Nephroprotective Ethno-medicinal Action of Selected Indian Medicinal Plants

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ABSTRACT
Medicinal plants may serve as a vital source of potentially advantageous new compounds for the development of effective therapy to action an array of kidney problems. Abounding herbs accept been accurate to be accomplishing as nephroprotective agents while abounding added are claimed to be nephroprotective but there is abridgement of any such accurate affirmation to abutment such claims. Developing a satisfactory herbal therapy to treat serve renal disorders requires systematic investigation of backdrop like acute renal failure, nephritic syndrome and chronic interstitial nephritis. Herbal medicines acquire alleviative backdrop due to the presence of their chemical components. An amount of extracts of accustomed articles and comestible antioxidants accept bee n appear to appearance careful furnishings adjoin nephrotoxicity. Following herbal drugs accept apparent their almighty nephroprotective aftereffect due their antioxidant, diuretic, anti-inflammatory, antispasmodic properties. The present review is aimed to elucidate the list of nephroprotective medicinal plants, which are scientifically proved in treating renal disorders.

Keywords: Nephroprotective, therapy, antioxidant and anti-spasmodic.

INTRODUCTION
Demand for medicinal plants is accretion in both developing and developed countries. Research on medicinal plants is one of the arch areas of analysis globally. However, there is a need to pay closer attention to the affair of bioactivity-safety appraisal and attention of medicinal plants. Kidney failure is one of the most common diseases from a lot of accepted diseases in India. Many plants accept been acclimated for analysis of kidney failure in acceptable arrangement of anesthetic throughout the world. Indeed along with dietary measures, plant preparation formed the base of the treatment of the ache until the accession of allopathic medicine. Ethno-medicinal plants can be acclimated to advice apprehend the charge for dialysis by treating the causes and aftereffect of renal failure, as well as reducing the many adverse effect of dialysis. [1] Nephrotoxicity can be authentic as renal disease or dysfunction that arises as an absolute or aberrant aftereffect of exposure to medicines, and environmental or industrial chemicals. Several factors accept been articular which accomplish the kidney accessible to toxic injury due to indigenous medicines. This includes urine pH, High blood flow rate, high endothelial surface area, high metabolic activity, active uptake by

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tubular cell and medullary interstitial concentration. The toxins may abuse the tubules directly, at the website of adulteration carriage or concentration, or by inducing renal ischemia, hemoglobinuria or myoglobinuria. Continued acknowledgment and acknowledgment to top doses can access the severity of renal failure. [2] The nephrotoxic effect of cyclosporine, aminoglycoside antibiotics, cisplatin, amphotericin-B, beta-lactam antibiotics and Indomethacin are reviewed. These drugs were produce produced nephrotoxicity because they are most frequently causes of renal injury in children. In addition, their nephrotoxicity is acquired by altered mechanisms. Several generalizations can be made, however. First, agents who could cause tubular accident tend to be accessory in their baneful effects, [3] This review attempts to portray the discovery and development of medicine from galenical to genomical, with a focus on the potential and role of medicinal plants. Ayurveda is an acceptable Indian system of medicine getting accomplished for thousands of years. Ethnomedicinal studies are generally cogent in absolute locally important bulb breed abnormally for the analysis of awkward drug. [4-6]

IDENTIFICATION OF RESEARCH PROBLEM
It is, therefore, not surprising that kidney and urinary tract diseases are ranked 12th in the list of major causes of death in the world by the World Health Organization (WHO). The incidence kidney failure (or chronic Kidney disease) has doubled the last 15 years. It is estimated that currently there are over 1 million people worldwide who are alive on dialysis or with a functioning graft. Diabetes, hypertension is an important cause of kidney failure.

There are approximately 7.85 million people suffering from chronic kidney failure in India. It is estimated that over 600000 patients will require treatment but 90% patients who suffer from kidney disease are not able to afford the cost of treatment. The crisis of kidney shortage is a global phenomenon and it is worst in Asian countries. In Ayurveda (Indian system of medicine), various kidney disorder have been identified and their treatment have been prescribed. In the present study it is proposed to identify some of the plants used in ayurveda for their evaluation as renoprotective agents. [7]

MAIN METABOLIC ABNORMALITIES IN PATIENTS WITH RENAL FAILURE [8]
- Anorexia – reduced oral nutrient intake
- Gastrointestinal consequences of uraemia
- Restrictive diets
- Uremic toxicity - inadequate dialysis prescription
- Metabolic acidosis
- Endocrine factors (PTH, insulin resistance etc.)
- Peripheral insulin resistance
- Impairment of lipolysis
- Low grade inflammatory state activation of protein catabolism

