Available online at www.ijpsdronline.com

International Journal of Pharmaceutical Sciences and Drug Research 2017; 9(2): 44-54

Review Article

ISSN: 0975-248X
CODEN (USA): IJPSPP

Nephroprotective Ethno-medicinal Action of Selected Indian Medicinal Plants

AK Srivastava[1*], D Kaushik[1], AK Shrivastava[2], VK Lal[3]

[1]*Agra Public Pharmacy College, Agra-282007, Uttar Pradesh, India*
[2]*Nandini Nagar Mahavidyalay, College of Pharmacy, Nawabganj- 224001, Uttar Pradesh, India*
[3]*Sagar Herbal & Research Centre, Barabanki-255001, Uttar Pradesh, India*

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 been 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.

DOI: 10.25004/IJPSDR.2017.090202 **Int. J. Pharm. Sci. Drug Res. 2017; 9(2): 44-54**

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

***Corresponding author: Mr. Anuj Kumar Srivastava,**
Agra Public Pharmacy College, Agra-282007, Uttar Pradesh, India; **Tel.:** +91-7465057756;
E-mail: anuj_pharmacognosy@rediffmail.com
Received: 05 February, 2017; **Accepted:** 09 March, 2017

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, hypertensions are 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 D_3 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 postischemic 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 extractd 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]

Ifosfamide Nephrotoxicity

Ifosfamide is a known simple of cyclophosphamide. Despite the fact that cyclophosphamide is not nephrotoxic, ifosfamide, 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 impediment because of precious stone development in the tubular cells. Acyclovir may prompt to the development of intratubular precious stones, which show up as birefringent 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 vasoconstriction
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]

Table 1: Administration of Medications/Chemicals

S. No.	Drugs/ Chemicals	Dose	Effect on kidney
1.	Glycerol	8-10 ml/kg, *i.m.*	Induction of ARF
2.	Gentamycin	40–200 mg/kg for 4–10 days, Dose 100 mg/kg, *i.p.* for 5 days	Induction of ARF.
3.	Cisplatin	5–40 mg/kg, *i.p.*	Induction of ARF.
4.	NSAIDs Acetaminophen	375–3000 mg/kg, *i.p.*	Induction of ARF
5.	Ifosfamide	50–1100 mg/kg, *i.p.*	induction of ARF
6.	Potassium dichromate	15 mg/kg, *s.c.*	Induction of ARF
7.	Radio contrast media (Diatrizoate)	2–10 ml/kg, *i.v.*	Induction of ARF

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 uroliathaitic. 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]

