

NEPHROPROTECTIVE POTENTIAL OF MEDICINAL PLANTS AND HERBAL MEDICINES: A REVIEW ON NATURAL NEPHROPROTECTIVE AGENTS

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ABSTRACT

Renal disorders have always remained a major area of concern for health. Medicinal plants may serve as a vital source of potentially useful new compounds for the development of effective therapy to combat a variety of kidney problems. Incidence of kidney diseases leading to kidney failure is increasing day by day. Many herbs have been proven to be effectual as nephroprotective agents. Various chemicals in common use are potential renal toxins. The use of herbal drugs for the prevention and treatment of various diseases is constantly developing. Some herbal therapy to treat severe renal disorders requires systematic investigation of properties like acute renal failure, nephritic syndrome and chronic interstitial nephritis. Herbal medicines possess curative properties due to the presence of their phytochemicals. Nephrotoxicity is an inherent adverse effect of certain antibiotics, anticancer drugs and other synthetic drugs. Various natural products and dietary antioxidants have exhibited protective effects against nephrotoxicity. Various herbal drugs have shown their potent nephroprotective effect due their antioxidant, diuretic, anti-inflammatory, antispasmodic properties. In this review, study the nephroprotective medicinal plants and herbal medicines which are scientifically proved in treating renal disorders.

KEYWORDS: Nephro Toxicity, Medicinal Plants, Nephroprotective Agents, Renal Disorders.

INTRODUCTION

The traditional medicines (or herbal drugs) have been existed in therapeutic practice before the development of modern medicine. Traditional medicine is the therapeutic experience of generations of practicing physicians of indigenous system of medicine. Traditional preparations comprise medicinal plants, minerals and organic matter etc. Herbal drugs

constitute only those traditional medicines which primarily use medicinal plant preparations for therapy. A large section of the world's population believes in traditional medicine, despite the great advancements in allopathic medicine. Research is underway in many colleges of alternative medicine to cope with modern maladies.

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Several herbal folklore surveys provide a glimpse of the ethano-pharmacological potential of herbs used by the villagers and tribals for the treatment of various diseases (Rajagopal, et al., 2013; Lakshmi et al., 2012).

Nephrotoxicity is one of the most common kidney problems and occurs when body is exposed to a drug or toxin (Porter and Bennett. 1981). Various therapeutic agents can adversely affect the kidney resulting in acute renal failure, chronic interstitial nephritis and nephritic syndrome because there is high number of potent drugs like aminoglycosides, NSAID's, chemotherapeutic agents have been added to the therapeutic armory in recent years (Hoitsma et al., 1991). Exposure to chemical reagents like ethylene glycol, carbon tetrachloride, sodium oxalate and heavy metals like lead, cadmium, mercury, and arsenic also induces nephrotoxicity. Prompt recognition of the disease and cessation of responsible drugs are usually the only necessary therapy (Paller. 1990). Nephroprotectives are possess protective activity against Nephrotoxicity. Medicinal plants have curative properties due to the presence of various complex chemical compounds. Various herbs are use for the cure of renal disorders (<http://farmacists.blogspot.com>). Co-administration of various medicinal plants that possessing nephroprotective activity along with different nephrotoxic agents which may attenuate its toxicity. The term renal failure mainly denotes failure of the excretory function of kidney, leading to retention of nitrogenous waste products of metabolism in the blood (Gourley. 2000). , There is a failure of regulation of fluid and electrolyte balance along with endocrine dysfunction. The renal failure is fundamentally categorized into acute and chronic renal failure (Barry et al., 2000). Acute renal failure (ARF) refers to the sudden and usually reversible loss of renal function which develops over a period of days or weeks. There are many causes for ARF which mainly includes

acute tubular necrosis that commonly accounts for 85% of incidence. Mostly acute tubular necrosis occurs either due to ischemia or toxins. The toxins may be exogenous or endogenous. The exogenous agents are radio contrast agents, cyclosporine, antibiotics, chemotherapeutics, organic solvents, acetaminophen and illegal abortifacients (Gourley. 2000; Barry et al., 2000). Chronic renal failure (CRF) is an irreversible deterioration in the renal function which classically develops over a period of years, leading to loss of excretory metabolic and endocrine functions. Various causes of renal failure has been recognized like hypertension, diabetes mellitus, antineoplastic agents like cyclophosphamide, vincristin and cisplatin etc (Gourley. 2000).

PLANTS AS NEPHROPROTECTIVE AGENTS

Medicinal plants have curative properties due to the presence of various complex chemical substances and cure of kidney disease (Ramya Pydi et al., 2011). Sources of herbs, which have been reported for the possible uses in nephritic disorders in the literature, are as follows.

ASPARAGUS RACEMOSUS

The decoction of the whole plant of *Asparagus racemosus* is used for treatment of the kidney (Melookunnel.1996).

ACHYROCLINE SATUREIODES

Hydro alcoholic extract of *A. satureioides* might change renal ion transport, it affects gastrointestinal reabsorption (Rocha et al., 1994).

ANGELICA RADIX (ROOT)

The effect of *A. radix* root on the nephrotoxicity, caused by i.p. use of 3 mg/kg cis-diaminedichloroplatinum (CDDP) was examined in mice (Sugiyama et al., 1994).

ARCTOSTAPHYLOS UVA-URSI

The effect of the dry extract from the leaves of *A. uva-ursi* was tested on the course of acute coli bacillary pyelonephritis in rats (Nikolayev et al., 1996).

ASWAGANDHA

The protective action of Aswagandha (*Withania somnifera*) on cadmium induced toxicity in mice kidney. Mice were fed with cadmium chloride along with Aswagandha extract and Aswagandha extract alone (1.14 g/kg body weight) for 20 days. Aswagandha is capable of reducing toxicity caused by cadmium (Panday, 1997).

AERVA LANATA

Aerva lanata (Pasanabheda, Chaya, Gorakhganja) belongs to the family Amaranthaceae (Variers and Vaidya Sala, 1994). The *A. lanata* plant have α -amyrin, campesterol, β -sitosterol, its palmitate, chrysin and flavonoid glucosides (Khare, 2007). Canthin-6-one and β -carboline alkaloids were isolated from *A. lanata* (Zapesochnaya et al., 1992). Four new alkaloids viz, aervine, methylaervine, aervoside and aervolanine were isolated (Vaidyaratnam et al., 1994). The plant was reported for various activities like diuretic, hepato protective (Majumdar et al., 1999), antidiabetic (Vetrichelvan and Jegadeesan, 2002), antimicrobial (Chowdhury et al., 2002), anthelmintic and demulcent activity (Guhabhakshi et al., 1999). *A. lanata* also shows its effect on cisplatin and gentamycin model of ARF (Shirwaikar et al., 2004). The ethanolic extract of the entire plant of *A. lanata* was tested as nephroprotective agent in cisplatin and gentamicin induced acute renal injury in rats. In the curative regimen, the extract at dose levels of 75, 150 and 300 mg/kg showed dose-dependent reduction in the elevated blood urea and serum creatinine in the cisplatin

model. In the gentamicin model the rats in the preventive regimen also showed good response to the ethanol extract at 300 mg/kg. The ethanolic extract of *A. lanata* possesses marked nephroprotective activity with minimal toxicity and could offer a promising role in the treatment of ARF caused by nephrotoxins like cisplatin and gentamicin (Shirwaikar et al., 2004).

