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON CREATININE CLEARANCE

Group	t-value	p-value	Significant
Normal control vs. Toxic control	10.72	0.000001	Yes
Reference control vs. Toxic Control	19.48	<0.000001	Yes
MECG (125mg/kg) vs. Toxic Control	3.59	0.004933	Yes
MECG (250 mg/kg) vs. Toxic Control	9.50	0.000003	Yes
MECG (500 mg/kg) vs. Toxic Control	9.88	0.000002	Yes

Methanolic extract of *Coccinia grandis* (MECG-500 mg/kg) and reference control groups had values closest to normal control, suggesting strong protection or restoration of kidney function.

All treatment groups show statistically significant improvement in creatinine clearance compared to the toxic control group.

Assessment of Oxidative Stress Parameter: The assessment of oxidative stress parameters is crucial to understanding the protective effects of the methanolic extract of *Coccinia grandis* against oxidative damage in nephrotoxicity models. Malondialdehyde (MDA) {nmol/mg} levels are quantified as a marker of lipid peroxidation and oxidative damage to cell membranes.

TABLE 6: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON MALONDIALDEHYDE (MDA)

Groups	Drug Treatment	Malondialdehyde (MDA)
I	Normal Control	7.56±0.232
II	Toxic Control	16.23±2.653
III	Reference Control	7.45±0.853
IV	MECG (125mg/kg)	9.86±0.121
V	MECG (250mg/kg)	8.56±0.743
VI	MECG (500mg/kg)	7.45±0.522

TABLE 6A: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *COCCINIA GRANDIS* (MECG) ON MALONDIALDEHYDE (MDA)

Group's Comparison	t-value	p-value	Significant (p < 0.05)?
Normal control vs. Toxic control	3.26	0.0089	Yes
Reference control vs. Toxic Control	3.28	0.0087	Yes
MECG (125mg/kg) vs. Toxic Control	2.37	0.039	Yes
MECG (250 mg/kg) vs. Toxic Control	2.54	0.030	Yes
MECG (500 mg/kg) vs. Toxic Control	3.21	0.0096	Yes

All treatment groups (including MECG (125mg/kg), MECG (250mg/kg), and MECG (500mg/kg)) showed significant reductions in MDA levels compared to the Toxic Control group, indicating protection against lipid peroxidation.

Assessment of Enzymatic Parameters: Superoxide dismutase (SOD), catalase (CAT), and glutathione peroxidase (GPx) are key enzymes in the body's antioxidant defense system, working together to neutralize harmful reactive oxygen species.

Changes in their activities provide important insights into how the body responds to oxidative stress, as alterations in these enzymes can indicate heightened oxidative damage or adaptive protective mechanisms.

TABLE 7: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* ON SUPEROXIDE DISMUTASE (SOD), CATALASE (CAT) AND GLUTATHIONE PEROXIDISE (GPx)

Groups	Drug Treatment	Superoxide dismutase (SOD) {nmol/mg}	Catalase (CAT) {nmol/mg}	Glutathione peroxidise (GPx) {nmol/mg}
I	Normal Control	20.11±1.631	219.56±1.74	25.56±0.52
II	Toxic Control	7.53±0.423	104.94±0.37	14.48±0.448
III	Reference Control	18.50±0.44	201.45±2.652	21.56±1.78
IV	MECG (125mg/kg)	9.45±0.342	132.11±4.234	14.99±0.43

V	MECG (250mg/kg)	11.89±0.303	158.39±4.091	16.33±0.399
VI	MECG (500mg/kg)	15.84±0.64	180.6±1.575	19.27±1.53

TABLE 7A: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON SUPEROXIDE DISMUTASE (SOD)

Group's Comparison	t (SOD)	p (SOD)	Sig (SOD)
Normal control vs. Toxic control	7.47	0.000021	Yes
Reference control vs. Toxic Control	17.97	<0.000001	Yes
MECG (125mg/kg) vs. Toxic Control	3.53	0.0055	Yes
MECG (250 mg/kg) vs. Toxic Control	8.38	0.000008	Yes
MECG (500 mg/kg) vs. Toxic Control	10.83	0.000001	Yes

TABLE 7B: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON CATALASE (CAT)

Group's Comparison	t (CAT)	p (CAT)	Sig (CAT)
Normal control vs. Toxic control	64.43	<0.000001	Yes
Reference control vs. Toxic Control	36.04	<0.000001	Yes
MECG (125mg/kg) vs. Toxic Control	6.39	0.000079	Yes
MECG (250 mg/kg) vs. Toxic Control	13.01	<0.000001	Yes
MECG (500 mg/kg) vs. Toxic Control	46.76	<0.000001	Yes