Table 2 : List of Nephroprotective Medicinal Plants

S. No.	Plant name	Family	Part used	Screening method
1.	*Adhatoda zeylanica*	Acanthaceae	Leaves	Gentamycin
2.	*Aegle marmelos*	Rutaceaeae	Leaves	Gentamycin
3.	*Aerva javanica*	Amaranthaceae	Fresh roots	Cisplatin
4.	*Aerva lanata*	Amaranthaceae	Whole plant	Cisplatin
5.	*Allium sativum L*	Amaryllidaceae	Garlic	Gentamycin
6.	*Aloe barbadensis*	Xanthorrhoeaceae	Leaves	Cisplatin & Gentamycin
7.	*Avuri kudineer*	Fabaceae	Roots and Leaves	Cisplatin
8.	*Bauhinia variegate*	Caesalpiniaceae	Stems	Gentamycin
9.	*Berberris aristata*	Berberidaceae	Root bark	Cisplatin
10.	*Boerhaavia diffusa*	Nyctaginaceae	Leaves	Cisplatin
11.	*Butea monosperma*	Fabaceae	Whole plant	Gentamycin
12.	*Carica papaya*	Caricaceae	Seeds	Cisplatin
13.	*Cassia auriculata*	Fabaceae	Root	Gentamycin
14.	*Casuarina equisetifolia*	Casuarinaceae	Dried leaves	Gentamycin
15.	*Cichorium intybus*	Asteraceae	Aerial Parts	Cisplatin
16.	*Clitoria ternatea*	Papilionaceae	Whole plant	APAP-induced
17.	*Crataeva nurvula*	Capparidaceae	Fruit	Gentamycin
18.	*Curcuma longa*	Zingeberaceae	Rhizome	Cadmium induced
19.	*Dichrostachys cinera*	Mimosaceae	Roots	Cisplatin
20.	*Diospyros lotus*	Ebenaceae	Seeds	Gentamycin
21.	*Elephantophus scaber*	Asteraceae	Leaves	Gentamycin
22.	*Emblica officinalis*	Euphorbiaceae	Fruits	Gentamycin
23.	*Ficus religiosa*	Moraceae	Dried latex	Cisplatin
24.	*Ficus racemosa*	Moraceae	Stem bark	Gentamycin
25.	Ginkgo biloba	Ginkgoceae	Leaves	Gentamycin
26.	*Harungana madagascarienis*	Hypericaceae	Root	Acetaaminophen
27.	*Ichnocarpus frutescens*	Apocynaceae	Whole plants	Cisplatin
28.	*Kalanchoe pinnata*	Crassulaceae	Leaves	Gentamycin
29.	*Kigelia africana*	Bignoniaceae	Fruits	Cisplatin
30.	*Lantana camara*	Verbenaceae	Roots	Gentamycin
31.	*Mammea africana*	Guttiferae	Stem bark	Acetaminophen
32.	*Momordica tuberosa*	Cucurbitaceae	Dried tubers	Cisplatin, Gentamycin & Acetaminophen
33.	*Moringa pterygosperma*	Moringaceae	Leaves	Acetaminophen
34.	*Mulberry (Morus Sp.)*	Moaraceae	Leaves	Acetaminophen
35.	Oroxylum indicum	Bignoniaceae	Whole plant	Gentamycin
36.	*Panax ginseng*	Araliacea	Roots	Cisplatin
37.	*Pedalium murex*	Pedaliaceae	Dried fruits	Cisplatin & Gentamycin
38.	*Phaseolus radiatus*	Leguminosae	Seeds	Gentamycin
39.	*Phyllanthus amarus*	Euphorbiaceae	Seeds	Gentamycin
40.	*Phyllanthus niruri*	Euphorbiaceae	Leaves	Gentamycin
41.	*Pimpinella tirupatiensis*	Apiaceae	Whole plant	Acetaminophen
42.	*Pimpinella tirupatiensis*	Apiaceae	Whole plant	Acetaminophen
43.	*Piper cubeba*	Piperaceae	Dried berries	Gentamycin
44.	*Plectranthus amboinicus*	Lamiaceae	Leaves	Acetaminophen
45.	*Pongamia pinnata*	Papilionaceae	Flowers	Cisplatin
46.	*Portula oleracea*	Portulaceae	Leaves and Stem	Cisplatin
47.	*Rhazya stricta*	Apocynaceae	Leaves	Gentamycin
48.	*Rubia cardifolia Linn*	Rubiaceae	Root	Ethylene glycol
49.	*Saccharum officinarum*	Poaceae	Jaggery	Acetaminophen
50.	*Salviae officinalis*	Lamiaceae	Whole plant	Cisplatin
51.	*Sida cordifolia*	Malvacea	Leaves & Root	Gentamycin
52.	*Solanum xanthocarpum*	Solanaceae	Fruit	Cisplatin & Gentamycin
53.	*Tinospora cardifolia*	Menispermeacea	Stem	Cisplatin
54.	*Tribulus terrestris*	Zygophyllaceae	Fruits	Gentamycin
55.	*Vitex negundo linn*	Verbenaceae	Bark	Chemical
56.	*Withania somnifera*	Solanaceae	Roots	Gentamycin
57.	*Zingiber officinale roscoe*	Zingiberaceae	Ginger Rhizome	Gentamycin