- Augmented catabolic response to inter current disease
- Metabolic acidosis
- Hyperparathyroidisms, uremic bone disease
- Impairment of vitamin D₃ activation

DIFFERENT TYPES OF NEPHROTOXICITY
Aminoglycoside Nephrotoxicity
Aminoglycosides preferentially affect the proximal tubular cells. These agents are freely filtered by the glomeruli and quickly taken up by the proximal tubular epithelial cells, where they are incorporated into lysosomes after first interacting with phospholipids on the brush border membranes. They exert their main toxic effect within the tubular cell by altering phospholipids metabolism. In addition to their direct effect on cells, Aminoglycosides cause renal vasoconstriction. The critical factors in the development of acute kidney injury (AKI) secondary to aminoglycoside nephrotoxicity are dosing and duration of therapy. Aminoglycoside take-up by the tubules is a saturable marvel, so take-up is restricted after a solitary measurement. Consequently, a solitary every day huge measurement is desirable over 3 dosages for each day. One measurement for each day probably causes less amassing in the tubular cells once the immersion point is reached. [9-10]

Amphotericin B Nephrotoxicity
Amphotericin B ties to sterols in cell films, in this way making pores that bargain layer uprightness and increment layer penetrability. It ties to ergosterol in contagious cell dividers as well as to cholesterol in human cell films; this is the thing that records for its nephrotoxicity. Trademark electrolyte variations from the norm incorporate squandering of potassium and magnesium auxiliary to expanded penetrability of the phone layers. The back-break of hydrogen particles in the gathering conduit prompts to distal renal tubular acidosis (dRTA). [11-12] Lipid-based preparations of amphotericin B decrease but do not eliminate the nephrotoxicity compared with traditional amphotericin B. This may be due to a direct nephrotoxic effect of the conventional preparation. [13]

Contrast-Induced Nephropathy
In spite of the fact that the pathogenesis of contrast-induced nephropathy (CIN) remains not entirely comprehended, it is doubtlessly the consequence of renal vasoconstriction and direct renal tubular epithelial cell poisonous quality. Current hypotheses in regards to CIN danger incorporate a mix of direct cytotoxicity with postsischemic reperfusion harm bringing about oxygen free radical creation prompting to endothelial damage. [14-15]

Calcineurin Inhibitor Nephrotoxicity
Cyclosporine and tacrolimus cause acute kidney injury (AKI) by initiating afferent and efferent arteriolar vasoconstriction. Steady harm can prompt to interstitial fibrosis. Tacrolimus has been appeared to bring about
thrombotic microangiopathy therefore of endothelial injury. [16-17]  

Cisplatin Nephrotoxicity  
Cisplatin more often than not influences the proximal tubules principally with some optional impact on the glomeruli and distal tubules. Cisplatin is discharged basically in the pee, bringing about extracted medication levels, which energize take-up into the phones by uninvolved dispersion or dynamic take-up. Cisplatin is steady in the circulatory system yet gets to be hydrolyzed in the chloride-poor cell condition. It is the hydrolyzed metabolite that ties DNA, RNA, proteins, and phospholipids, bringing on cytotoxicity. [18]  

Iosfamide Nephrotoxicity  
Iosfamide is a known simple of cyclophosphamide. Despite the fact that cyclophosphamide is not nephrotoxic, iosfamide, by ethicalness of its metabolite chloroacetaldehyde, is harmful to the tubular cells, with special association of the proximal tubule prompting to Fanconi syndrome. [19-20]  

Foscarnet Nephrotoxicity  
Foscarnet, which is utilized to treat safe cytomegalovirus (CMV) diseases, causes intense interstitial nephritis and intratubular precious stone arrangement. Notwithstanding precious stone arrangement, this can be comprised of calcium salts or sodium salts, chelation of calcium by foscarnet prompts to hypocalcemia. [21-22]  

Crystal-Forming Drug Nephrotoxicity  
Sulfa drugs, acyclovir, methotrexate, ethylene glycol, and protease inhibitors like indinavir cause acute kidney injury (AKI) by tubular impendiment because of precious stone development in the tubular cells. Acyclovir may prompt to the development of intratubular precious stones, which show up as bilefringing needle-molded gems and can evoke an intense interstitial nephritis. [23-24]  

Rhabdomyolysis  
Rhabdomyolysis alludes to the breakdown of skeletal muscle strands, which prompts to the arrival of conceivably nephrotoxic intracellular substance into the course. Acute kidney injury (AKI) creates in this setting by means of the accompanying 3 instruments:  
   a. Renal vasocostriction  
   b. Heme-interceded proximal tubular cell toxicity  
   c. Intratubular cast arrangement.