ALLIUM ASCALONICUM

The clinical use of an immunosuppressive cyclosporine A (CsA) is limited by its serious nephrotoxic effect. Shallot (*Allium ascalonicum* L.) has been shown to possess antioxidative and free radical scavenging activities. The possible beneficial effect of shallot extract on renal injury caused by CsA. Male Wistar rats were treated orally with vehicle, CsA (25 mg/kg), shallot extracts (1 g/kg), and CsA plus shallot extract for 21 days. Renal function, tissue malondialdehyde (MDA) and glutathione (GSH) levels were tested 24 h after the last treatment. CsA-induced nephrotoxicity was evidenced by increased blood urea nitrogen and serum creatinine, but decreased urea and creatinine clearance. The kidney of CsA treated rats exhibited severe tubular necrosis. CsA also induced oxidative stress, as indicated by increased renal MDA and reduced GSH concentrations. Use of shallot extract along with CsA counteracted the deleterious effects of CsA on renal dysfunction, oxidative stress markers. The protective potential of shallot extract against CsA nephrotoxicity and suggest a significant role of its antioxidant property to this beneficial effect (Wongmekiat et al., 2008).

AEGLE MARMELOS

Nephroprotective activity of an aqueous extract of the leaves of *Aegle marmelos* in rats. The aqueous extract of the plant was used at three doses (250, 500, and 750 mg/kg, p.o) to wistar rats in gentamicin model. The extract of the

plant normalized the serum creatinine, urea and blood urea nitrogen levels in gentamicin toxicity indicating a nephro-protective effect (Kore et al., 2011).

AERVA JAVANICA

Aerva javanica Juss. ex Schult is medicinal plant belonging to the family Amaranthaceae. *A. javanica* is an anthelmintic, diuretic, demulcent. It is also used for the treatment of headache (Soliman. 2006; Chopra et al., 1956). The decoction of the plant is used to remove swellings, applied to acne like conditions of the face (Gaze. 1940). The aqueous extracts of *A. javanica* roots were exhibited nephroprotective activity. The cisplatin injury was evidenced by the elevated biochemical markers and histopathological features of acute tubular necrosis. The aqueous extract at the dose level of 400 mg/kg body weight was found to normalize the elevated biochemical markers and bring about a marked recovery in kidneys as evidenced (Chopra et al., 1956; Gaze. 1940).

ASTRAGALI RADIX

The effects of aqueous extract of *Astragali Radix* (ARE) on the oxidative stress status and endothelial nitric oxide synthase level in adriamycin (ADR) nephropathy rats were tested. The ADR nephropathy rats were randomly treated with ARE (2.5 g/kg/d), or benazepril (10 mg/kg/d, angiotensin-converting enzyme inhibitor (ACEI) group) for ten weeks. Serum urea nitrogen, creatinine, albumin, total protein, cholesterol and 24-h urinary protein concentration were determined. Renal cortex catalase (CAT), glutathione peroxidase (GSH-Px), superoxide dismutase (SOD), malondialdehyde (MDA) activities, and 24-h urinary $\text{NO}_3^-/\text{NO}_2^-$ excretion were determined. Renal cortex cyclic guano sine monophosphate (cGMP) level was measured by enzyme immunoassay. The ARE and ACEI treatments could remarkably reduce more 24 h urinary

protein excretion than that in ADR group and there was no difference between ARE and ACEI group. Renal cortex CAT, GSH-Px activities in ARE and ACEI group were significantly higher than ADR group, and renal cortex SOD activity in ARE group was higher than ADR group. Renal cortex MDA activity, cGMP level, and glomerular and tubular eNOS expression in ARE and ACEI group were lower than that in ADR group, and 24-h urinary $\text{NO}_3^-/\text{NO}_2^-$ excretion in ARE group was lower than ADR group. Renal cortex MDA content, cGMP content expression in glomerulus were strongly positively associated with 24 h urinary protein excretion. The ARE may ameliorate the proteinuria and inhibiting the oxidative injury in ADR nephropathy rats (You et al., 2011).

BAUHINIA VARIEGATE

The nephroprotective effect of ethanolic extract of *Bauhinia variegata* stem against cisplatin induced nephropathy was tested in rats. The protective action of the plant against cisplatin induced nephropathy (Pani et al., 2011).

CARISSA OPACA

Carissa opaca fruit constitutes flavonoids possessing antioxidant activities. Effect of methanolic extract of 25 *C. opaca* fruit (MFC) and its derived fractions; n-hexane (HFC), ethyl acetate (EFC), chloroform (CFC), buta- 26 nol (BFC) and aqueous extract (AFC) against carbon tetrachloride (CCl_4) induced nephrotoxicity was studied. Intraperitoneal (i.p) dose of 20% CCl_4 (0.5 ml/kg b.w) was administered twice a week for 8 weeks to a 28 group of rat. Other groups were given CCl_4 and various fractions of *C. opaca* fruit (200 mg/kg bw). CCl_4 treatment depleted GSH contents and activities of antioxidant enzymes; CAT, POD, SOD, GST, GSR, 30GSH-Px, and QR in kidney samples. High level of renal lipid peroxides (TBARS), H_2O_2 , DNA injuries and histopathological lesions were

observed in CCl₄ test group. The CCl₄ increased RBCs, WBCs, urea, urobilinogen and creatinine in urine while BUN, creatinine, urobilinogen, direct and total bilirubin, and nitrite in serum. Treatment of various fractions attenuates the toxicity of CCl₄ and weight of body and kidneys reversed towards the normal level. The presence of myricetin, isoquercetin, apige-35 nin and orientin in CFC, AFC and MFC with evident protective effects. The *C. opaca* fruit is a useful functional food for preventing kidney disorders (Khan et al., 2011).

CROTON ZAMBESICUS

The kidney protective effect of ethanolic root extract of *Croton zambesicus* against gentamicin-induced kidney injury in rats. The root extract (27-81 mg/kg) was used to rats for eight days with concurrent use of gentamicin (100 mg/kg) daily for the same period of time. Protective effect of the extract was tested in serum levels of creatinine, urea, and uric acid as well as some ions like sodium, potassium and chloride. Use of the root extract significantly reduced histopathological changes in the kidneys of the extract-treated rats especially in the rats treated with lower doses of the extract (27 and 54 mg/kg).

The levels of serum urea and creatinine were also reduced significantly at these doses with no observable effect on the levels of uric acid and ions. The kidney protective activity of this extract could be due to its antioxidant and free radical scavenging activities (Okokon et al., 2011).

CRATAEVA RELEGIOSA

The bark of *Crataeva relegiosa* is useful in the urinary disorders and kidney stone remover. The crude drug contains an active principle lupeol, a triterpenoid which is mainly involved in the pharmacological activities (Patil et al., 2011).

CASSIA AURICULATA

Effect of *Cassia auriculata* Linn. root extract on cisplatin and gentamicin induced renal injury was studied. The alcoholic extract normalized the raised blood urea and serum creatinine levels. The reduction in serum creatinine levels was observed only in the group treated with 600 mg/kg. In the gentamicin model the alcoholic extract at 600mg/kg dose reduced the blood urea and serum creatinine level effectively in both the curative as well as the preventive therapy (Shirwaikar et al., 2005).

CLERODENDRON TRICHOTOMUM

Intravenous use of the extract to rats and dogs, elicited renal vasodilatation, increased urine flow and urinary sodium excretion (Lu et al., 1994).

CAMELLIA SINENSIS

In rats given 2 mg of green tea tannin mixture, the methyl guanidine (uremic toxin) excretion was significantly decreased indicating a possible radical scavenging action (Yokozawa et al., 1992).

CRATAEVA NURVALA

Lupeol, isolated from *Crataeva nurvala* stem bark in doses of 40 and 80 mg/kg body weight, p.o, for 10 days, decreased the concentration of blood urea nitrogen, creatinine and lipid peroxidation and increased glutathione and catalase activities in cisplatin (5mg/kg body weight, i.p) induced nephrotoxicity in rats. The increased glutathione and catalase activities are indicative of antioxidant properties of lupeol (Shirwaikar et al., 2004).

