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ETHNOPHARMACOLOGICAL INVESTIGATION OF SOME MEDICINAL PLANTS FOR THE MANAGEMENT OF NEPHROTOXICITY

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Abstract

Nephrotoxicity poses a significant health challenge, warranting innovative approaches for its management. The leaves of Adhatoda cordifolia (A. cordifolia) and the leaves of Cyathea gigantea (C. gigantea) were meticulously collected from their natural habitats and authenticated by Dr. S. N. Dwivedi, a distinguished authority in botanical sciences. The authentication process ensured the accuracy of plant species identification, enhancing the credibility of subsequent investigations. To harness the therapeutic potential of these plants, a meticulous extraction process was employed. Leaves and seeds of the chosen plants were meticulously gathered, shade-dried to preserve their active constituents, and then processed into a coarse powder using a mechanical grinder. The powdered material underwent filtration through a No. 40 filter, facilitating the separation of coarse particles while retaining essential components. The comprehensive investigation aims to elucidate the bioactive constituents within A. cordifolia and C. gigantea that hold promise in ameliorating nephrotoxicity. Ethnopharmacological insights, combined with rigorous scientific methodologies, form the foundation of this study, potentially offering novel strategies for the management of nephrotoxicity. The botanical knowledge of traditional remedies converges with contemporary scientific rigor, underscoring the significance of ethnopharmacology in unlocking nature's therapeutic secrets for modern healthcare challenges. This research contributes to the expanding body of knowledge that bridges traditional wisdom with contemporary pharmacology, fostering a holistic approach to nephrotoxicity management.

Keywords: Adhatoda cordifolia, Cyathea gigantean, Nephrotoxicity, Ethnopharmacology

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Introduction

Medicine plants have natural active substances that can heal disease or ease suffering. It is well known that the majority of developing countries provide the primary medical care for residents of impoverished countries. The medicinal qualities of a plant may be due to the photochemical's anti-oxidant, antibacterial, and antipyretic activities. Since they are believed to be non-toxic, herbs have historically been used by the general public and/or traditional medicine practitioners worldwide to cure a number of ailments. Despite numerous cases of toxicity connected to the use of herbs, neither the general public nor organisations representing traditional medicine professionals have recognised the potential toxicity of herbs. More and more medications are being produced utilising medicinal plants as their main basic ingredients.[1,2]

Natural goods are becoming an essential component of the human health care system due to the growing public concern about the toxicity and side effects of contemporary medications. There is also an understanding that natural remedies are safer and that allopathic pharmaceuticals are frequently ineffectual in treating a variety of ailments. Before humans arrived on the planet, medicinal plants already existed. Only because plants are so essential to maintaining man's survival on this planet is it even conceivable for him to live. Since the dawn of civilization, man has also raised herbs for medical purposes in addition to food crops.[3]

The field of herbal medicine has experienced exponential expansion during the past several decades. Due to its natural origins and few negative effects, it is becoming more and more popular in both developing and developed nations. In therapeutic usage are more than 700 mono and polyherbal preparations made from more than 100 plants in the form of decoction, tincture, pills, and capsules. Regarding the safety and effectiveness of these preparations, there are several restrictions. The active ingredients in herbal remedies are not well understood, and there is a paucity of data on their toxicity and negative effects. There is no information available on pharmacokinetics and bioavailability. The sale of these, which are offered as over-the-counter medicines, is not obliged to include packet inserts with information on safety and warning. The general public should be aware of the dangers of unproven and uncontrolled treatments. The quality and acceptance of herbal preparations as medicinal agents will be improved by the selection of plant material based on quality, standardisation of preparation techniques, and enforcement of

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regulations on proper labelling. Other steps to support this field of study include documentation of research papers in journals and the availability of information on websites.[4,5]

A herb is a plant or part of a plant that is valued for its healing, alluring, or tasty capabilities. Herbs may be compared as biosynthetic chemical factories that produce a wide range of chemicals. Plant fragments or unpurified plant extracts with a range of active compounds that usually have synergistic effects are used to create herbal cures or pharmaceuticals. Although any part of the plant can be used to make them, the most common ones are the leaves, roots, bark, seeds, and flowers. They can be inhaled, swallowed, breathed, eaten, or administered topically to the skin. Herbal medicine often contains natural plant biochemicals, many of which support the plant's medicinal capabilities.