ADMINISTRATION OF MEDICATIONS/ CHEMICALS FOR ANIMAL SCREENING [25]  
Acute renal failure (ARF) can be incited in exploratory creature by organization of different medication and chemicals, taking after are the widely utilized techniques by which ARF can be prompted in trial creatures shown in Table 1.

MEDICINAL HERBS AGAINST NEPHROTOXICITY  
During different method of extraction most frequently are maceration, percolations and soxhletion of crude drugs with different solvents like aqueous, ethanolic, hydroalcoholic, methanolic have been used for extraction of phyto-constituents responsible for nephroprotective action. The extracts are often used as nephroprotective activity such as aqueous, ethanolic, hydroalcoholic and methanolic extract are mainly used against commonly drug induced nephrotoxicity and some of the medicinal plants are cited in Table 2. [26-38]  

<p>| Table 1: Administration of Medications/Chemicals |</p>
<table>
<thead>
<tr>
<th>S. No.</th>
<th>Drugs/Chemicals</th>
<th>Dose</th>
<th>Effect on kidney</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Glycerol</td>
<td>8-10 ml/kg, i.m.</td>
<td>Induction of ARF</td>
</tr>
<tr>
<td>2.</td>
<td>Gentamycin</td>
<td>40-200 mg/kg for 4–10 days, Dose 100 mg/kg, i.p. for 5 days</td>
<td>Induction of ARF</td>
</tr>
<tr>
<td>3.</td>
<td>Cisplatin</td>
<td>5–40 mg/kg, i.p.</td>
<td>Induction of ARF</td>
</tr>
<tr>
<td>4.</td>
<td>NSAIDs</td>
<td>375–3000 mg/kg, i.p.</td>
<td>Induction of ARF</td>
</tr>
<tr>
<td>5.</td>
<td>Iosfamide</td>
<td>50–1100 mg/kg, i.p.</td>
<td>Induction of ARF</td>
</tr>
<tr>
<td>6.</td>
<td>Potassium dichromate</td>
<td>15 mg/kg, s.c.</td>
<td>Induction of ARF</td>
</tr>
<tr>
<td>7.</td>
<td>Radio contrast media (Diatrizoate)</td>
<td>2–10 ml/kg, i.v.</td>
<td>Induction of ARF</td>
</tr>
</tbody>
</table>

BERGENIA LIGULATA (PASHADBHED)  
Bergenia ligulata (Haw.) Sternb. plants belonging to family Saxifragaceae. It is otherwise called Elephant's Ears. It is an evergreen lasting herb developing to 0.3 m by 0.5 m. Bergenia ligulata is utilized as a part of customary ayurvedic pharmaceutical for the treatment of a few sicknesses in Nepal, India, Pakistan, Bhutan and some different nations shown in figure 1.

Fig. 1: Morphology of Bergenia ligulata (an) Entire Plant (b) Root

Reported Ethno-medicinal Uses  
It has astringent, tonic, hostile to sorbutic and purgative properties. Likewise, it is given in aspiratory friendship, looseness of the bowels, ulcers, dysuria, spleen broadening, hack, and fever. The wounded rhizomes are connected in the eye ailments, bubbles, cuts and antibacterial, mitigating, anticancer, hostile to diabetic and against uroliathatic. The Bergenia ligulata root, rhizome, and entire plant are utilized for kidney and bladder stones and urinary issues. A juice or powder of the entire plant is utilized to treat urinary inconveniences in Nepal. [39-49]
Reported Phytoconstituents

The study on rhizomes of Bergenia ligulata depicted the confinement of various concoction constituents as coumarins: bergenin; 11-O-galloylbergenin, and protocateche. Paashaanolactone (4(4′-β-glucopyranosyloxy-1′-benzoyloxy)-6-methyltetrahydropryan-2-one) another compound was disconnected from the rhizomes of Bergenia ligulata. The rhizomes were found to contain higher centralization of bergenin, catech, gallic corrosive and (+)-afzelchin than different parts of the plants which was evaluated by a basic strategy for sufficient measurement by utilizing slight layer chromatography in toluene: ethyl acetic acid.
 derivation: formic corrosive (4:6:1, v/v) dissolvable framework which was affirmed through HPLC technique. [50-55]