Reported Phytoconstituents

The study on rhizomes of *Bergenia ligulata* depicted the confinement of various concoction constituents as coumarins: bergenin; 11-O-galloyl; bergenin, 11-O-P hydrozybenzoyl; bergenin, 11-O-brotocatechuoyl; bergenin, 4-O-galloys. Flavonoids: catechin (+) afzelchin; avicularin, catechin; eriodictyol–7-O-β–D-glucopyranoside; reynoutrin. Benzenoids: arbutin; arbutin, 6-O-p-hydroxy-benzoyl; arbutin, baenzoic corrosive, 4-hydroxy. catechin, quercetin–3-0-catechin, bergenim, 4-Ogalloylbergenin, and protocatechic. Paashaanolactone (4(4′-β-glucopyranosyloxy-1′-benzoyloxy)-6-methyltetrahydropyran-2-one) another compound was disconnected from the rhizomes of *Bergenia ligulata*. The rhizomes were found to contain higher centralization of bergenin, catechin, gallic corrosive and (+) - afzelechin than different parts of the plants which was evaluated by a basic strategy for synchronous 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 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 actuating 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), *Crateva 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 Gorakshaganja in Ayurveda arrangement of prescription. It is considered as one among the couple of natural wellsprings of Pashanabheda. The plant is broadly utilized as a part of urinary issue like Ashmari (Urinary calculi), Mootrakrichra (Dysuria), Mootravikara and so on by a large portion of the Ayurveda and Siddha specialists in southern India, for the sake of Pashanabheda. [60]

Fig. 2: Morphology of *Aerva lanata* Plant

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, supparative, diuretic and lithontriptic. 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, bryophynol and two homologous phenanthrene subsidiaries 2(9-decenyl) - phenanthrene (I) and 2-(undecenyl) - phenanthrene (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-orthoacetate and bufadienolidebryophyllin B were likewise disengaged. Botulin, β-sitosterol, amyrin, plant hentriacontane, campesterol, stigmasterol, kaempferol, propionic corrosive, β-carboline-I, aervoside and aervolanine. Four new alkaloids-aervine (10-hydroxy canthin-6-one), methylaervine (10-methoxycanthin-6-one), aervoside (10-β-D-glucopyranosyloxycanthin-6-one), and aervolanine (3-(6-methyoxy-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.

Sodium and potassium level in pee test was additionally evaluated. Nephroprotective movement of JZS against gentamycin-prompted 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 nephroprotecitve 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

Coleus aromaticus (*Syn*: *Coleus amboinicus* 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 antilithiotic, 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, chacicol and flavonoids. Quercetin, apigenin, luteolin, salvigenin, genkwanin and essential oil in the leaves have been reported. Monoterpenes and sesquiterpenes have been reported from Coleus aromaticus limonene, linalool, myrcene and thymol, alpha-amorphene, beta 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 anti-oxidative 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) Friuts (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., trioctanyl dotrioctanoate 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 ethanolic 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 hepatoprotective and nephroprotective 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 nephroprotector 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, urine to serum creatinine ratio, lipid peroxidation, gluthione, 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 near 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, cyanogenetic, 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]

Fig. 5: Morphology of *Cynodon dactylon* (a) Arial Part (b) entire plant

Reported Phytochemical

The phytochemical analysis showed that the plant contained flavanoids, alkaloids, glycosides, terpenoides, triterpenoids steroids, saponins, tannins, resins, phytosterols, 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* Hexadecanoic acid, ethyl ester linolenic acid, ethy ester d-mannose 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-dihydroxy-6-methyl 57%, benzofuran, 2,3-dihydro 39%, 2-furancarboxaldehyde, 48%,decanoic acid, ethyl ester 63%, d-mannose 20%, Ar-tumerone 31%, tumerone 23%, tricyclo[6.3.0.0(1,5)]undec-2-en-4one,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 asiatica* 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 epiflourescence 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 in different animal models. The nephroprotective activity is probably due to the presence phyto-constituents 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.