CRATAEVA NURVALA

Crataeva nurvala Buch-Ham, family Cappariaceae commonly known as Varuna, is an evergreen tree indigenous to India (Parvin et

al., 2012). The potentiality of *C. nurvala* extract and its active principle, particularly lupeol as diuretic, anti-inflammatory, antioxidant, cardio-protective, hepatoprotective, lithonotriptic, anti-rheumatic, anti-periodic, contraceptive, anti-protozoal, rubifacient and vesicant (Farjana et al., 2012). The alcoholic extract of *C. nurvala* 250 and 500 mg/kg for 10 days showed protective activity against cisplatin 5 mg/kg induced nephrotoxicity. The alcoholic extract has significantly altered the dysfunction of renal proximal tubule cells by decreasing the concentration of blood urea nitrogen, creatinine, lipid peroxidation, glutathione and catalase (Shelkea et al., 2011). Use of aqueous extract of *C. nurvala* 200 and 400 mg/kg for 28 days showed protective activity against ethylene glycol induced nephrotoxicity (Sridhar et al., 2011).

CORDYCEPS SINENSIS

The simultaneous use of the plant *Cordyceps sinensis* with gentamicin protects the proximal tubular cells from gentamicin toxicity. The use of *C. sinensis* after establishment of kanamycin induced acute renal failure reduced the recovery time significantly compared to control group (Zhan.1992).

COCOS NUCIFERA (COCONUT)

Rats, fed with methyl deficient diet, developed renal necrosis with acute renal failure. The renal protective effect was evidenced by less or no mortality and increased survival time in the methyl-deficient rats receiving coconut oil, as well as by a reduced incidence and severity of the renal lesions as tested by renal weight, type (tubular and cortical necrosis or repair) and extent (grade) of the renal damage. (Monserrat et al., 1995).

CARICA PAPAYA

Carica papaya Linn, family caricaceae. *Carica papaya* is a rich source of phytoconstituents

mainly carpaine, dehydrocarpaine, pseudocarpaine. It has various traditional remedies and pharmacological activities like antioxidant, wound healing, hepatoprotective, anti inflammation, antibacterial, analgesic, heart tonic, anthelminthic and to treats ringworm, high blood pressure, stomachache, skin sores, fungal infections, cancer and prevents rheumatism, psoriasis. The aqueous seed extract of *C. papaya* has been tested by CCl₄ induced renal injury in rats as a dose and time-dependent study. The *C. papaya* extract has nephroprotective effect on CCl₄ renal injured rats, an effect which could be mediated by the phytoconstituents present in it either antioxidant and/or free radical scavengers (Mabberly. 1987; Doughari et al., 2007; Olagunju et al., 2009).

DRYNARIA FORTUNE

The flavonoid fraction (FF) from *Drynaria fortune* was tested to determine its biological activity expression in acute renal failure in Guinea pigs and mercuric chloride treated mice. Guinea pigs received 100 mg/kg of gentamicin and 10 mg/kg of FF. the FF treatment prevented the GM toxicity. Mice were treated once with 6 mg/kg of mercuric chloride, followed by 10 mg/kg of FF. In conclusion, the FF prevents nephrotoxicity, improves kidney function and promotes kidney primary epithelial tubular cell regeneration (Long M et al., 2005).

DOLICHOS BIFLORUS

The extract of *Dolichos biflorus* contains phytonutrients like alkaloids, flavonoids and isoflavone. Use of it significantly lowered the level of thiobarbituric acid reacting substances (TBARS) and enhanced the level of glutathione (GSH), catalase (CAT) and superoxide dismutase (SOD), thus protecting the tissues from oxidative stress (Muthu et al., 2006).

DIDYMOCARPUS PEDICELLATA

Ethanol extract of the aerial parts of *Didymocarpus pedicellata* exhibited significant antioxidant and protective activity against ferric nitriloacetate induced renal oxidative stress, nephrotoxicity and tumor promotion response. The extract provided significant protection against and dose-dependently protected against ferric nitriloacetate mediated damage to lipids and DNA. The nephroprotective activity of the plant is attributed to polyphenolic compounds. The study supported use of plant in the treatment of kidney diseases (Kaur. 2007).

DESMODIUM CANADENSE

The effect of the dry extract of the aerial parts of *D. canadense* on the course of CCl₄ induced acute renal insufficiency was studied in male albino rats. A marked nephroprotective effect was obtained with a dose of 50 mg/kg, with regeneration of the functional activity of the kidneys. The protective effect of the extract may be explained by its antioxidant activity which is due to the high content of phenolic compounds (Nikolayev et al., 1996).

ECHINACEA PALLID

The hydro alcohol extract of *Echinacea pallida* given to mice in association with the i.p use of cisplatin exhibited protective effects expressed by a diminished loss and faster recovery of the animal's body weight. Pretreatment with *E. pallida* also decreased cisplatin nephrotoxicity (Mustea.1997).

ERUCA SATIVA

Mercuric chloride (HgCl₂) is a well-known nephrotoxic agent. The role of oxidative stress in HgCl₂ induced nephrotoxicity. *Eruca sativa* is widely used in folklore medicines and has a good reputation as a remedy of renal ailments. The antioxidant potential of ethanolic extract of

E. sativa seeds was determined and its protective effect on HgCl₂ induced renal toxicity was tested. The extract was found to possess a potent antioxidant effect, with a large amount of polyphenols and a high reducing ability. The extract revealed glucoerucin and flavonoids to be the major antioxidantst. The *E. sativa* extract significantly scavenged several reactive oxygen species (ROS) and reactive nitrogen species (RNS). Feeding of the extract to rats afforded a significant protection against HgCl₂ induced renal toxicity. Subcutaneous use of 4 mg/kg body weight HgCl₂ induced renal injury evident as a marked elevation in serum creatinine and blood urea nitrogen levels. Oxidative modulation of renal tissues following HgCl₂ exposure was evident from a significant elevation in lipid peroxidation and attenuation in glutathione (GSH) contents and activities of antioxidant enzymes viz., catalase (CAT), glutathione peroxidase (GPX), superoxide dismutase (SOD) and glutathione reductase (GR). Oral use of *E. sativa* extract to rats at a dose regimen: 50–200 mg/kg body weight for 7 days prior to HgCl₂ treatment significantly and dose dependently protected. The *E. sativa* seeds to possess a potent antioxidant and renal protective activity and preclude oxidative damage inflicted to the kidney (Alam et al., 2007).

EPHEDRA DISTACHYA

Use of *E. distachya* an extract caused decrease in the concentration of urea nitrogen, creatinine. methyl guanidine and guanidinosuccinic acid in serum of rats significantly (Yokozawa et al., 1995).

FICUS RELIGIOSA

Ficus religiosa (L.), commonly known as pepal, family Moraceae plants have been used in traditional Indian medicine for various range of ailments. Traditionally the bark is used as an antibacterial, antiprotozoal, antiviral,

astringent, antidiarrhoeal, gonorrhoea, ulcers, and skin diseases (Kalpana and Rishi. 2009). The leaves reported antivenom activity and regulates the menstrual cycle (Chopra and Chopra. 1958). *F. religiosa* fruits contain flavonols namely kaempferol, quercetin, and myricetin (Bushra and Farooq. 2008). The possible potential, nephroprotective and curative role of the methanolic extract of *F. religiosa* was used against cisplatin (5mg/kg, i.p.) induced nephrotoxicity. A single dose of cisplatin induced shows the increased levels of urea and creatinine in serum and it was significantly recovered by 400mg/kg in curative and protective groups. The enzyme estimation in kidney tissue has found that increased malondialdehyde and decreased reduced glutathione (GSH). The nephrotoxicity induced by cisplatin due oxidative stress and methanolic extract of *F. religiosa* latex may have nephroprotective and curative activity (Bushra and Farooq. 2008).