**Reported Pharmacological Activity**

The poisonous quality strategy was embraced from Ghosh et al., (1998) and the intense harmfulness considers have been depicted by Byatti VB et al. [56-57]

Protective effects of Neeri: NS-RF (a home grown definition produced for enhancing renal capacities) on substantial metal (lead acetic acid derivation) instigated nephrotoxicity in Wistar pale skinned person rats. Lead acetic acid derivation is considered as a noteworthy nephrotoxicity acting specialist bringing on direct harm through various pathways including oxidative anxiety. Lead acetic acid derivation (8 mg/kg i.p. for a month and a half) initiated huge oxidative anxiety and nephrotoxicity in rats; demonstrated by expanded levels of serum creatinine, serum urea, urinary protein, urinary glucose; and decreased levels of serum egg whites, serum add up to proteins, urinary creatinine; and furthermore the auxiliary harm in kidney. Co-treatment with NS-RF (1640 and 3280mg/kg, p.o. for a month and a half) fundamentally keep the modified serum and urinary biochemical parameters and histological renal tubular harms by lead acetic acid derivation. Convincingly, NS-RF is a powerful nephro-defensive plan shielding kidneys from nephrotoxins including oxidative harm prompted by lead acetate. [58]

ELKP-1 is a polyherbal formulation containing standardized extracts of Tribulus terrestris (120 mg), Cretea nurvala (25 mg), Bergenia ligulata (10 mg), Andrographis paniculata (50 mg), Tinospora cordifolia (75 mg), Boerhavia diffusa (75 mg), Solanum nigrum (25 mg), Eclipta alba (50 mg) and Terminalia chebula (20 mg). [59]

**AERVA LANATA**

Aerva lanata (Linn) Juss. ex Schult plant belonging to Amaranthaceae family is usually distinguished and known as Gorakshaganka in Ayurveda arrangement of prescription. It is considered as one among the couple of natural wellsprings of Pashanabhed. The plant is broadly utilized as a part of urinary issue like Ashmari (Urinary calculi), Mootakrichra (Dysuria), Mootravikara and so on by a large portion of the Ayurveda and Siddha specialists in southern India, for the sake of Pashanabhed. [60]

**Reported Ethno-medicinal Uses**

Aerva lanata Linn. (Amaranthaceae) is an herbaceous enduring weed developing wild in the tropical districts and Western Ghats of India. Aerva lanata has been asserted to be helpful as diuretic, anthelmintic, hostile to diabetic, expectorant, hepatoprotective, Antimicrobial, cytotoxicity movement, urolithiasis and calming. The plant is astringent, severe, cooling, emollient, vermifuge, suppurative, diuretic and lithotriptic. It is helpful to treat bubbles, cephalalgia, hack, strangury and lithiasis. The plant has helpful restorative esteem, the extract is demonstrated for nephroprotective movement, diuretic impact, cytotoxicity, cell reinforcement, immunomodulatory impact, diuretic impact, calming impact, antimicrobial action, hepatoprotective action, and hostile to hyperglycemic effect. [61-64]

**Reported Phytochemicals**

Chemical constituents from this plant are bryophyllol, bryophollone, bryophollenone, bryophylin and two homologous phanthenre subsidiaries 2(9-decenyl) -phenanthenre (I) and 2- (undecenyl) -phenanthenre (II) from leaves; 18α-oleanane, ψ-taraxasterol, α-and β- amyrins and their acetic acid derivations were separated. Powerful cytotoxic mixes bersaldegenin-1,3, 5-orthocacetate and bufadienolidobryophyllin B were likewise disengaged. Botulin, β-sitosterol, amyrin, plant hentriacontane, campesterol, stigmasterol, kaempferol, propionic corrosive, β-carbonile-1, aervoside and aervolane. Four new alkaloids-aervine (10-hydroxy canthin-6-one), methyl aervine (10-methoxycanthin-6-one), aervoside (10-β-D-glucopyranosylcanthin-6-one), and aervolane (3-(6-methoxy-β-carbolin-1-yl) propionic corrosive), and furthermore the known alkaloids canthin-6-one and 3-(β-carbolin-1-yl) propionic corrosive have been disengaged from the herb Aerva lanata Juss. Their structures have been set up on the premise of concoction and phantom characteristics. [65]

