

A Review on Nephroprotective Herbs and Herbal Formulations

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ABSTRACT

Renal disorders have always remained a major area of concern for physicians since a long time. It is the 9th leading cause of death in United States. Incidence of kidney diseases leading to kidney failure is increasing day by day. A large number of chemicals in common use are potential renal toxins. The use of herbal drugs for the prevention and treatment of various diseases is constantly developing throughout the world. Nephrotoxicity is an inherent adverse effect of certain antibiotics, anticancer drugs and other synthetic molecules. A number of extracts of natural products and dietary antioxidants have been reported to show protective effects against nephrotoxicity. Following herbal drugs have shown their potent nephroprotective effect due their antioxidant, diuretic, anti-inflammatory, antispasmodic properties.

Keywords: Nephro toxicity, Nephro protection, Free radicals, Medicinal plants.

INTRODUCTION

The WHO has recently reported that traditional medicines (including herbal drugs) have been existing in therapeutic practice even hundred years before the development of modern medicine. Traditional medicine is the synthesis of 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. India has produced some well-defined systems of medicine. Indian systems of medicine hold that health is a dynamic process, not just an absence of disease. These systems are more patient centered and less invasive. The idea that health involves both the mind and body, emphasized in Indian philosophy and medicine is getting worldwide attention today. Research is underway in many schools of alternative medicine to cope with modern maladies.

Several herbal folklore surveys conducted in the recent past provide a glimpse of the ethnopharmacological potential of herbs used by the villagers and tribals of India for the treatment of various diseases. This increases the scope for new herbal drug development by

the use of pharmacognostical, phytochemical and pharmacological methods.

Plants as nephroprotective agents

Nephroprotective agents are the substances which possess protective activity against nephrotoxicity. Medicinal plants have curative properties due to the presence of various complex chemical substances. Ancient literature has prescribed various herbs for the cure of kidney disease (Ramya Pydi et.al 2011). Co-administration of various medicinal plants possessing nephroprotective activity along with different nephrotoxic agents may attenuate its toxicity. Sources of herbs, which have been documented for the possible uses in nephrotic disorders in the literature, are as follows.

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).

Rheum species

Effect of *R. officinale* extract treatment on urine composition in rats with adenine-induced renal failure was studied. Administration 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).

Cordyceps sinensis

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

Punarnava

Observations on the clinical, experimental and immunological studies on "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).

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).

Zingiber officinale

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

Vitis vinifera

Cortisone, *Mercurius corrossivus* (a homeopathic drug) and an aqueous extract of *Vitis vinifera* were used for controlling nephrotoxicosis caused by citrinin in mice. These drugs were administered to toxin treated mice regularly for 20 weeks. Analysis of blood as well as histopathological examination of kidney revealed that combination of drugs had significantly positive effect and up to 41% recovery was achieved (Bilgrami and Jeswal. 1993).

Tribulus terrestris

Simultaneous administration of *Tribulus terrestris* (200 mg/kg/day/p.o.) and gentamicin to female rats decreased the gentamicin-induced nephrotoxicity in both structural and functional terms. The effects were comparable to that of verapamil. *Tribulus terrestris* was found to reduce the MDA production in kidney in experimental animals (Nagarkatti. 1994).

Achyrocline satureioides

Hydro alcoholic extract of *A. satureioides* might change renal ion transport, based on observations that it affects gastro-intestinal reabsorption (Rocha et.al.1994).

***Angelica radix* (Root)**

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

Clerodendron trichotomum

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

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).

Icacina trichantha

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

***Cocos nucifera* (Coconut)**

Rats, fed with methyl deficient diet, developed renal necrosis with acute renal failure. The aim of this experiment was to explore further the role of coconut oil in this experimental model. 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 evaluated by renal weight, type (tubular and cortical necrosis or repair) and extent (grade) of the renal damage. (Monserrat et.al.1995).

Ephedra distachya

Administration 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).

Terminalia chebula (Haleela)

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

Taraxacum officinale

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

Asparagus racemosus

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

Ocimum sanctum

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

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).

Desmodium canadense

The effect of the dry extract obtained from the aerial parts of *D. canadense* on the course of CCl₄ induced acute renal insufficiency was studied in male albino rats, A marked nephro-protective effect was obtained with a dose of 50 mg/kg, with regeneration of the functional activity of the kidneys early in the pathological process. 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).