FAGOPYRUM ESCULENTUM (BUCKWHEAT)

In ischemia reperfused control rats, the activities of antioxidative enzymes in renal tissue, blood and renal parameters were deviated from the normal range, indicating dysfunction of the kidney. In contrast, when buckwheat extract was given orally for 20 consecutive days before ischemia and reperfusion, the activities of the antioxidative enzymes viz. superoxide dismutase, catalase and glutathione peroxidase were higher, while thiobarbituric acid reactive substance level in serum and renal tissue was lower in the treated rats as compared to the control. Decreased levels of urea nitrogen and creatinine in serum exhibited a protective effect against the renal dysfunction caused by ischemia and recirculation. Buck wheat extract had a protective effect on cultured proximal tubule cells subjected to hypoxia reoxygenation

probably by preventing oxygen free radicals from attacking the cell membrane (Yokozawa et al., 2001).

FICUS RACEMOSA

The protective effects of aqueous and alcoholic extracts of the bark of *Ficus racemosa* in cisplatin induced mice were studied. The drug extract significantly protects the toxicity produced by cisplatin by elevating the blood urea and serum creatinine levels (Shivalinge Gowda et al., 2011).

GINKGO BILOBA

G. biloba leaf extract exhibited good protection against gentamicin induced nephrotoxicity in rats. Significant reduction in lipid peroxidation, urea and creatinine has been reported (Niazi, 1994). The *G. biloba* Ext. (300 mg/kg BW) was used orally 2 days before and 8 days concurrently with gentamicin (80 mg/kg BW). The supplementation with *G. biloba* extract may be helpful to reduce gentamicin nephrotoxicity (Naidu et al., 2000).

GERANIUM THUNBERGII

Effects of geranin (tannin) extracted from the herb *Geranium thunbergii* on puromycin amino nucleoside (PA) nephritis was studied in rats. The urine protein excretion in female rats (140-160g) receiving PA on the 7th day after the injection of PA reached its maximum on 14th day, but in animals treated intramuscularly with geranin (10 mg/kg) the urinary protein was reduced by approximately 35%.

The increase in serum cholesterol and lipid peroxide produced by PA was also suppressed by geranin. The degree of abnormality in glomerular epithelial cells was lower in the rats treated with geranin, after the PA injection than in the rats treated with PA alone (Nakanishi.1999).

GREEN TEA

Cisplatin (CP) an anticancer drug is known to induce nephrotoxicity, which limits its long term clinical use. Green tea (GT), consumed since ancient times is known for its numerous health benefits. It has been shown to improve kidney functions of acute renal failure. The GT can prevent CP-induced nephrotoxic and other deleterious effects. A nephrotoxic dose of CP was co-administered to control and GT-fed male Wistar rats every fifth day for 25 days. The effect of GT was determined on CP-induced alterations in various serum parameters and on enzymes of carbohydrate metabolism, brush border membrane, and antioxidant defense system in renal cortex and medulla. CP nephrotoxicity was recorded by increased serum creatinine and blood urea nitrogen. The CP increased the activities of lactate dehydrogenase and acid phosphatase whereas, the activities of malate dehydrogenase, glucose-6-phosphatase, superoxide dismutase, catalase, and ^{32}P transport significantly decreased. GT consumption increased the activities of the enzymes of carbohydrate metabolism, brush border membrane, oxidative stress, and ^{32}P transport. GT ameliorated CP-induced nephrotoxic and other deleterious effects due to its intrinsic biochemical/antioxidant properties (Sara A. Khan et al., 2009).

GRAPE SEED EXTRACT

Grape seed extract in ethylene glycol (EG) induced nephrotoxicity in mice was studied for its nephroprotective activity. Mice received grape seed extract 100mg/kg was given after EG (2ml/kg p.o) use. Grape seed extract in mice produced significant reduction of urinary LDH, blood urea, creatinine and dilated tubules lined by normal intact epithelium indicating recovery. The renoprotective effect of *Vitis vinifera* seed extract is due to improvement in antioxidant status (Miller et al., 2005).

GLYCYRRHIZIN

The effects of glycyrrhizin (200 mg/kg/day) on renal function in association with the regulation of aquaporin 2 water channel in rats with gentamicin (100 mg/kg/day)-induced acute renal failure was tested. Polyuria in rats with gentamicin-induced acute renal failure was associated with down-regulation of renal aquaporin 2 in the inner and outer renal medulla, and cortex. Glycyrrhizin use restored the expression of aquaporin 2 with paralleled changes in urine output. Changes in renal functional parameters, such as creatinine clearance, urinary osmolality, and solute-free reabsorption, accompanying acute renal failure were also partially restored after administration of glycyrrhizin. Histological changes in rats with gentamicin-induced acute renal failure were also abrogated by glycyrrhizin treatment. The glycyrrhizin treatment could ameliorate renal defects in rats with acute renal failure induced by gentamicin (Sohn et al., 2003).

GARLIC EXTRACT

Aged garlic extract (AGE), an antioxidant, has a protective role in this experimental model of male Wistar rats were studied. AGE was given at a dose of (1.2 mL/kg/12 hours) followed by GM (70 mg/kg/12 hours). These alterations were prevented or ameliorated by AGE treatment. The protective effect of AGE was associated with the decrease in the oxidative stress and the preservation of manganese superoxide dismutase (Mn-SOD), GPx, and glutathione reductase (GR) activities in renal cortex. The AGE may be a useful agent for the prevention of GM nephrotoxicity (Maldonado et al., 2003).

HEMIDESCUS INDICUS

The treatment with *H. indicus* helped in the management of renal impairment, which was induced by gentamicin in rats. Various kidney

function tests for gentamicin, along with the results from the plant treated group, and is in comparison with the results found for the gentamicin recovery group. The plant shows promise as an adjunct therapy alongside aminoglycosides as it reduces nephrotoxicity caused by aminoglycosides (Magala et al., 2004).

HIRSUTELLA SINENSIS

Hirsutella sinensis can inhibit the production of TGF-beta1 and CTGF, factors that promote the extracellular matrix (ECM) synthesis and TIMP-1 and PAI-1, factors that antagonize ECM degradation in kidney tissues, thus alleviating renal interstitial fibrosis and improving renal function in CAAN (chronic aristolochic acid nephropathy (Zhu et al., 2007).

HARUNGANA MADAGASCARIENSIS

In African traditional medicine, decoctions from different parts of *Harungana madagascariensis* (L.) are highly valued in the treatment of various human diseases including drug related renal disease. The effects of pretreatments with single daily oral 100-500 mg/kg/day of the root aqueous extract of *H. madagascariensis* were tested in acute and repeated dose acetaminophen nephrotoxic rats for 24 hours and 14 days, respectively, using renal function parameters—serum urea (UR), uric acid (UA) and creatinine (CR). Treatment with i.p acetaminophen for 24 hours and 14 days induced significant elevations in the serum concentrations of UR, UA and CR, varying degrees of tubular necrosis on histology and varying degrees of alterations in the hematological parameters in acute and repeated dose acetaminophen nephrotoxic rats, respectively. Oral doses of the extract significantly attenuated elevations in the serum concentrations of UR, UA and CR, and improved diffuse tubular necrosis in both models of acetaminophen nephrotoxicity. The extract also

significantly improved packed cell volume (PCV), hemoglobin (Hb), and total leucocyte count (TLC) levels but non-significant increase in the mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean corpuscular hemoglobin concentration (MCHC), in the repeated acetaminophen model. The *Harungana* extract protects against acetaminophen nephrotoxicity (Adeneye et al., 2008).

ICACINA TRICHANTHA

Methanolic extract of *icacina trichantha* tuber was found to be effective in CCl₄ induced nephrotoxicity. The rats treated only with CCl₄ lost weight but those treated with CCl₄ and extract gained weight. Histopathological examination of the kidney revealed complete protection against CCl₄ induced nephrotoxicity (Asuzu.1995).