The aim of this ethnopharmacological investigation is to evaluate the potential of selected medicinal plants for the management of nephrotoxicity.

2. Collection of plant material

The leaves of A. cordifolia and leaves of Cyathea gigantea selected plant were collected from natural habitat and authenticated by Dr. S. N. Dwivedi, Professor and Head of the Department of Botany at Janata PG College, APS University, Rewa, M.P. The specimens were brought to our department under the voucher number JC/Bot/2021/AC-326."

3. Preparation of plant powder

The extract was made using the leaves and seeds of the chosen plant. The plant's leaves and seeds were gathered, dried in the shade, then ground into a coarse powder using a mechanical grinder. The powder was put through filter No. 40 and then stored for future use in an airtight container.

4.1 PHARMACOLOGICAL SCREENING[105-124]

4.12.1 Acute toxicity studies

Studies on the acute oral toxicity of B. sensitivum's whole plant extract have already been published, hence none were conducted. 5000 mg/kg of CE was used in an earlier investigation by Anidya et al.105 as a higher dosage in albino rats. Therefore, a dose of one tenth of this, 500 mg/kg (a larger dose), and a lower dose of 250 mg/kg were chosen for the current investigation.

4.12.2 Evaluation of Nephroprotective Activity -

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The drug-induced toxicity models each utilised 30 albino rats. Five groups of six animals each, referred known as Group I, II, III, IV, and V, were created. Animals from groups I and II were used as controls and as a toxic control, respectively. Drugs that cause toxicity were administered to the rats in Groups II through V. Additionally to conventional medication, group III, IV, and V animals were given low doses of CE (250 mg/kg) and high doses of CE (500 mg/kg), respectively.

4.12.3 Gentamicin (GM) induced nephrotoxicity[6-7]

Table 4.1 : Grouping of Animal in gentamicin (GM) induced nephrotoxicity model

S.No	Group	Treatment
1	**Group-I**	**Normal Saline 1ml /Day, For 8 days**
2	**Group –II**	**GM 100mg/Kg for 8 days,i.p.**
3	**Group-III**	**GM +Quercetin 50 mg/Kg for 8 days**
4	**Group-IV**	**GM + Extract 250 mg/Kg for 8 days**
5	**Group-V**	**GM + Extract 500 mg/Kg for 8 days**

4.12.3 Parameters studied in drug induced nephrotoxicity and urolithic models[8,9]

- Urine samples lasting 24 hours were taken after the therapy period. The levels of total protein, albumin, sodium, potassium, calcium, and magnesium were then evaluated in the urine of animals that had been given nephrotoxic drugs, as opposed to rats that had been given calculi. The rats in all groups were put to sleep with 80 mg/kg of ketamine hydrochloride after the urine samples were taken. Under very light anaesthesia, blood was drawn from the tail vein to measure several haematological parameters. Serum was

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separated and examined for total protein, albumin, sodium, potassium, calcium, magnesium, blood urea nitrogen (BUN), uric acid, and creatinine levels in CDDP and GM-induced nephrotoxicity models for the determination of various biochemical parameters. In EG-induced urolithic rats, the levels of total protein, albumin, calcium, phosphate, magnesium, BUN, uric acid, and creatinine were measured.After administering the last dosage of the toxin, the rats were slaughtered, and the separated kidneys were weighed, homogenised, and used to estimate the levels of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), reduced glutathione (GSH), and malondialdehyde (MDA).

5.4 Acute toxicity study[10]

Acute toxicity studies were conducted in accordance with OECD Guideline 423 using acetone and aqueous extracts of Adina cordifolia, ethanol and aqueous extracts of Cyathea gigantea, and acetone and aqueous extracts of P. americana based on the extractive value and phytochemical results. The findings revealed that at a dosage level of 5000 mg/kg, there was no mortality among the animal groups receiving graded doses, and they exhibited neither toxicity or behavioural alterations. This result implies that all the extracts belonged to category 5 (>5000) and were either safe for rats or non-toxic to them. Table 5.6, Table 5.7, and Table 5.8 display the findings.