Arctostaphylos uva-ursi

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

Echinacea pallida

The hydro alcohol standardized extract of *Echinacea pallida* given to mice in association with the intraperitoneal administration 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 estimated from the level of kidney homogenate oxygen consumption (Mustea.1997).

Aswagandha

The protective effect of "Aswagandha" (*Withania somnifera*) on cadmium induced toxicity in mice kidney has been studied. Mice were fed with cadmium chloride along with Aswagandha extract and Aswagandha extract alone (1.14 g/kg body weight) for 20 days. A result based on lipid peroxidation indicates that Aswagandha is capable of reducing toxicity caused by cadmium (Panday.1997).

Vicia faba (Baqila)

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. *Vicia faba* is a ubiquitous plant rich in easily absorbable L-DOPA. Following ingestion of 40 g freshly chopped *V. faba* containing 120-130 mg of L-DOPA, plasma L-DOPA, urinary sodium and DA excretion increased significantly. *V. faba* might be of value in treating conditions such as hypertension, heart failure, renal failure, and liver cirrhosis in which natriuresis and diuresis are medically beneficial (Vered et.al.1997).

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).

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 *Sanguisorbae radix* extract, renal dysfunction was attenuated and the increases in serum urea nitrogen and Cr induced by LPS were significantly reduced. The administration of *Sanguisorbae radix* extract also effectively lowered serum nitrite/nitrate level. A similar effect was observed on the iNOS activity. These results indicate that *Sanguisorbae radix* extract contributes to the regulation of renal function under conditions where there is excessive generation of NO (Chen C. P et. al.1999).

Geranium thunbergii

Effects of geranin (tannin) extracted from the herb *Geranium thunbergii* on puromycin amino nucleoside (PA) nephritis were 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. Observation by electron microscopy revealed that 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).

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).

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). *G. biloba* Ext. (300 mg/kg BW) was administered orally 2 days before and 8 days concurrently with gentamicin (80 mg/kg BW). The study showed that supplementation with *Ginkgo biloba* extract may be helpful to reduce gentamicin nephrotoxicity (Naidu et. al.2000).

***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 demonstrated a protective effect against the renal dysfunction caused by ischemia and recirculation. On the other hand it was demonstrated that 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).

Solanum nigrum

The 50% ethanol extract of the whole plant of *Solanum nigrum* was tested in vitro for its cytoprotection against gentamicin-induced toxicity on Vero cells. Cytotoxicity was significantly inhibited as assessed by the Trypan blue exclusion assay and mitochondrial dehydrogenase activity (MTT) assay. The test extract also exhibited significant hydroxyl radical scavenging potential, thus suggesting its probable mechanism of cytoprotection (Prasanth Kumar V et. al. 2001).

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 BW was given after EG (2ml/kg BW p.o) administration. Grape seed extract in mice produced significant reduction of urinary LDH, blood urea, creatinine & dilated tubules lined by normal intact epithelium indicating recovery. The results suggest that the Reno protective effect of *Vitis vinifera* seed extract is due to improvement in antioxidant status (Miller et.al. 2005).

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).

Rhazya stricta

Crude 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).

Pongamia pinnata

Ethanol extract of the flowers of *Pongamia pinnata* was studied for its protective effect against cisplatin and gentamicin induced renal injury in rats. When the extract (300 and 600mg/kg) was administered 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 (600mg/kg) normalized the raised blood urea and serum creatinine levels (Shirwaikar et. al.2003).

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 investigated. 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 administration 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 above results suggest that glycyrrhizin treatment could ameliorate renal defects in rats with acute renal failure induced by gentamicin (Sohn E J 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). Nephrotoxicity was made evident by:

1. The increase in blood urea nitrogen and plasma creatinine.
2. The decrease in plasma glutathione peroxidase (GPx) activity and the urinary increase in N-acetyl-beta-D-

glucosaminidase activity and total protein.

3. Necrosis of proximal tubular cells.
4. Increase in the renal levels of oxidative stress markers: nitro tyrosine and protein carbonyl groups and the decrease in manganese superoxide dismutase (Mn-SOD), GPx, and glutathione reductase (GR) activities.