REFERENCE

1. Talele BD, Mahajan R, Chopda MK, Nemade N. Nephroprotective Plants: A Review. Int J Pharmacy Pharm Sci. 2012; 4:8-16.
2. Singh NP, Prakash A. Nephrotoxic Potential of Herbal Drugs. JIMSA. 2011; 24: 79-81.
3. Mendoza SA. Nephrotoxic Drugs. Pediatr Nephrol. 1988; 2:466-76.
4. Chopra RN, Nayar SL, Chopra IC. Glossary of Indian Medicinal Plants, National Institute of Science Communication (CSIR), New Delhi 1999.
5. Gupta AK. Sharma N. Tendon. Reviews on Indian Medicinal Plants I-IV, ICMR, New Delhi. 2004.
6. Jain SK. Dictionary of Indian Folkmedicine and Ethnobotany, 1991, pp. 311.
7. Nigeria: Tackling Challenges Facing Kidney Failure Patients: Alarming Facts about Kidney Disease | Medindia
8. Normal J, William E, Jhon J *et al*. Management of acute renal failure in the pediatric patient. Hemofiltration versus hemodialysis. Am J Kidney Dis. 1997; 30:84-88.
9. Lopez-Novoa JM, Quiros Y, Vicente L, Morales AI, Lopez-Hernandez FJ. New insights into the mechanism of aminoglycoside nephrotoxicity: an integrative point of view. Kidney Int. 2011; 79:33-45.
10. Rougier F, Claude D, Maurin M, Maire P. Aminoglycoside nephrotoxicity. Curr Drug Targets Infect Disord. 2004; 4: 153-162.
11. Safdar A, Ma J, Saliba F, Dupont B, Wingard JR, Hachem RY, et al. Drug-induced nephrotoxicity caused by amphotericin B lipid complex and liposomal amphotericin B: a review and meta-analysis. Medicine (Baltimore). 2010; 89:236-44.
12. Goldman RD, Koren G. Amphotericin B nephrotoxicity in children. J Pediatr Hematol Oncol. 2004; 26:421-426.
13. Mistro S, Maciel Ide M, de Menezes RG, Maia ZP, Schooley RT, Badaró R. Does lipid emulsion reduce amphotericin B nephrotoxicity? A systematic review and meta-analysis. Clin Infect Dis. 2012; 54:1774-1777.
14. Lencioni R, Fattori R, Morana G, Stacul F. Contrast-induced nephropathy in patients undergoing computed tomography (CONNECT) - a clinical problem in daily practice? A multicenter observational study. Acta Radiol. 2010; 51:741-750.
15. Arana E, Catala-Lopez F. Contrast-induced nephropathy in patients at risk of renal failure undergoing computed tomography: systematic review and meta-analysis of randomized controlled trials. Med Clin (Barc). 2010; 135:343-350.].