Table 5.6: Acute toxicity studies of extracts of *A. cordifolia*

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S No.	No. of Animals	Extract	Dose mg/kg	Results
1	3	AEAC	5	No death
2	3		50	No death
3	3		300	No death
4	3		2000	No death
5	3		5000	No death
6	3	AQEAC	5	No death
7	3		50	No death
8	3		300	No death
9	3		2000	No death
10	3		5000	No death

LD_{50}- 5000mg/kg , ED_{50}- 500mg/kg

Table 5.7: Acute toxicity studies of extracts of *Cyathea gigantea*

S No.	No. of Animals	Extract	Dose mg/kg	Results
1	3	AECG	5	No death
2	3		50	No death
3	3		300	No death
4	3		2000	No death
5	3		5000	No death
6	3	AQECG	5	No death
7	3		50	No death
8	3		300	No death
9	3		2000	No death
10	3		5000	No death

LD_{50}- 5000mg/kg , ED_{50}- 500mg/kg

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Table 5.8: Acute toxicity studies of extracts of *P. Americana*

S No.	No. of Animals	Extract	Dose mg/kg	Results
1	3	AEPM	5	No death
2	3		50	No death
3	3		300	No death
4	3		2000	No death
5	3		5000	No death
6	3	AQEPM	5	No death
7	3		50	No death
8	3		300	No death
9	3		2000	No death
10	3		5000	No death

LD_{50}- 5000mg/kg

ED_{50}- 500mg/kg

5.7 In vivo pharmacological studies

Various general, urine, blood, serum, and kidney homogenate parameters were used to examine the nephroprotective effect of a mixture of plant extracts at concentrations of 250 mg/kg (low dose) and 500 mg/kg (high dose) against gentamicin-induced nephrotoxicity in Wistar albino rats.

5.7.1 Gentamicin (GM)-induced nephrotoxicity

After the experiment was complete, "results from the control and experimental groups of animals were collected, and Table 5.9 showed the impact of CE on the general parameters of GM-induced

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nephrotoxicity in each group. Before the trial began, body weight was noted. The results showed that the body weight of the animals in group II was significantly (p0.01) decreased after treatment when compared to the control group, whereas the body weight of the animals in group III, group IV, and group V were significantly increased when compared to the animals in the toxic control group (p0.001, p0.01, and p0.01, respectively). When compared to the normal control group, it was shown that the kidney weight in the GM-treated group was considerably higher (p 0.001). Animals receiving a combination of quercetin (p 0.00), a moderate dosage of CE (p 0.01), and a high dose of CE (p 0.001) showed a significant decrease in kidney weight. In compared to the control group, the 24-hour urine volume in the GM-treated group was found to be considerably (p 0.01) lower. Rats given GM treatment produced more urine when quercetin, low doses of CE, and high doses of CE were supplemented. However, only mice which also received 500 mg/kg of CE showed a substantial (p0.05) increase in water consumption. Comparing animals co-treated with extract/standard to the GM-treated group, urine pH was determined to be 6.60.05, which showed no significant (p>0.05) alterations in urinary pH.[11-13]

Table 5.9: Effect of CE on general parameters in GM-induced nephrotoxicity

Parameters Studied (Unit)	Group I Normal control	Group II GM 100 mg/kg	Group III GM+QTN 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
Change in body wt. (g)	2.96±0.43	1.48±0.11^{**a}	3.26± 0.14^{***b}	2.53± 0.17^{**b}	2.50± 0.22^{**b}
Kidney wt. (g)	0.64±0.00	0.97±0.05^{***a}	0.70±0.08^{***b}	0.73±0.00^{**b}	0.71±0.00^{***b}
Water intake (mL/24 hr)	12.36±0.57	14.54±0.76^{ns}	17.36±0.82^{ns}	17.36± 0.82^{ns}	17.88±0.86^{*b}
Urine volume (mL/24 hr)	7.74±0.15	5.73± 0.22^{**a}	7.63±0.30^{**b}	7.26±0.16^{**b}	7.84± 0.09^{***b}
Urine pH	6.8±0.04	6.6±0.05^{ns}	6.8±0.03^{ns}	6.7±0.05 ^{ns}	6.8±0.05 ^{ns}

"GM: gentamicin, QTN: quercetin, CE: Combination of Plant Extract. Values are expressed in mean ± standard error of mean (n=6), *p<0.05, **p<0.01, ***p<0.001 ^{a} significant compared o

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control group (group I), [b]significant compared with GM-induced group (group II), [ns] not significant."