TABLE 7C: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON GLUTATHIONE PEROXIDISE (GPx)

Group's Comparison	t (GPx)	p (GPx)	Sig (GPx)
Normal control vs. Toxic control	16.14	<0.000001	Yes
Reference control vs. Toxic Control	3.86	0.0032	Yes
MECG (125mg/kg) vs. Toxic Control	0.82	0.4306	No
MECG (250 mg/kg) vs. Toxic Control	3.08	0.0116	Yes
MECG (500 mg/kg) vs. Toxic Control	3.00	0.0132	Yes

All treatment groups showed significant improvements in the antioxidant enzymes SOD and CAT compared to the toxic group. However, the response of GPx varied across treatments. The methanolic extract of *C. grandis* at 125 mg/kg (MECG-125) did not produce a significant improvement in GPx levels ($p = 0.43$). In contrast, the higher doses MECG-250 and MECG-500 as well as the reference control group, demonstrated significant increases in GPx activity, indicating a dose-dependent enhancement of this antioxidant defense enzyme.

Assessment of Non-Enzymatic Antioxidant Parameter: Reduced glutathione (GSH) is a key intracellular antioxidant that protects cells from oxidative stress by neutralizing free radicals. Evaluating GSH levels helps in understanding the antioxidant potential or toxicity of substances such as plant extracts.

TABLE 8: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON REDUCED GLUTATHIONE (GSH)

Groups	Drug Treatment	Reduced glutathione (GSH) {nmol/mg}
I	Normal Control	21.65±0.662
II	Toxic Control	9.02±0.4532
III	Reference Control	19.67±0.821
IV	MECG (125mg/kg)	10.65±1.174
V	MECG (250mg/kg)	15.56±0.812
VI	MECG (500mg/kg)	17.18±0.6312

TABLE 8A: THE EFFECTS OF THE DIFFERENT DOSES OF METHANOLIC EXTRACT OF *C. GRANDIS* (MECG) ON REDUCED GLUTATHIONE (GSH)

Group	t-value	p-value	Significant (p < 0.05)
Normal control vs. toxic control	15.74	0.0001	Yes
Reference control vs. Toxic Control	11.36	0.0001	Yes
MECG (125mg/kg) vs. Toxic Control	1.30	0.2243	No
MECG (250 mg/kg) vs. Toxic Control	7.03	0.0001	Yes
MECG (500 mg/kg) vs. Toxic Control	10.50	0.0001	Yes

Normal control, Reference control, MECG-250mg/kg, and MECG-500 mg/kg show significantly higher GSH levels compared to the toxic group ($p < 0.05$). The MECG-125 mg/kg group does not show a statistically significant difference ($p = 0.2243$).

Histopathological Studies: Histopathological examination revealed clear differences among the experimental groups. In the normal control group, kidney sections displayed a typical arrangement of nephrotic bundles, with both the cortex and medulla appearing normal. The glomeruli showed well-organized podocytes, and both the proximal and distal convoluted tubules were intact. In contrast, the nephrotoxic group exhibited pronounced pathological changes, including coagulative and diffuse necrosis, severe glomerulonephritis characterized by glomerular condensation and infiltration of inflammatory cells, as well as marked hemorrhage, edema, and narrowing of renal arterioles. The reference control group, treated with N-acetyl cysteine, showed normal kidney histology with no evidence of necrosis, indicating effective protection. The extract-treated groups demonstrated varying degrees of improvement. Kidneys from rats treated with MECG-125 mg/kg and MECG-250 mg/kg exhibited moderate tubular degeneration, mild edema, and necrotic changes with swollen tubular epithelium. In the MECG-500 mg/kg group, moderate signs of regeneration were evident, including chromatolysis in the tubular structures, along with stripping of tubular epithelium and intertubular edema, suggesting partial recovery at higher doses.