16. Lee JP, Heo NJ, Joo KW, Yi NJ, Suh KS, Moon KC, *et al*. Risk factors for consequent kidney impairment and differential impact of liver transplantation on renal function. Nephrol Dial Transplant. 2010; 25:2772-2785.
17. Hamour IM, Omar F, Lyster HS, Palmer A, Banner NR. Chronic kidney disease after heart transplantation. Nephrol Dial Transplant. 2009; 24:1655-1662.
18. Detrenis S, Meschi M, Musini S, Savazzi G. Lights and shadows on the pathogenesis of contrast-induced nephropathy: state of the art. Nephrol Dial Transplant. 2005; 20:1542-1550.
19. Chen N, Aleksa K, Woodland C, Rieder M, Koren G. The effect of N-acetylcysteine on ifosfamide-induced nephrotoxicity: in vitro studies in renal tubular cells. Transl Res. 2007; 150: 51-57.
20. Nissim I, Horyn O, Daikhin Y, Nissim I, Luhovyy B, Phillips PC, *et al*. Ifosfamide-induced nephrotoxicity: mechanism and prevention. Cancer Res. 2006; 66:7824-7831.
21. Deray G, Martinez F, Katlama C, Levaltier B, Beaufils H, Danis M, *et al*. Foscarnet nephrotoxicity: mechanism, incidence and prevention. Am J Nephrol. 1989; 9:316-321.
22. Maurice-Estepa L, Daudon M, Katlama C, Jouanneau C, Sazdovitch V, Lacour B, *et al*. Identification of crystals in kidneys of AIDS patients treated with foscarnet. Am J Kidney Dis. 1998; 32:392-400.
23. Rho M, Perazella MA. Nephrotoxicity associated with antiretroviral therapy in HIV-infected patients. Curr Drug Saf. 2007; 2:147-54.
24. Izzedine H, Launay-Vacher V, Deray G. Antiviral drug-induced nephrotoxicity. Am J Kidney Dis. 2005;45:804-17
25. Singh AP, Muthuraman A, Jaggi AS, Singh N, Grover K, Dhawan R. Animal models of acute renal failure. Pharmacol Reports 2012; 64: 31-44.
26. El-Tantawy WH, Mohamed SAH, Al-Haleem ENA. Evaluation of biochemical effects of *Casuarina equisetifolia* extract on gentamycin-induced nephrotoxicity and oxidative stress in rats. Phytochemical analysis. J Clinic Biochem Nutr. 2013; **53**: 158–165.
27. Prusty KB, Harish B, Mamatha CH. Evaluation of nephroprotective activity of the methanolic extract of leaves of *Bauhinia variegate* Linn, (Family-Caesalpiniaceae). J Pharma Sci Tech. 2012; 2:16-19.
28. Kavitha AV, Jagadeesan G. Role of *Tribulus terrestris* (Linn.) (Zygophyllacea) against mercuric chloride induced nephrotoxicity in mice, *Mus musculus* (Linn.). J Environ Biol. 2006; 27:397-400.