**Reported Pharmacological Activity**

PPABTF (100 mg/kg) did not demonstrate any lethality as prove of perceptions that included changes in skin and hide, eyes and mucous films, respiratory, circulatory, autonomic and focal sensory systems, somatomotor movement and conduct design. Perceptions of tremors, writhings Antidiabetic movement of alkaloids of Aerva lanata salivation, the runs, dormancy, rest and extreme lethargies were under-taken. No indications of any strange conduct or any mortality were seen amid the review time frame. At that point 1/fifth and 1/tenth dosages were chosen for further reviews according to OECD (2000) guidelines. [66-67]

Jawarish Zarooni Sada (JZS) is one such polyherbal planning containing 15 fixings, for the most part depicted to be diuretic and nephroprotective. Thusly, in the present review ethanol and water extracts of JZS (300 mg each) were explored for diuretic movement by measuring the aggregate pee yield over a time of 6 h.

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**Fig. 2: Morphology of Aerva lanata Plant**

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Sodium and potassium level in pee test was additionally evaluated. Nephroprotective movement of JZS against gentamycin-promoted nephrotoxicity was explored by regulating JZS alongside high measurements of gentamycin (40 mg/kg) and rise of serum urea and serum creatinine was taken as the list of nephrotoxicity. JZS indicated huge diuretic and nephroprotective effect. [68] The impact of ethanolic extract of Aerva lanata was contemplated on Mercuric chloride incited renal harm in rats. Oral organization of ethanolic extract of A. lanata (200 mg/kg and 400 mg/kg) successfully repressed the levels of marker catalysts, cell reinforcement chemicals, lipid profile, protein and lipid peroxidation when contrasted with the ordinary gatherings. Greasy invasion, greasy degeneration and corruption saw in mercuric chloride treated gatherings were totally missing in histology of the liver and kidney areas of the creatures treated with the extract. It is stipulated that the extract treated gatherings were mostly shielded from hepatocellular harm created by mercuric chloride. The outcomes recommend that the ethanolic extract of A. lanata have critical potential as nephroprotective agent. [69]

The ethanol extract of the whole plant of Aerva lanata was considered for its nephroprotective movement in cisplatin and gentamycin-induced renal damage in albino rats of either sex. In the healing regimen, the extract at measurements levels of 75, 150 and 300 mg/kg demonstrated dosage subordinate lessening in the raised blood urea and serum creatinine and standardized the histopathological changes in the remedial regimen. In the gentamycin display the rats in the preventive regimen likewise demonstrated great reaction to the ethanol separate at 300 mg/kg. The discoveries recommend that the ethanol extract of Aerva lanata has stamped nephroprotective action with insignificant lethality and could offer a promising part in the treatment of acute renal damage brought about by nephrotoxins like cisplatin and gentamycin. [70] The natural medication Sirupeelai Kudineer i.e. the decoction of entire plant of Aerva lanata. Linn. the plant which is by and large generally utilized as a part of Siddha System of Medicine, is assessed for Nephroprotective action in creature show. The Nephroprotective action of the medication in Gentamycin models was assessed in Wistar rats. The rats in prophylactic gathering were treated with the decoction of Aerva lanata at the dosage of 270 mg (5.4 ml) and 500 mg (10.0 ml)/kg. The Gentamycin models of rats treated with the medication at the measurement of 500.0 mg/kg orally for 10 days demonstrated huge decrease in the level of Blood urea (P < 0.02) and Serum Creatinine with the criticalness of (P < 0.05). Histopathology additionally uncovers the decrease in the level of renal damage. [71]

**COLEUS AROMATICUS**

*Coles aromaticus* (Syn: *Coles ambionicus* Lour. & *Plectranthus amboinicus*) is a tender fleshy perennial plant belonging to the family Lamiaceae with an oregano-like flavor and odour. Native to Southern and Eastern Africa, from South Africa and Swaziland to Angola and Mozambique and north to Kenya and Tanzania. It is used as a decorative plant in many houses in south India.