MORCHELLA ESCULENTA

Morchella esculenta (L) Pers. is an excellently edible and delicious morel mushroom found growing in the temperate forests. The mycelium of this mushroom is widely used as a flavoring agent. The protective effect of the aqueous-ethanol extract of cultured mycelium of *M. esculenta* against cisplatin and gentamicin induced acute renal toxicity in mice. Cisplatin and gentamicin when used induced a marked renal failure, characterized by a significant increase in serum urea and creatinine concentrations. Treatment with the extract at 250 and 500 mg/kg body weight decreased the cisplatin and gentamicin induced increase in serum creatinine and urea levels. Treatment with the extract also restored the depleted antioxidant defense system. The decreased activity of superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and reduced glutathione (GSH) in the kidneys consequent to cisplatin and gentamicin use was significantly elevated. The enhanced renal

antioxidant defense system also prevented the tissue lipid peroxidation. The aqueous-ethanol extract of morel mushroom, *M. esculenta* mycelium protected cisplatin and gentamicin induced nephrotoxicity possibly by enhancing renal antioxidant system. The potential therapeutic use of morel mushroom mycelium as a novel nephroprotective agent (Nitha et al., 2008).

MORINGA OLEIFERA

Oxidative stress due to abnormal production of reactive oxygen species has been implicated in the nephrotoxicity induced by gentamicin. The nephroprotective effect of aqueous ethanolic extract of *M. oleifera* leaves (150 and 300 mg/kg) was tested against gentamicin-induced (80 mg/kg) renal injury in rabbits. Serum urea and creatinine levels were tested as the markers of renal nephrotoxicity. Serum urea and creatinine levels were reduced in the *M. oleifera* (150 and 300 mg/kg) plus gentamicin treated groups. Kidney of intoxicated rabbits groups which received *M. oleifera* extract showed reparative tendencies. A highly significant elevation was observed in lipid peroxidation (LPO) level in the kidneys of gentamicin-intoxicated rabbits whereas combined treatment of *M. oleifera* and gentamicin group showed a highly significant depletion in LPO. The aqueous-ethanolic extract of *M. oleifera* leaves attenuates renal injury in rabbits treated with gentamicin, possibly by inhibiting lipid peroxidation (Ouédraogo et al., 2011).

NIGELLA SATIVA

Oral treatment of rats with *N. sativa* oil (0.5, 1.0 or 2.0 ml/kg/day) would ameliorate nephrotoxicity of GM (80 mg/kg/day i.m) concomitantly with the oil. Nephrotoxicity was tested by measurement of concentrations of urea, creatinine and total antioxidant status (TAS) in plasma and reduced glutathione (GSH)

and TAS in kidney cortex. The GM treatment caused moderate proximal tubular damage, significantly increased the concentrations of creatinine and urea, and decreased that of TAS and GSH. Treatment with *N. sativa* oil produced a dose-dependent amelioration of the biochemical and histological indices of GM nephrotoxicity that was significant at the two higher doses used, and it increased GSH and TAS concentrations in renal cortex and enhanced growth. The *N. sativa* may be useful in ameliorating signs of GM nephrotoxicity in rats (Ali et al., 2004).

ORTHOSIPHON STAMINEUS

Leaves of this plant have been used as diuretic, and to treat rheumatism, abdominal pain, kidney and bladder inflammation, edema, gout and hypertension (Hegnauer, 1966). Scientific studies have found that the leaves exhibit dynamic pharmacological properties such as, antioxidant, antibacterial, hepatoprotective, anti-inflammatory, cytotoxic, diuretic, antihypertensive and vasodilative properties (Chung et al., 1998). More than twenty phenolic compounds were isolated from this plant including lipophilic flavones, flavonol glycosides and caffeic acid derivatives such as rosmarinic acid and 2,3-dicaffeoyltartaric acid (Sumaryono et al., 1991). The nephroprotective activity of *orthosiphon stamineus*, family Lamiaceae (*Labiatae*) revealed the presence of flavonoids, tannins, saponins, phenols and terpenoids. The drug is found to be potent diuretic which causes excretion of sodium and potassium. The plant material is nephroprotective activity in rats. Gentamicin is an extensively used aminoglycoside antibiotic, even at normal therapeutic dose level. The drug was used i.p at a dose of 80mg/kg weight for 9 days. The methanolic extract of *orthosiphon stamineus* benth was evaluated for its nephroprotective activity using rat model. Gentamicin is an extensively used

aminoglycoside antibiotic (Chung et al., 1998). Histopathological sections showed marked glomerular, peritubular and blood vessel congestion. These increased levels of serum creatinine, blood urea, urinary protein and extent of renal damage were decreased by the methanolic extract of *O. stamineus* at both dose levels that is 100 and 200 mg/kg body weight in rats (Kannappan. 2010).

OCIMUM SANCTUM

Seeds of *Ocimum sanctum* are useful in complaints of the urinary system (Melookunnel. 1996).

PIMPINELLA TIRUPATIENSIS

Pimpinella tirupatiensis (Apiaceae) is an herbaceous medicinal plant used to treat cough, stomach, liver problems, asthma, ulcer and tooth ache in Asian countries. Acetaminophen (APAP) in at high doses causes liver and kidney necrosis in man and animals. The nephroprotective and antioxidant activities of the ethanol extract of *P. tirupatiensis* in two dose levels of 500mg/kg & 750 mg/kg B/W respectively on APAP induced toxicity in rats. There is an increase in the levels of serum urea and creatinine along with an increase in the body weight and reduction in the levels of uric acid in APAP induced groups. These values are retrieved significantly by treatment with *P. tirupatiensis* extracts at two different doses. The antioxidant studies reveal that the levels of renal SOD, CAT, GSH and GPx in the APAP treated animals are increased significantly along with a reduced MDA content in ethanol extract of *P. tirupatiensis* treated groups. Histopathological changes also reveal the protective nature of the *P. tirupatiensis* extract against acetaminophen induced necrotic damage of renal tissues. The ethanol extract of *P. tirupatiensis* can prevent renal damage from APAP induced nephrotoxicity in rats and it is

likely to be mediated through its antioxidant activities (Palani et al., 2009).

PARONYCHIA ARGENTEA

Renal protection and antiurolithiasic effects of two extracts of *Paronychia argentea* (PA), a traditional Algerian plant known as Algerian tea, were evaluated. The aqueous extract (APA) or the butanolic extract (BPA) of aerial parts could prevent or reduce calculi aggregation in experimental calcium oxalate (Ox) nephrolithiasis in Wistar rats. The two extracts (APA and BPA) were used orally and daily, during 28 days to nephrolithiasic treated rats at the dose of 250, 500 mg/kg b.w. and 10, 20 mg/kg b.w. respectively. Body weight, renal index, liver index, serum level of creatinine, uric acid, urea, K⁺, Ca²⁺, Mg²⁺, Na⁺ and transaminase (alanine aminotransferase, ALT; aspartate aminotransferase, AST), phosphatase alkaline activity (PAL) were evaluated following the 28 days treatment in rats. In addition histopathological changes in kidney and liver were stained in hematoxylin eosin (HE). The effect of the extracts could be advantageous in preventing urinary stone retention by reducing renal necrosis and thus inhibit crystal retention. In contradiction with APA, the two doses of BPA attenuated elevation in the serum creatinine and blood urea levels (nephroprotective effect). However, the increase in ALT (27%) and PAL (31-51%) serum levels and in the relative liver weights in the groups treated with doses of APA may indicate that this extract has not a hepatoprotective effect against oxalate toxicity. The use of the butanolic extract of aerial parts to rats with NaOx induced lithiasis, and reduced and prevented the growth of urinary stones in experimental calcium oxalate nephrolithiasis in rats (Bouanania et al., 2010).

PHYTOLACCA ROOTS

Water extract (100 mg/kg) of *Phytolacca* roots elicited moderate diuresis. The diuretic effect

of the extract is due to improving the renal hemodynamics (Kim et al., 1980).