29. Dubey T, Srivastava A, Nagar H, Mishra BK, Mishra SS. Nephroprotective activity of *Nelumbo nucifera* gaertn. roots, leaves and flowers on gentamycin induced nephrotoxicity. Asian J Pharma Edu Res. 2014, **3**: 134-151.
30. Saleh IA. Evaluation of the hepatroprotective and nephroprotective activities of *Scrophularia hypericifolia* growing in Saudi Arabia. Saudi Pharma J. 2014; 22:258–263.
31. Yadav YC, Srivastav DN, Seth AK, Saini V, Yadav KS. Nephropharmacological activity of ethanolic extract *Lepidium sativum* L. seeds in albino rats using cisplatin induced acute renal failure. Int J Pharma Sci Rev Res. 2010: 64-68.
32. Chatterjee P, Mukherjee A, Nandy S. Protective effects of the aqueous leaf extract of *Aloe barbadensis* on gentamycin and cisplatin-induced nephrotoxic rat. Asian Pac J trop Biomed. 2012:S1754-S1763.
33. Gajjar KK, Aiwale AS, Anovadiya AP, Mevada AV, Baxi SN, Tripathi CB. Evaluation of nephroprotective effect of hydroalcoholic extract of *Cyperus scariosus* Linn. in gentamycin-induced acute kidney injury in *wistar* albino rats. Jundishapur J Nat Pharm Prod. 2016; 11: e34452.
34. Dhibi S, Bouzenna H, Samout N, Tlili Z, Elfeki A, Hfaiedh N. Nephroprotective and antioxidant properties of *Artemisia arborescens* hydroalcoholic extract against oestroprogestative-induced kidney damages in rats. Biomed Pharmacother. 2016; 82:520-527.
35. Gandhi S, Srinivasan BP, Akarte AS. Potential nephrotoxic effects produced by steroidal saponins from hydro alcoholic extract of *Tribulus terrestris* in STZ-induced diabetic rats. Toxicol. Mech. Methods. 2013; **23**:548-557.
36. Kaksaheb JK, Shete RKV, Kale BN, Borade AS. Protective Role of Hydroalcoholic Extract of Ficus carica In Gentamycin Induced Nephrotoxicity In Rats. Int. J. of Pharm. Life Sci. 2011; 2: 791-796, 979.
37. Patel S Rajashekhar I. Role of Plants as Nephroprotective agents – A Review. Int J Therap Applications. 2015; 26: 6-14
38. Srivastava AK, Kaushik D, Shrivastava AK, Lal VK. Curative Effect of Natural Healars for the Treatment of Kidney Disorders: A Review. J Ayur Integ Med. (Paper Submitted with refrence no. JAIM_2017_115)
39. Encyclopaedia of World Medicinal Plants, Vol I, T. Pullaiah, 2006, pp. 311.
40. Chauhan R, Ruby KM, Dwivedi J. *Bergenia ciliata* Mine of Medicinal Properties: A Review. Int J Pharma Sci Rev Res. 2012; 15:20.
41. Chowdhary S, Verma DL, Kumar H. Biodiversity and traditional knowledge of Bergenia spp. in Kumaun Himalaya. New York Science Journal. 2009; 2(6):105-8.
42. Bahu CP, Seshadri RT. Advances in Research In "Indian Medicine, "Pashanbedi" Drugs Forurinary Calculus, Udupa K.N. (eds). 1970:77-98.
43. Harsoliya MS, Pathan JK, Khan N, Bhatt D, Patel UM. Effect of Ethanolic Extracts of *Bergenia ligulata*, *Nigella sativa* and Combination on Calcium oxalate Urolithiasis in Rats. Int Drug Formulation Res. 2011; 2: 268-280.
44. Pant S, Samant SS, Arya SC. Diversity and Indigenous Household Remedies of The Inhabitants Surrounding Mornaula Reserve Forest In West Himalaya. Ind J Trad Knowledge. 2009; 8: 606-610.
45. Samal PK, Dhyani PP, Dollo M. Indigenous Medicinal Practices of Bhotia Tribal Community in Indian Central Himalaya. Ind J Trad Knowledge. 2010; 1: 140-144.
46. Sharma HK, Chhangte L, Dolui AK. Traditional Medicinal Plants in Mizoram, India. Fitoterapia. 2001; 72: 146-161.
47. Ballabh B, Chaurasia OP, Ahmeda Z, Singha SB. Traditional Medicinal Plants of Cold Desert Ladakh Used Against Kidney And Urinary Disorders. J Ethnopharmacol. 2008; 118:331-339.
48. Kumar V, Tyagi D. Review on phytochemical, ethnomedical and biological studies of medically useful genus *Bergenia.* Int J Curr Microbiol App Sci. (2013) 2(5): 328-334.