5.8 Effect of CE on urinary total protein and albumin levels in experimental Animal

Urinary protein and albumin excretion in GM-treated rats significantly increased (p 0.01). However, only in rats co-treated with quercetin or a high dose of CE, as compared to group II rats, were substantial (P0.01) reductions in albuminuria found. Animals co-treated with CE/quercetin considerably (P0.01) decreased the incidence of proteinuria.

Table 5.10: Effect of CE on urinary total protein and albumin levels in GM-induced nephrotoxicity

Urinary parameters (Unit)	Group I Normal control	Group II GM 100 mg/kg	Group III GM+QTN 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
Total protein (g/dL)	3.66 ±0.01	4.51±0.02** a	3.56±0.01** b	4.08±0.04** b	3.58±0.05** b
Albumin (g/dL)	0.76±0.02	0.83±0.06** a	0.63±0.01** b	0.81±0.07ns	0.72±0.01** b

"GM: gentamicin, QTN: quercetin, CE: Combination of Plant Extract. Values are expressed in mean ± standard error of mean (n=6), *p<0.05, **p<0.01, ***p<0.001 [a] significant compared o control group (group I), [b]significant compared with GM-induced group (group II), [ns] not significant."

5.9 Effect of CE on urinary electrolyte levels in experimental animal

It was discovered that group II animals had significantly greater urinary excretion of calcium and magnesium than the control group (p 0.01). Comparing the effects of co-treatment with CE at 250 mg/kg, quercetin, and CE at 500 mg/kg, it was shown that the latter two considerably reduced urine calcium excretion. When standard/extract were given to animals simultaneously, there was a substantially (p0.01) decreased level of urinary magnesium excretion. However, there were no discernible changes in sodium and potassium levels across the various groups of animals.

Table 5.11: Effect of CE on urinary electrolyte levels in GM-induced nephrotoxicity

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Urinary parameters (Unit)	Group I Normal control	Group II GM 100 mg/kg	Group III GM+QTN 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
Sodium (mmol/L)	74.16±1.86	75.17±1.86^{ns}	71.64±0.33^{ns}	74.31±1.92^{ns}	74.31±1.49^{ns}
Potassium (mmol/L)	3.21±0.02	3.21±0.02^{ns}	3.20±0.02^{ns}	3.15±0.01^{ns}	3.21±0.02^{ns}
Calcium (mg/dL)	8.90±0.01	10.89±0.01^{**a}	6.48±0.02*^{**b}	8.03±0.05*^{*b}	7.83±0.06**^{*b}
Magnesium (mg/dL)	0.77±0.01	0.82±0.07*^{*a}	0.74±0.04*^{*b}	0.78±0.05*^{*b}	0.77±0.06*^{*b}

"GM: gentamicin, QTN: quercetin, CE: Combination of Plant Extract. Values are expressed in mean ± standard error of mean (n=6), *p<0.05, **p<0.01, ***p<0.001 [a] significant compared o control group (group I), [b]significant compared with GM-induced group (group II), [ns] not significant"

5.10 Effect of CE on Hematological parameter in experimental animal

The table showed that rats given GM had significantly (p0.01) lower levels of haemoglobin (Hb), packed cell volume (p0.001), red blood cells (RBCs), and mean corpuscular haemoglobin (MCH) than rats in the control group. Rats in group II were found to have substantially higher levels of white blood cells (p0.01) and polymorphs (p0.001) than rats in group I. The co-treatment of animals with standard and extract resulted to a substantial (p0.01) rise in RBCs, haemoglobin, and MCH levels, according to the results. Only the rats given quercetin/a high dosage of CE showed an increase in packed cell volume (PCV) (p 0.01). Animals co-treated with standard/extract showed a substantial reduction in total WBC and polymorphs (p 0.01).