PUNARNAVA

Punarnava (*Boerhaavia diffusa*) reveal diuretic effect equivalent to furosemide. Punarnava increases serum protein level and decreases urinary protein excretion in patients of nephrotic syndrome. Increase was also noted in the level of immunoglobulin and lower immune complexes after one month of medication in patients of nephrotic syndrome. Clinically Punarnava was proved to be a useful and safe drug in patients of nephrotic syndrome (Singh.1992).

PORTULACA PILOSA

Hydro alcoholic extract of *P. pilosa* causes an increase in K excretion without a concomitant change in water diuresis or Na excretion (Rocha et al., 1994).

PANAX GINSENG

The protective effect of two natural antioxidants, ginsenoside rb-1 and quercetin isolated from *Panax ginseng*, on acute nephritis induced by puromycin amino nucleoside (pa) has been reported. The protective action of rb-1 and quercetin were evidenced by their ability to suppress the formation of phosphatidylcholine hydro peroxide in the plasma, liver and kidney. Another beneficial effect noted from these natural antioxidants, was increased glutathione peroxidase activity in the blood. The severity of pa-induced acute nephritis was found to be ameliorated by the antioxidative action of these two flavonoids (Lim.1998).

PINUS DENSIFLORA

The effect of pine leaf extract and its constituent compounds, gallic acid and galloyl gallic acid, on cell injury was determined in the

cultured renal epithelial cell line, LLC-PK-I. (Yokozawa et al., 1999).

PEDALIUM MUREX

Pedaliium murex is used as herbal medicine, family Pedaliaceae. Fruit extract of this plant contains many phytochemicals such as carbohydrates, flavonoids, alkaloids, glycosides, steroids, phenols, saponins, tannins and fixed oils & fats (Mozhi et al., 2011). The effects of these bioactive components showed diverse pharmacological properties like antioxidant, anti-diabetic (Kumar and Krishnamoorthy. 2011), antibacterial (Balamurugan et al., 2010), aphrodisiac, anti-inflammatory activity (Devi et al., 2010) and nephroprotective property (Shelke et al., 2009). The ethanolic extract of dried fruits of *P. murex* Linn was tested for its nephroprotective activity. Nephrotoxicity was induced in rats by i.p use of cisplatin 5mg/kg. Effect of concurrent use of *P. 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 ethanolic extract of dried fruits of *P. murex* has an excellent nephroprotective activity as compared to cystone.

PONGAMIA PINNATA

Ethanolic extract of the flowers of *P. pinnata* was studied for its protective effect against cisplatin and gentamicin induced renal injury in rats. When the extract (300 and 600mg/kg) was used orally for 10 days following cisplatin (5mg/kg i.p) on day 5, toxicity of cisplatin, as measured by loss of body weight, elevated blood urea and serum creatinine declined significantly. Similarly in gentamicin (40mg/kg s.c) induced renal injury, the extract (600 mg/kg) normalized the raised blood urea and serum creatinine levels (Shirwaikar et al.,2003).

RHAZYA STRICTA

Water extract of leaf of *Rhazya stricta* in higher doses 0.5 and 1 g/kg showed dose related amelioration in the indices of GM induced nephrotoxicity. It increased SOD activity and GSH concentration and decreased that of lipid peroxides in the kidney cortex (Ali. 2002).

RAPHANUS SATIVUS

The leaf juice of *Raphanus sativus* is prescribed in difficulty in passing urine as well as in the closure of urinary passage. Root juice of the same is used in urinary troubles and seeds are found to be effective in increasing the excretion (Melookunnel. 1996).

RHEUM SPECIES

Effect of *R. officinale* extract treatment on urine composition in rats with adenine-induced renal failure was studied. Use of the rhubarb (*R. officinale*) extract markedly increased the urinary excretion of both urea and creatinine, indicating an improvement of renal clearance in the uremic state. A number of significant differences in the amino acid levels of the urine were observed (Yokozawa et al., 1984).

SOLANUM NIGRUM

The 50% ethanol extract of the whole plant of *S. nigrum* was tested in vitro for its cytoprotection against gentamicin-induced toxicity on Vero cells. Cytotoxicity was significantly inhibited. The test extract exhibited significant hydroxyl radical scavenging potential, thus suggesting its probable mechanism of cytoprotection (Kumar et al., 2001).

SALVIAE RADIX

Salviae radix extract (SRE) exerts a beneficial effect against cisplatin induced renal failure in rabbits. Rabbits were pretreated with SRE orally followed by cisplatin injection (5mg/kg ip).

Cisplatin injection caused a reduction in GFR, which was accompanied by an increase in serum creatinine levels. The fractional Na₊ excretion and lipid peroxidation were also increased. All these changes were prevented by SRE pretreatment. Cisplatin treatment *invitro* in renal cortical slices increased LDH release and lipid peroxidation, which was prevented by SRE and its effect, may be attributed to its antioxidant action (Jeong et al., 2001).

STRYCHNOS POTATORUM

Strychnos potatorum Linn, Loganiaceae (Agharkar. 1991). According to Ayurveda, the seeds are acrid, alexipharmic, lithotriptic and cure strangury, urinary discharges, head ailments etc. Roots cure all types of leucoderma whereas fruits are useful in eye diseases, thirst, poisoning and hallucinations. The ripe fruit is emetic, diaphoretic, alexiteric, cures inflammation, anaemia, jaundice (Gupta et al., 2006). According to Unani system of medicine, seeds are bitter, astringent to bowels, aphrodisiac, tonic, diuretic and good for the liver, kidney complaints, gonorrhoea, colic etc (Oudhia. 2004). Since kidney is involved in the clearance of toxins and xenobiotics, it may be more prone to attack by various challenges. A large number of these agents may cause damage to these organs by oxidative stress. The ethanolic extract of *S. potatorum* seeds was tested for its nephroprotective effect in rats. The seeds of *S. potatorum* possess marked nephroprotective activity and could have a promising role in the treatment of acute renal injury induced by nephrotoxins, especially gentamicin.

SANGUISORBAE RADIX

The effect of *Sanguisorbae radix* extract, a traditional crude drug, was investigated in renal dysfunction induced by lipopolysaccharide (LPS) endotoxin. Injection of LPS in rats resulted in a sharp rise in the serum levels of urea nitrogen

and creatinine (Cr), indicating impairment of renal function. Nitrite and nitrate levels and the activity of inducible nitric oxide synthase (iNOS), an enzyme which participates in NO synthesis, were also significantly increased in the serum of LPS-treated rats compared with normal rats. In rats pretreated with *S. radix* extract, renal dysfunction was attenuated and the increases in serum urea nitrogen and Cr induced by LPS were significantly reduced. The use of *S. radix* extract also effectively lowered serum nitrite/nitrate level. A similar effect was observed on the iNOS activity. The *S. radix* extract contributes to the regulation of renal function under conditions where there is excessive generation of NO (Chen et al., 1999).

SMILAX CHINA

Smilax china L., popularly known as "Jin Gang Ten", has been widely used as a traditional herbal medicine for the treatment of gout, rheumatoid arthritis and other diseases for a long time in China. The effect of *S. china* L. on hyperuricemia and renal dysfunction in induced hyperuricemic animals. Five fractions (petroleum ether, chloroform, ethyl acetate, n-butanol and residual ethanol fraction) of *Smilax china* L. were orally used to potassium oxonate induced hyperuricemic mice for three days. The xanthine oxidase inhibitory activities and modes of action of nine compounds isolated from ethyl acetate fraction (EAF) were then examined in vitro. Finally, different dosages of EAF were used to 10% fructose-induced hyperuricemic rats. EAF (250 mg/kg) exhibited stronger anti-hyperuricemic activity in hyperuricemic mice compared with the other four fractions. Caffeic acid, resveratrol, rutin and oxyresveratrol isolated from EAF showed different inhibitory activities on xanthine oxidase in vitro and exhibited competitive or mixed inhibitory actions. Moreover, EAF (125, 250 and 500 mg/kg) markedly reversed the serum uric acid level, fractional excretion of

urate and blood urea nitrogen to their normal states, and prevented the renal damage against tubulointerstitial pathologies in hyperuricemic rats. These findings show that *Smilax china* L. exhibits anti-hyperuricemic and nephroprotective activity in hyperuricemic animals (Lvji Chena et al., 2011).