Fig. 3: Morphology of Coleus aromaticus (a) Arial Part (b) Leaf

**Reported Ethno-medicinal Uses**

*C. aromaticus* is a common medicinal herb in India for example; the leaves are used in treatment of common cold, cough and headache. They have also been shown to have antithiolotic, antiepileptic, chemo-preventive and antioxidant properties. Disorders of the digestive system are treated by using *C. aromaticus* for stomach pain, nausea, vomiting, and mouth infections; also it is used as purgatives and as anthelmintics. It is popular in the treatment of dyspepsia, indigestion, diarrhea and as carminative Moreover; it is the most frequently cited species for the treatment of burns, wounds, sores, insect bites and skin allergies, for the treatment of chronic coughs, asthma, bronchitis and *Mycobacterium tuberculosis*. It has also been reported to have been used for fevers microbial infections viruses like Herpes simplex virus-I and HIV Besides, the plant is reported to relieve kidney troubles, decrease vaginal discharges, treat urinary diseases and is drunk after child birth. It is also useful in the treatment of congestive heart failure nervous disorders, epilepsy like convulsions, meningitis and to alleviate conjunctivitis, [72-78]

**Reported Phytochemicals**

Several compounds of different chemical groups have been isolated from this plant including carvacrol, caryophyllene, thymol, eugenol, patchoulane, chariccol and flavonoids. Quercetin, apigenin, luteolin, salvigenin, genkwain and essential oil in the leaves have been reported. Monoterpenes and sesquiterpenes have been reported from Coleus aromaticus limonene, linalool, myrcene and thymol, alpha-cubebene and phenolics. [79]

**Reported Pharmacological Activities**

In the present studies of sub acute toxicity reveals that no mortalities or evidence of adverse effects have been observed in Balb C mice following acute oral administration at the highest dose of 2000 mg/kg crude extracts of PAS. In sub acute toxicity study daily oral administration of methanol extract 200 and 400 mg/kg...
body wt of PAS for up to 28 days did not result in death or significant changes in body weight, hematological and biochemical parameters. [80]

The methanolic extract of Plectranthus amboinicus (Lour) Spreng at dose of 200, 400 mg/kg orally for every 24 h for 28 days did not produce any mortality in tested animals. No sign of observable toxicity was detected during the experimental period. [81]

An in-vivo study of nephroprotective effect of aqueous extract of Plectranthus amboinicus on Glycerol induced Acute Renal Failure (ARF) was carried out on albino rats. The blood biochemical parameters like urea, uric acid and creatinine were estimated along with histopathological studies of the kidney. The result shows significant nephroprotective activity of aqueous extract of P. amboinicus at 500 mg/kg. The presence of quercetin plays a significant nephroprotective effect. [82]

The Juice from Plectranthus amboinicus (PA) leaves is commonly used for illnesses including liver and renal conditions in the Asian sub-continent. Acetaminophen (APAP), used as an analgesic, produces liver and kidney necrosis in mammals at high doses. The ethanol extract of PA at two doses of 250 and 500 mg/kg b w on APAP-induced toxicity in rats. The Ethanolic extract of PA rescued these phenotypes by increasing antioxidant responses as assessed by biochemistry and histopathology. Statistical data suggested that the ethanol extract of PA possess nephroprotective and antioxidant effects against APAP-induced nephrotoxicity and strong diuretics effect in rats. [83]

PEDALIUM MUREX

Pedalium murex (P. murex) Linn is the medicinal plant belonging to family Pedaliaceae and it is annual herb, which grows abundantly on the sea costs in South India, Srilanka, Ceylon, Mexico and tropical Africa. In and around Visakhapatnam the plant is very prolific after summer rains.

Fig. 4: Morphology of Pedalium murex (a) Arial Part (b) Fruits (c) Powder

Reported Ethno-medicinal Uses

Fruits are considered as demulcent, diuretic, antispasmodic, antiseptic and aphrodisiac. Juice of fruit is believed to dissolve the kidney stone. It is a cooling tonic, purifies blood, act as and removes stone from the bladder. An infusion or extract prepared from the leaves, stems and fruits in cold water of Pedalium murex are found to be useful in the treatment of disorders of urinary systems such as gonorrhea, dysuria, and incontinence of urine etc. [84-87]

Reported Phytochemicals

Pedalium murex contains flavonoids, tri-terpenoids, lipids, steroids, phenolic acids, carbohydrates and amino acids. Especially fruits contain alkaloids, flavonoids (pedalitin and dinatin). The chemical composition of P. murex fruits consist of alkaloids (3.5%-5.0%), resins, carbohydrates, saponins, stable oil, aromatic oil, triterpenoids, and glycosides, and also two more significant flavonoids i.e., triotcanyl drotiocanoate and 2, 4, 5-trihydroxy-5, 7-dimethoxy flavones. P. murex includes some essential flavonoids like dinatin and 7-glucoronide, diosmetin and its 7-glucoronide, pedalin and pedalitin (3’4,5,6-tetrahydroxy-7-methoxyflavone) in its leaves. Moreover, steroids, alkaloids, saponins, proteins and resins are extracted as well. The root is enclosed with unique Phenolic compounds like phenol 2-(5,6-dimethyl pyrazinyl) methyl. [88-89]