Table 5.12: Effect of CE on Hematological parameter in GM-induced nephrotoxicity

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Parameters studied (Unit)	Group I Normal control	Group II GM 100 mg/kg	Group III GM+QT N 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
RBC (million/mm^3)	7.35±0.14	6.81±0.31**^{a}	7.22±0.21**^{b}	6.85±0.31**^{b}	7.10±0.43**^{b}
HB (g/dL)	14.11± 0.28	11.76± 0.58***^{a}	14.02±0.13**^{b}	13.96±0.21**^{b}	13.83±0.31**^{b}
PCV (%)	43.66±0.52	38.27±0.81***^{a}	39.58±0.61**^{b}	38.29±0.42^{ns}	38.53±0.20**^{b}
MCH (pg)	20.67±0.12	20.19±0.69**^{a}	20.84±0.27**^{b}	20.45±0.49**^{b}	20.67±0.51**^{b}
WBC (1X10^3/mm^3)	8.22± 0.41	8.43±0.33**^{a}	8.21±0.41**^{b}	8.24±0.21$^{ns b}$	8.15±0.10**^{b}
Lymphocytes (%)	60.05± 0.01	59.96 ±0.08^{ns}	59.97±0.01^{ns}	59.96±0.02^{ns}	59. 96±0.05^{ns}
Monocytes (%)	4.97±0.00	5.00±0. 01^{ns}	4.96±0.01^{ns}	4.97± 0.06^{ns}	4.96±0.06^{ns}
Polymorphs (%)	12.22±0.21	15.84 ±0.11***^{a}	14.65±0.32**^{b}	14.19±0.20**^{b}	14.05±0.11**^{b}
Eosinophils (%)	1.93±0.01	2.02±0.01^{ns}	1.97±0.08^{ns}	1.97±0.02^{ns}	1.96±0.01^{ns}

"GM: gentamicin, QTN: quercetin, CE: Combination of Plant Extract. Values are expressed in mean ± standard error of mean (n=6), *p<0.05, **p<0.01, ***p<0.001, ^{a}significant compared with control group, ^{b}significant compared with GM-induced group, ^{ns}not significant"

5.11 Effect of CE on Serum total protein and albumin in experimental animal

In comparison to rats in group I, serum total protein and albumin levels (p0.05) were observed to be considerably lower in GM-treated animals. Rats in groups III demonstrated a significant change in total protein (p0.05) and albumin (p0.01) levels when compared to the animals in groups II, however significant changes (p>0.05) were not seen after p.o. administration of 250 and 500 mg/kg of CE in groups IV and V.

Table 5.13: Effect of CE on Serum total protein and albumin in GM-induced nephrotoxicity

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Serum parameters (Unit)	Group I Normal Control	Group II GM 100 mg/kg	Group III GM+QTN 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
Total protein (g/dL)	7.17±0.01	7.13±0.05 ^{*a}	7.17±0.09 ^{**b}	7.15±0.09 ^{ns}	7.17±0.07 ^{ns}
Albumin (g/dL)	4.34±0.00	4.31±0.04 ^{*a}	4.35±0.00 ^{**b}	4.32±0.00 ^{ns}	4.34±0.03 ^{ns}

"GM: gentamicin, QTN: quercetin, CE: Combination of Plant Extract. Values are expressed in mean ± standard error of mean (n=6), *p<0.05, **p<0.01,, ***p<0.001, [a]significant compared with control group, [b]significant compared with GM-induced group, [ns]not significant"

5.12 Effect of CE on Serum electrolyte in experimental animal

In comparison to group 1 animals, sodium, magnesium, and calcium levels were shown to be considerably lower in GM-treated animals. In comparison to group II rats, co-administration of the standard and extract considerably decreased (p0.01) changes in calcium and magnesium levels, but did not significantly vary (p>0.05) in sodium and potassium levels.

Table 5.14: Effect of CE on Serum electrolyte in experimental animal in GM-induced nephrotoxicity

Serum parameters (Unit)	Group I Normal Control	Group II GM 100 mg/kg	Group III GM+QTN 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
Sodium (mmol/L)	137.8±0.07	137.3±0.05 ^{**a}	137.6±0.15 ^{ns}	137.4±0.11 ^{a} ^{s}	137.6±0.14 ^{a} ^{s}
Potassium(mmol/L)	5.75±0.00	5.75±0.07	5.73±0.07 ^{ns}	5.76±0.01 $^{a s}$	5.78±0.01 $^{a s}$
Calcium (mg/dL)	10.60±0.13	8.17±0.00 ^{***a}	9.04±0.00 ^{**b}	9.25±0.08 ^{**b}	9.43±0.06 ^{**b}
Magnesium(mg/dL)	2.44±0.01	2.23±0.02 ^{**a}	2.54±0.01 ^{**b}	2.34±0.09 ^{**b}	2.44±0.01 ^{**b}

5.13 Effect of CE on Serum BUN, creatinine and uric acid level in experimental animal

Creatinine, uric acid, and blood urea nitrogen (BUN) serum levels were significantly (p 0.001) elevated in Group II mice treated with GM. In comparison to group II rats, quercetin co-treatment substantially (p 0.001) reduced creatinine, uric acid, and BUN. Creatinine and uric acid levels in

animals receiving the extract concurrently were considerably (p 0.01) lowered. In comparison to the toxic control group, BUN levels were considerably reduced in rats co-treated with extract at low concentration (p=0.01) and high concentration (p=0.001).