SIDA RHOMBOIDEA

Nephrotoxicity was induced in rats with gentamicin (GM) (100 mg/kg bodyweight (i.p.) for 8 days) and were treated with *Sida rhomboidea* (SR) extract (200 and 400 mg/kg bodyweight (p.o.) for 8 days) or 0.5% carboxymethyl cellulose (vehicle). Plasma and urine urea and creatinine, renal enzymatic and nonenzymatic antioxidants along with lipid peroxidation were tested. The GM treatment induced significant elevation in plasma and urine urea, creatinine, renal lipid peroxidation along with significant decrement in renal enzymatic and non-enzymatic antioxidants. SR treatment to GM treated rats (GM+SR) recorded significant decrement in plasma and urine urea and creatinine, renal lipid peroxidation along with significant increment in renal enzymatic and nonenzymatic antioxidants. The SR leaf extract ameliorates GM induced nephrotoxicity and renal dysfunction and thus validates its ethno medicinal use (Menaka et al., 2010).

TECOMA STANS

The nephroprotective activity of ethyl acetate extract of dried flowers of *Tecoma Stans* for its protective effects on gentamicin-induced nephrotoxicity in albino rats. Nephrotoxicity was induced in albino rats by i.p use of gentamicin 80 mg/kg/day for eight days. Effect of concurrent use of ethyl acetate floral extract of *T. stans* at a dose of 100, 200 and 300 mg/kg/day given by oral route was determined using serum creatinine, serum uric acid, blood urea nitrogen and serum urea as indicators of

kidney damage. As nephrotoxicity of gentamicin is known to involve induction of oxidative stress, *in vitro* antioxidant and free radical-scavenging activity of this extract was also evaluated. The ethyl acetate floral extract of *T. stans* significantly protected rat kidneys from gentamicin-induced histopathological changes. Gentamicin-induced glomerular congestion, peritubular and blood vessel congestion, epithelial desquamation, accumulation of inflammatory cells and necrosis of the kidney cells were found to be reduced in the groups receiving the ethyl acetate floral extract of *Tecoma stans* along with gentamicin in a dose dependent manner. The floral extract also reduced the gentamicin-induced increase in serum creatinine, serum uric acid, blood urea nitrogen and serum urea levels. The important role of reactive oxygen species (ROS) and the relation to renal dysfunction and point to the therapeutic potential of *T. stans* in gentamicin induced nephrotoxicity (Raju et al., 2011).

TERMINALIA CHEBULA (HALEELA)

The extract of *T. chebula* have possess uremic toxin decreasing action in rats. It lowers the serum concentrations of urea nitrogen, creatinine, methyl guanidine and guanidinosuccinic acid significantly (Yokozava et al., 1995).

TARAXACUM OFFICINALE

The roots of *Taraxacum officinale* are used in chronic disorders of kidney (Melookunnel. 1996).

TRIBULUS TERRESTRIS

Simultaneous use of *Tribulus terrestris* (200 mg/kg/day/p.o.) and gentamicin to female rats decreased the gentamicin - induced nephrotoxicity. The effects were comparable to that of verapamil (Nagarkatti. 1994).

VICIA FABA (BAQLA)

Dopamine (DA) is known to increase diuresis and natriuresis through its action on renal dopaminergic receptors. Augmentation of intra renal DA concentration by enhancement of its *in situ* production greatly depends on the availability of its precursor L-DOPA to the sites of its renal decarboxylation. *V. faba* is rich in easily absorbable LDOPA. Following ingestion of 40 g freshly chopped *V. faba* containing 120-130 mg of LDOPA, plasma L-DOPA, urinary sodium and DA excretion increased significantly. *V. faba* might be of value in treating conditions like hypertension, heart failure, renal failure and liver cirrhosis in which natriuresis and diuresis are medically beneficial (Vered et al., 1997).

VITIS VINIFERA

Cortisone, *Mercurius corrossivus* (a homeopathic drug) and an aqueous extract of *V. vinifera* were used for controlling nephrotoxicosis caused by citrinin in mice. These drugs were used to toxin treated mice regularly for 20 weeks. Combination of drugs had significantly positive effect and up to 41% recovery was achieved (Bilgrami and Jeswal. 1993).

VERNONIA CINEREA

V. cinerea, family Asteraceae (Oriental legman, Indian Medicinal plants, 1994). Mainly it consists of 38% fatty oil, plant contains β -amyrin acetate, β -amyrinbenzoate; lupeol and its acetate, β -sitosterol, stigmasterol, a-spinasterol, and also contains flavonoids, glycosides, tannins and carbohydrates (Bhande et al., 2010). The different parts of *V. cinerea* has been possess hypoglycemic and anti-diabetic (Sy et al., 2005), anti-pyretic (Guptha et al., 2003), anti-bacterial (Guptha et al., 2003), diuretic and anti-diuretic (Adeboye et al., 1997), anti-inflammatory (Mazumder et al., 2003), free radicals scavenging (Kumar and Khuuttan.

2009), analgesic activities (Iwalewa et al., 2003). The alcoholic extracts of aerial parts of *V. cinerea* has been tested for the effect of petroleum ether, ethyl acetate on cisplatin-induced nephrotoxicity at a dose of 6mg/kg, i.p. in rats. The alcoholic extract showed pronounced curative activity and the ethyl acetate extract has exhibited good prophylactic activity and petroleum ether extract showed moderate protection for both curative and prophylactic models against cisplatin-induced toxicity.

VERNONIA CINEREA

Effect of petroleum ether, ethyl acetate, and alcoholic extracts of aerial parts of *Vernonia cinerea* on Cisplatin induced nephrotoxicity was studied in rats. The nephroprotector activity of the plant was assessed in prophylactic and curative models. Among the three extracts, alcoholic extract showed pronounced curative activity, ethyl acetate extract exhibited good prophylactic activity and petroleum ether extract showed moderate protection in both curative and prophylactic models against cisplatin induced toxicity (Sreedevi A et al., 2011).

ZINGIBER OFFICINALE

The pharmacokinetics of (60)-gingerol obtained from the rhizomes of ginger (*Zingiber officinale*) were tested in rats with acute renal failure induced by bilateral nephrectomy and those with acute hepatic failure induced by single oral use of CCl₄ to clarify the contribution of the kidney and liver in the elimination process of (6)-gingerol (Naora et al., 1992).

PLANT FORMULATIONS AS NEPHRO PROTECTIVE AGENTS

BANADEQUL BUZOOR

A Unani formulation "Banadequl Buzoor" was tested for nephroprotective activity. The

formulation was found to decrease the serum urea and serum creatinine levels significantly which was increased by the use of gentamicin (Anwar. 1999).

CHAI-LING-TANG

A Chinese poly herbal formulation was used along with prednisone to 37 children with steroidal dependent nephrotic syndrome (SDNS). After treatment with Chai-ling-tang, relapse was markedly improved, time for negative conversion of protein urea was shortened, prednisone dosage was significantly reduced and side effects were eased. Children with SDNS treated with prednisone and cyclophosphamide served as control. The short- and long-term relapse and average prednisone dose were similar in the two groups. Chai-ling-tang may be useful with SDNS for those who fail to respond to or manifest severe toxic effects to cytotoxic agents (Yun.1995).