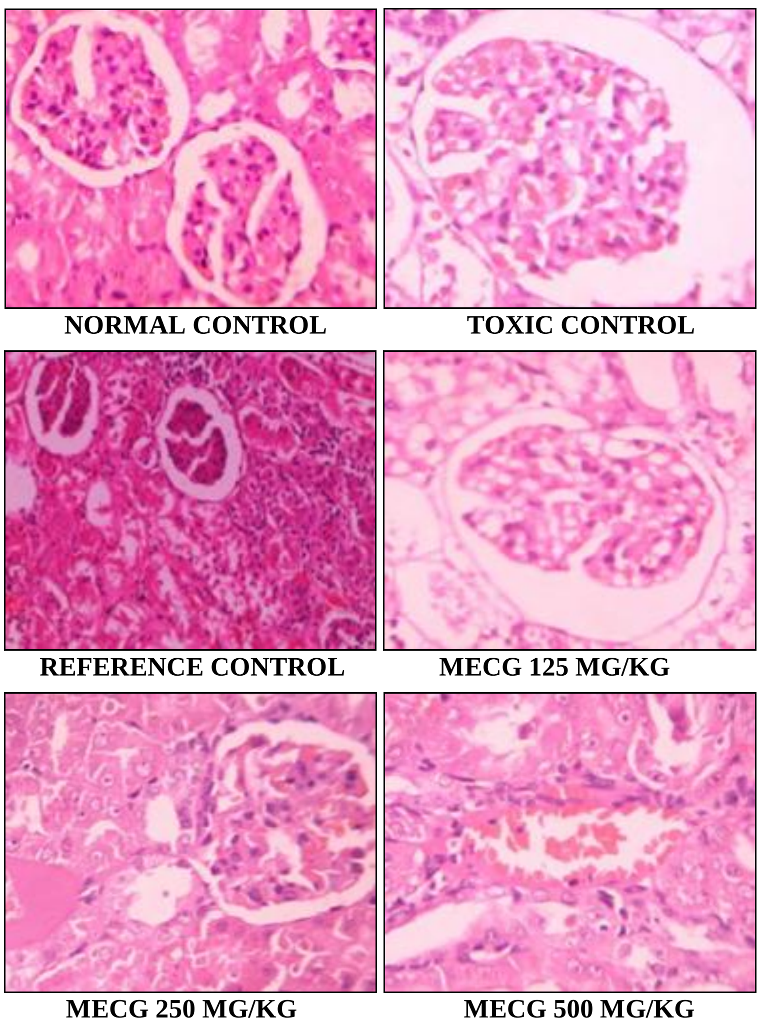

FIG. 2: PHOTOMICROGRAPHS OF KIDNEY TISSUE SECTION

DISCUSSION: Nephrotoxicity is a common clinical condition characterized by a rapid decline in renal function, resulting in elevated serum creatinine and blood urea levels. Although acute renal failure can be managed with limited chemical treatments, many synthetic nephroprotective agents produce adverse effects, increasing interest in traditional medicine for safer alternatives. [24]Various herbs have long been used globally to treat kidney ailments, and ethnomedicinal plants remain valuable for reducing renal damage and delaying the need for dialysis. *Coccinia grandis* leaves contain flavonoids, terpenoids, tannins, alkaloids, saponins, and anthraquinones phytochemicals known for strong antioxidant potential and acute toxicity studies confirm the safety of its methanolic extract. Acetaminophen overdose, though mainly hepatotoxic, can also induce nephrotoxicity through the cytochrome P450–mediated formation of NAPQI. Excess NAPQI depletes glutathione, triggers oxidative stress, and damages renal tubular cells, particularly in the metabolically active S3 segment, where mitochondrial dysfunction, lipid peroxidation, and inflammation contribute to acute tubular necrosis and impaired renal function [25, 26, 27].

In the present study, acetaminophen-treated rats showed significant weight loss, reduced glomerular filtration rate, elevated serum creatinine, increased blood urea nitrogen (BUN), and decreased creatinine clearance, confirming acute renal failure. Administration of *Coccinia grandis* extract (125, 250, and 500 mg/kg) significantly reduced serum creatinine and BUN levels while improving renal function. Acetaminophen toxicity also elevated malondialdehyde (MDA), indicating enhanced lipid peroxidation, whereas *Coccinia grandis* effectively suppressed this rise, demonstrating strong antioxidant protection. Additionally, the extract prevented the depletion of endogenous antioxidant enzymes SOD, CAT, GSH, and GPx whose activities were otherwise reduced by acetaminophen. Restoration of these enzymatic antioxidants suggests that the extract mitigates oxidative stress–mediated renal injury. Overall, the findings confirm that *Coccinia grandis* exerts significant nephroprotective effects against acetaminophen-induced nephrotoxicity.

CONCLUSION: In conclusion, a methanolic extract of *Coccinia grandis* leaves shown statistically significant nephroprotective action. The plant extract's recognized flavonoid concentration and antioxidant qualities may have contributed to its nephroprotective effect. More research on the histology of the liver and spleen is possible, and clinical investigations are necessary to identify the active phytoconstituents with strong nephroprotective effects.

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CONFLICTS OF INTEREST: Nil

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