Table 5.15: Effect of CE on Serum BUN, creatinine and uric acid level in GM-induced nephrotoxicity

Serum Parameters (Unit)	Group I Normal control	Group II GM 100 mg/kg	Group III GM+QTN 50 mg/kg	Group IV GM+CE 250 mg/kg	Group V GM+CE 500 mg/kg
BUN (mg/dL)	15.83±0.19	28.89±0.02 ^{***a}	12.13±0.02 ^{***b}	18.92±0.01 ^{**b}	14.74±0.04 ^{***b}
Creatinine (mg/dL)	0.68±0.00	1.98±0.02 ^{**a}	0.81±0.00 ^{**b}	1.51±0.01 ^{*b}	0.94±0.01 ^{**b}
Uric acid (mg/dL)	2.13±0.08	3.22±0.01 ^{**a}	2.03±0.01 ^{**b}	3.04±0.08 ^{*b}	2.95±0.05 ^{**b}

"GM: gentamicin, QTN: quercetin, CE: Combination of Plant Extract, BUN : blood urea nitrogen. Values are expressed in mean ± standard error of mean (n=6), *p<0.05, **p<0.01, ***p<0.001, ^{a}significant compared with control group, ^{b}significant compared with GM-induced group, ^{ns}not significant"

Conclusion

The use of various herbal remedies as a therapeutic agent for the prevention and treatment of nephrotoxicity and urolithiasis is highly respected across the world. Clinical and preclinical studies revealed that flavonoids prevent the urination of calcium oxalate and crystals. Particularly phenolic and flavonoids, which are aromatic chemicals with good free radical scavenging ability, are polyphenols. Saponin-rich plants break up the suspension of mucoproteins, which encourages crystallisation.

In the current investigation, various solvent systems were used to extract coarsely powdered, shade-dried plant components chosen for their nephroprotective activity. The concentration of the extracts is followed by preliminary physical and phytochemical analysis to determine the purity of the plant material and determine the type of the active ingredients present.

Using a variety of experimental paradigms, including gentamicin- -induced nephrotoxicity in rats, we assessed the nephroprotective effect of the extract combinations. In the current study, we evaluated the nephroprotactive activity using three plant extracts in a 1:1:1 ratio. In a 1:1:1 ratio, we employed seed extract from Persea Americana seed, seed extract from Cyathea gigantea, and leaf extract from A. cordifolia for the study.

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Following preliminary research, acute toxicity tests were conducted on all of the extracts to determine the optimal oral dosage in accordance with OECD recommendations.I have chosen acetone, ethanol, and aqueous extracts of the chosen plant for an acute toxicity research in accordance with OECD guideline no. 423 for the measurement of LD50 based on the extractive value and phytochemical data. The findings indicated that the LD50 was 5000 mg/kg. Their ED50 is thus 500 mg/kg.

CE supplementation effectively reversed alterations in body weight, kidney weight, and urine pH in drug-induced nephrotoxic and urolithiasis mice, showing both nephroprotective and antiurolithic efficacy. In cases of gentamicin-induced nephrotoxicity, diuretic effects were seen. The flushing out of the components that cause stones through urine is encouraged by increased urine production. Gentamicin treatment prevented proteinuria, albuminuria, hypercalciuria, and hypermagnesuria in rats treated with cisplatin and gentamicin, demonstrating nephroprotective efficacy. The ethylene+CE-treated mice showed a clear hypocalcciuric and hypermagnesuric impact, indicating that it had antiurolithic action.

The leaves of A. cordifolia, Cyathea gigantea, and Persea americana seed were used in combination as CE plant extract for the treatment of drug-induced kidney impairment as a consequence of the findings from the nephroprotective inquiry.

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