COMPOUND FORMULATION CONTAINING CROCUS SATIVUS, NIGELLA SATIVA AND VITAMIN E

Cisplatin [cis-dichlorodiamineplatinum (II)] is a widely used chemotherapeutic drug that is toxic to the kidney. Concurrent administration of cysteine together with vitamin E, *Crocus sativus* and *Nigella sativa* reduced the toxicity of cisplatin in rats. When administered intraperitoneal for 5 alternate days with 3 mg/kg cisplatin, extract of *Crocus sativus* stigmas (50 mg/kg) and *Nigella sativa* seeds (50 mg/kg) significant reduction of blood urea nitrogen (BUN) and serum creatinine was observed. Also, used of *Crocus sativus* and *Nigella sativa* together with cisplatin partially reversed many of the kidney enzymes changes induced by cisplatin. The combination of *Crocus sativus* and *Nigella sativa* may be a promising compound for reducing cisplatin-toxic side effects including nephrotoxicity (El Daly.1998).

CYSTONE

Cystone, a polyherbal Ayurvedic preparation was found to protect rats partially but significantly against cisplatin induced renal toxicity, when given intraperitoneal 1 hr. before cisplatin (Rao and Rao.1998).

CARDIPRO

Clinical trials on CardiPro were conducted on 13 healthy male volunteers (age 40-57 years) by administering one capsule twice daily for 30 days. CardiPro contains extracts of *Terminalia arjuna*, *Emblca officinalis*, *Withania somnifera*, *Ocimum sanctum* and *Boerhaavia diffusa*. It is safe for use in humans and has a favorable cardiac profile. It brings down not only blood pressure and heart rate but also improves the serum lipid profile and renal functions (Mathur et al., 2001).

EKONGSAN

Ekongsan (containing plants like *Ginseng radix*, *Atractylis rhizome*, *Glycyrrhiza radix* and *Aurantii nobilispericarpium*) decreased cisplatin induced cytotoxicity on rabbit kidney proximal tubule and human renal cortical cells by MTT assays and sustained glucose consumption on cisplatin induced human renal cortical tissue. Levels of creatinine and blood urea nitrogen in serum after administration of cisplatin (0.75 mg/kg, i.p.) to Ekongsan (0.75 g/kg/d, p.o.) pretreated rats were markedly lower compared to those of cisplatin treated rats.

Moreover, the use of Ekongsan significantly inhibited the loss in body weight of cisplatin injected rats. The Ekongsan is an active prescription in protection against nephrotoxicity of cisplatin (Lee et al., 1998).

GINSENOID-RD

Ginsenoside-Rd has been proved to decrease

the severity of renal injury induced by cisplatin, in which proximal urinaferous tubules represent the main site of injury. When ginsenoside-Rd was given orally at a dose of 1 or 5 mg/kg body weight/day prior to cisplatin injection, the activities of the antioxidation enzymes superoxide dismutase and catalase were higher, while malondialdehyde levels in serum and renal tissue were lower in the treated rats than in the controls.

The levels of urea nitrogen and creatinine in serum were decreased in rats given ginsenoside-Rd. Decreased urinary levels of glucose, sodium and potassium reflected a protective action against the renal dysfunction caused by cisplatin. The ginsenoside-Rd affected cultured proximal tubule cells exposed to Cisplatin (Yokozava T et al., 2000).

JIAN-PI-QILI-SHU

A Chinese poly herbal formulation was found to be effective against cisplatin induced nephrotoxicity (Chang. 1992).

JAWARISH ZAROONI SADA (JZS)

Jawarish Zarooni Sada (JZS) is a polyherbal preparation containing 15 ingredients, mainly described to be diuretic and nephroprotective. Ethanolic and aqueous extracts of JSZ were tested for its diuretic activity and nephroprotection, studied in gentamicin model. The JZS showed significant diuretic activity (Afzal. 2004).

LIVER-KIDNEY CARE

The effect of 'Liver-Kidney Care' an Ayurvedic formulation. Each 325 mg capsule consisted of *Phyllanthus niruri* 125 mg, *Boerhaavia diffusa* 100 mg, and *Picrorrhiza kurroa* 100 mg. The formulation detoxifies, purifies and rejuvenates liver and kidney, naturally and effectively (Chaturvedi et al., 2003).

MORINGA OLEIFERA AND TINOSPORA CORDIFOLIA

Moringa oleifera, with a little opium and *Tinospora cordifolia* is useful in the inflammation of kidney (Melookunnel.1996).

NR-AG-1 AND NR-AG-2

Two formulations NR-AG-1 containing (*Crataeva nurvala*, *Dolichor biflorus*, *Tribulus terrestris*, *shilagi*) and NR-AG-2 containing (*Crataeva nurvala*, *Boerrhaavia diffusa*, *Saccharum officinarum*, *Butea frondosa*) were used to male rats along with gentamicin. Biochemical studies indicated that gentamicin (80 mg/kg/s.c./day) causes significant renal damage, which was prevented by both the formulations (Samiulla. 2000).

SHI-QUAN-DA-BU-TANT

A poly herbal Chinese formulation *Shi-quanda-bu-tant* was used for its protective effect on mice against cisplatin induced nephrotoxicity. Among the ingredients of the formulation, *Angelica radix* was more effective and it showed the strongest protective effect against the toxicity. The effectiveness of *A. radix* was found to be due to its constituent l-malate which was tested for nephroprotective activity (Sugiyama.1981).

SEEDS OF PAPAYA AND PUMPKIN FRUIT

The Nephroprotective test of ethanolic extract of the Papaya seed, PSE (*Carica papaya*, family-Caricaceae) and pumpkin seed, PSE (*Curcubita pepo*, family-Curcubitaceae). Cisplatin (10mg/kg, i.p.) used for the nephrotoxicity, which is the dose limiting side effect of the Cisplatin (Cis-diamine dichloro platinum-II). The ethanolic extract of PSE & PSE exhibited protection against cisplatin-induced nephrotoxicity. Antioxidant studies like nitric oxide scavenging activity, lipid peroxidation in

kidney is also supporting the nephroprotective activity of these seeds. This nephroprotective study also compared with chloroform extract of the dried Zinger roots, ZE (*Zingiber officinale*, Family-Zingiberaceae) and methimazole (Subal Debnath et al.,2010).

TONG FU XIE ZHUO

Chinese traditional medicine "Tong Fu Xie Zhuo" was tested for uremia. The treatment is better in combination with "Fu Zheng ". Also, the application of "Tong Fu Xie Zhuo" can replace "Ping Can Xi Feng" in the treatment of neurologic symptoms in uremia (Chen.1986).

TRIPTERYGIUM WILFORDII AND SALVIAE MILTIORRHIZAE

Tripterygium wilfordii polyglucoside combined with radix *Salviae miltiorrhizae* for treating purpuric nephritis was compared with the control group of using *T. wilfordii* polyglucoside. The average time of edema disappearing and blood pressure resuming to normal range was observed to be 8 days in control group, which was much better than those in first group (Yu.1992).

TRIBULUS TERRESTRIS AND CRATAEVA NURVULA

The indigenous drugs Gokshura (*Tribulus terrestris*) and Varun (*Crataeva nurvula*) have nephroprotective action against gentamicin induced nephrotoxicity in rats (Meher et al., 2001).

CONCLUSION

Medicinal plants play a prominent role against various diseases. A variety of medicinal plants have been reported for its significant nephroprotective activity. The nephro protective activity is probably due to the presence of flavanoids in all the few medicinal plants. The extracts of some medicinal plants have good potentials for use in kidney damage.

This review give evidential explore mechanism of action of medicinal plants against nephrotoxicity (Rajagopal, et al., 2013; Lakshmi et al., 2012). Hence, it is concluded that the herbal drug possesses nephroprotective activity which gives links to develop the future trials.

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