Reported Pharmacological Activities

Nephroprotective efficacy in rats with induced renal damage by cisplatin dosage (Cisplatin 5 mg/kg) was tested against ethanol extract of P. murex fruit. Losses in body weight, blood urea and serum creatinine were observed as kidney damage indicators by dosing 250 mg/kg orally concurrent ethanol extract of P. murex. Ethanolic extract was found very effective to prevent the kidney damage. Therefore, it can be concluded that cystone ethanolic extract of P. murex is significantly nephroprotective.

The nephroprotector activity of the ethanolic and aqueous extracts of fruits of Pedalium murex (600 mg/kg body weight, p.o.) against gentamycin-induced (100 mg/kg/d s.c) renal toxicity in rats. The effect of plant extracts were examined by estimating blood urea nitrogen, serum creatinine, urinary protein, urine to serum creatinine ratio, lipid peroxidation, gluthione, catalase in kidney. Co-administration of either ethanolic or aqueous extract with gentamycin was significantly prevented the renal injury protection both functionally and histological in dose dependent manner. The present study provides the corroborative scientific evidence for the folklore use of Pedalium murex in urinary troubles.

The ethanolic extract of dried fruits of Pedalium murex was evaluated for nephroprotective activity in Cisplatin (5 mg/kg) induced renal damage in wistar rats. Effect of concurrent administration of Pedalium murex ethanolic extract at a dose of 250 mg/kg given by oral route was determined using serum creatinine and blood urea and change in body weight as indicators of kidney damage. Cystone was used as standard drug. The extract significantly decreased the cisplatin induced nephrotoxicity. The study results show that the ethanolic extract of dried fruits of Pedalium murex is an excellent nephroprotective as compared to cystone.
The nephroprotective and nephrotoxic activity of the AEVM were assessed in rifampicin-induced hepatotoxic and nephrotoxic rats. Pretreatment with AEVM significantly prevented the physical, biochemical, and histological changes induced by rifampicin in the liver and kidney, respectively. The AEVM possessed statistically significant hepatoprotective and nephroprotective activity.

The nephroprotective activity of ethanolic extract of dried fruits of *Pedalium murex* Linn. Nephrotoxicity was induced in Wistar rats by intraperitoneal administration of Cisplatin 5mg/kg. Effect of concurrent administration of *Pedalium murex* ethanolic extract at a dose of 250 mg/kg given by oral route was determined using serum creatinine and blood urea and change in body weight as indicators of kidney damage. The study shows that the ethanolic extract of dried fruits of *Pedalium murex* is an excellent nephroprotective as compared to cystone.

The nephroprotective activity of the ethanolic and aqueous extracts of fruits of *Pedalium murex* (300 and 600 mg/kg body weight, p.o) against cadmium chloride-induced (3 mg/kg/d s.c) renal toxicity in rats were studied. The effect of plant extracts were examined in terms of blood urea nitrogen, serum creatinine, urinary protein, to urine to serum creatinine ratio, lipid peroxidation, glutathione, catalase in kidney. In present study, Cadmium induced nephrotoxicity characterized by significant elevation of serum markers levels, increased urinary protein excretion, raised LPO levels, reduced GSH and CAT levels, reduced creatinine clearance. Co-administration of either ethanolic or aqueous extract with CdCl2 was significantly prevented the renal injury in dose dependent manner.

The ethanolic fruit extract of *P. murex* to ethylene glycol intoxicated rats were reverted the levels of the liver and kidney markers to normal levels protecting liver and renal tissue from damage and also prevents the crystal retention in tissues. The levels of ACP and ALT AST, ALT in renal and hepatic tissues of ethylene glycol induced rats might be due to leakage of the enzymes in to the general circulation from the collateral circulation. LDH levels in serum, urine tissue were increased on ethylene glycol intoxications is due to the oxalate induced renal and hepatic cellular damage. [90-94]

**CYNODON DACTYLON**

*Cynodon dactylon* is commonly known as “Doob” (Hindi) and is termed as a creeper in India and also calles Bermuda grass, belongs to family Poaceae. It is native to East Africa, Asia, Australia and southern Europe. *Cynodon* is a weed and has been found to possess various potential medicinal properties. Morphological appearances are shown in figure 5.