49. http://prr.hec.gov.pk/chapters/1012-6.pdf.
50. Chandrareddy UD, Chawla AS, Mundkinajeddu D, Maurya R Handa SS. Paashaanolactone From *Bergenia Ligulata*. Phytochem. 1998; 47: 907-909.
51. Chandrareddy UD, Chawla AS, Mundkinajeddu D, Singh D, Handa SS, High Pressure Liquid Chromatographic Determination of Bergenin And (+) -Afzelechin From Different Parts of Paashaanbhed (*Bergenia ligulata* Yeo). Phytochem analysis. 1999; 10:44 – 47.
52. Dhalwala K, Shindev M, Biradara YS, Mahadika KR. Simultaneous Quantification of Bergenin, Catechin, and Gallic Acid from *Bergenia ciliata* and *Bergenia ligulata* By Using Thin-Layer Chromatography. J Food Comp Analysis. 2008; 21: 496-500.
53. Srivastava S, Rawat AKS, Simultaneous Determination of Bergenin and Gallic acid In Different *Bergenia* Species. J Plan Chromatograph-Modern TLC. 2007; 20: 275-277.
54. Chauhan SK, Singh B, Agrawal S. Simultaneous Determination of Bergenin and Gallic Acid In *Bergenia Ligulata* Wall By High-Performance Thin-Layer Chromatography. J Aoac Int. 2000; 83:1480-3.
55. Singh DP, Srivastava SK, Govindarajan R, Rawat AKS. High-Performance Liquid Chromatographic Determination of Bergenin in Different *Bergenia* Species. Acta Chromatographica. 2007; 19:246-252.
56. Ghosh MN. Fundamental of Experimental Pharmacology, 2nd Edition, Scientific Book Agency; pp. 174-198
57. Mazharul I, Iqbal A, Khan U, Muhammad A, Ahmad A, Shahbuddin. Bioactivity evaluation of *bergenia ciliate.* Pak J Pharma Sci. 2002; 15:15-33.
58. Barwal A, Kumari S, Verma SK, Goyal PK, Sharma I, Sharma S, Sharma AK. Evaluation of Herbal Formulation Neeri (NS-RF) For Protective Effect against Heavy Metal Induced Nephrotoxicity in Rats. Indo Am J Pharma Res. 2015; 5: 2790-2798.
59. Singh Y, Murgunanandam AV, Das SN, Rao AT, Agarwala SK. Reno-protective action of a herbal formulation (ELKP-1) in cisplatin-induced nephrotoxicity. Phytomedica. 1999; 20: 37-41.
60. Nagaratna A, Prakash L Hegde, Harini A. A Pharmacological Review on Gorakha Ganja (*Aerva lanata* (Linn) Juss. Ex. Schult). J Pharmacog Phytochem. 2014; 3: 253-257.
61. Pareta SK, Patra KC, Papiya M. Establishing the Principle of Herbal Therapy for Antiurolithiatic Activity: A Review. J Pharmacol Toxicol. 2011; 6: 321-332.
62. Akram A, Abdell AN, Mohamed FN. Urolithiasis In Tunisian Children: A Study of 100 Cases. Soudi J of Kidney Dis. Transplant. 2009; 2: 1096-1100.
63. Bapalal V. Some Controversial Drugs in Indian Medicines. 1st Edn; Chaukhambha Orientalia, 1982.
64. Yadav NP, Dixit VK. Hepatoprotective Activity of Leaves of *Kalanchoe Pinnata* Pers. J Ethnopharmacol. 2003; 86:197-202.
65. Shirwaikar A, Issac D, Malini S. Effect of *Aerva Lanata* on Cisplatin and Gentamycin Models of Acute Renal Failure. J Ethanopharmacol. 2004; 9:81–86.
66. Zapesochnaya GG, Pervykh LN, Kurkin, VA. A Study of the Herb *Aerva Lanata.* III. Alkaloids. Chemistry of Natural Compounds 1991; 27: 336-340.
67. Agrawal R, Sethiya NK, Mishra SH. Antidiabetic Activity of Alkaloids of *Aerva lanata* Roots on Streptozotocin-Nicotinamide Induced Type-II Diabetes in Rats. Pharm Biol. 2013: 1–8.
68. Afzal M, Khan NA, Ghufran A, Iqbal AM. Diuretic and nephroprotective effect of Jawarish Zarooni Sada—a polyherbal unani formulation. Innamuddin J Ethnopharmacol. 2004: 91 219–223.
69. Soumya PS, Poornima K, Kumar R, Kalaiselvi G, Gomathi M, Uma DC. Nephroprotective effect of *Aerva lanata* against Mercuric chloride induced renal injury in rats. J Pharmacy Res. 2011; 4: 2474
70. Vetrichelvan T, Jegadeesan M. Anti-diabetic activity of alcoholic extract of *Aerva lanata* (L.) Juss. ex Schultes in rats. J Ethnopharmacol. 2002; 80:103-107.