**Reported Ethno-medicinal Uses**

In traditional medicine it is used for indigestion and the treatment of wounds. It is reported to be alterative, antiseptic, aperients, astringent, cyanogetic, demulcent, depurative, diuretic, emollient, sudorific, and vulnerary; it is reported to be photosensitizing in animals, to cause contact dermatitis, and hay fever. It is folk remedy for anasarca, calculus, cancer, carbuncles, convulsions, cough, cramps, cystitis, diarrhea, dropsy, dysentery, epilepsy, headache, hemorrhage, hypertension, hysteria, insanity, laxative, measles, rubella, snakebite, sore stones, tumors, urogenital disorders, warts, and wounds. [95-99]

**Reported Phytochemical**

The phytochemical analysis showed that the plant contained flavanoids, alkaloids, glycosides, terpenoids, triterpenoids steroids, saponins, tannins, resins, phytoesters, reducing sugars, carbohydrates, proteins, volatile oils and fixed oils. [100-104] Quantitative estimation of phytoconstituents showed glycosides reached 12.2%, tannins 6.3%, alkaloids 0.1%, resins 1.0%, free reducing sugar 10% and total reducing sugar 12%. [105] Nutritional analysis showed that each 100 g contained (on a zero-moisture basis) 11.6 g protein, 2.1 g fat, 75.9 g total carbohydrate, 25.9 g fiber, 10.4 g ash, 530 mg Ca, 220 mg P, 112.0 mg Fe, 1630 mg K, 28 mg beta-carotene equivalent. [106] A total of 20 compounds were identified from the hydroalcoholic extract of the whole parts of *Cynodon dactylon* Hexadecanoc acid, ethyl ester linolenic acid, ethyl ester d-mannoze were the major components of the hydroalcoholic extract, and hexadecanoic acid ethyl ester was the most abundant one (17.49%). However, the isolated compounds were included: 3H-pyrazo-3-one, 2,4-dihydro-2,4,5-trimethyl 12%, 4H-pyran-4-one, 2,3-dihydro-3,5-dihyroxy-6-methyl 57%, benzoferan, 2,3-dihydro 39%, 2-furan-carboxaldehyde, 48%, decanoic acid, ethyl ester 63%, d-mannoze 20%, Ar-tumorene 31%, tumerone 23%, tricyclo[6.3.0.0(1,5)]undec-2-enone,2,3,5,9-tetramethyl,3,7,11,15-Tetramethyl-2-hexadecen-1-ol 10.35, hexadecanoic acid ethyl ester, phytol, 9,12-octadecadienoic acid ethyl ester, linolenic acid ethyl ester and octadecanoic acid ethyl ester. [107]

**Reported Pharmacological Activity**

The effect of aqueous extract of *Cynodon dactylon* on renal function in Streptozotocin (STZ) induced diabetic rats has been performed. STZ induced diabetic male rats showed significant decrease in the levels of serum total protein, which lead to the reduction in their body...
weight, and significant elevation in the levels of blood urea and serum creatinine were observed, when compared to normal rats. These levels were reverted in the STZ induced diabetic rats, treated with Cynodon dactylon extract and in those treated with glibenclamide, which was also demonstrated and correlated with the histopathological findings of the kidney tissue. The results of the study reveals that Cynodon dactylon aqueous extract effectively prevented the nephropathic changes induced by diabetes and this is the first study to report on nephroprotective effect of Cynodon dactylon with histological correlations. [108]

Cynodon dactylon and Gmelina asitica plants have shown potent protective activity against free radical which is evident through data obtained in various antioxidant assays. All the extracts tested revealed a protective effect on red blood cells against heat induced membrane damage and proteinase inhibition, which depicted its vital role in maintaining the integrity of the cell membrane. The promising results obtained through in vitro anti-oxidant and anti-inflammatory assay prompted us to evaluate nephroprotective potential of these plants using DNA fragmentation assay, epifluorescence assay and cytoprotective assay. Normal kidney cells (vero cells) were used for epifluorescence dual staining and DNA fragmentation assay using vitamin E as a positive control. [109]

As we gone through various studies on the treatment of kidney disorders, we can conclude that herbal plants play a unique and significant role as a nephroprotective ingredient in different animal models. The nephroprotective activity is probably due to the presence phytoconstituents like polyphenol and flavonoids in medicinal plants. The present review study give evidential explore of medicinal plants against experimentally induced nephrotoxicity. Hence the review study is concluded that the herbal drug possesses nephroprotective activity and it has been proved by different animal models give many links to develop economical polyherbal formulations in the future trials.

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