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 Mn-SOD, GPx, and GR activities in renal cortex. These data suggest that AGE may be a useful agent for the prevention of GM-nephrotoxicity (Maldonado P. D et.al.2003).

Aerva lanata

The ethanol extract of whole plant of *Aerva lanata* was found to possess marked nephroprotective activity with minimal toxicity in cisplatin and gentamicin induced acute renal injury in albino rats of either sex. In the curative regimen, the extract at dose levels of 75,150, and 300mg/kg showed dose dependent reduction in the elevated blood urea and serum creatinine levels and normalized the histopathological changes in the curative regimen. (Shirwaikar et.al. 2004).

Nigella sativa

In this work, tested whether 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 evaluated histopathologically and by measurement of concentrations of urea, creatinine and total antioxidant status (TAS) in plasma and reduced glutathione (GSH) and TAS in kidney cortex. The results indicated that 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 results suggest that *N. sativa* may be useful in ameliorating signs of GM nephrotoxicity in rats (Ali B H et.al.2004).

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).

Hemidescus indicus

The treatment with *H. indicus* helped in the management of renal impairment, which was induced by gentamicin in rats. This is evident from the results obtained for 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. A histological examination of kidneys also supports the findings from hematological evaluations. The plant shows promise as an adjunct therapy alongside aminoglycosides as it reduces nephrotoxicity caused by aminoglycosides (Magala S et.al.2004).

Cassia auriculata

Effect of *Cassia auriculata* Linn. Root extract on cisplatin and gentamicin induced renal injury was studied. In the cisplatin model, the alcoholic extract normalized the raised blood urea and serum creatinine levels. The histopathological pictures supported the biochemical findings. 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 regimen (Shirwaikar et.al.2005).

Drynaria fortunei

The flavonoid fraction (FF) from *Drynaria fortunei* was investigated to determine its biological activity expression in three acute renal failure animal models Guinea pigs & mercuric chloride treated mice. Guinea pigs received 100 mg/kg of gentamicin & 10 mg/kg of FF. FF treatment prevented the GM toxicity, ie; the increase in BUN and creatinine levels. Mice were treated once with 6 mg/kg of mercuric chloride, followed by 10 mg/kg of FF. BUN and creatinine levels were found to be significantly higher on the mercuric chloride treatment and are ameliorated by FF treatment. In conclusion, the present study suggests that 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 such as alkaloids, flavonoids & isoflavone. Administration 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 A K et. al.2006).

Eruca sativa

Mercuric chloride (HgCl₂) is a well-known nephrotoxic agent. Increasing number of evidences suggest 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. In the present study, the antioxidant potential of ethanolic extract of *E. sativa* seeds was determined and its protective effect on HgCl₂ induced renal toxicity was investigated. The extract was found to possess a potent antioxidant effect, with a large amount of polyphenols and a high reducing ability. HPLC analysis of the extract revealed glucoerucin and flavonoids to be the major antioxidants present in it. *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 administration of 4 mg/kg body weight HgCl₂ induced renal injury evident as a marked elevation in serum creatinine and blood urea nitrogen levels, and histopathological changes such as necrosis, edema and congestion of stroma and glomeruli. 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 administration 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 against alterations in all these diagnostic parameters. The data obtained in the present study suggests *E. sativa* seeds to possess a potent antioxidant and renal protective activity and preclude oxidative damage inflicted to the kidney (Sarwar Alam M et.al.2007).

Didymocarpus pedicellata

Ethanolic extract of the aerial parts of *Didymocarpus pedicellata* demonstrated significant

antioxidant and protective activity against ferric nitriloacetate induced renal oxidative stress, nephrotoxicity and tumor promotion response. Further the extract provided significant protection against. The extract also significantly 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 further supported ancient use of plant in the treatment of kidney diseases (Kaur G. 2007).

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 Y. Fet.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. In the current study, effects of pretreatments with single daily oral 100 – 500 mg/kg/day of the root aqueous extract of *Harungana madagascariensis* were investigated 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). Effects of the extract pretreatments on the hematological and renal histological profile in acetaminophen nephrotoxic rats were also evaluated. Results showed that treatment with intraperitoneal acetaminophen for 24 hours and 14 days induced significant ($p < 0.05$, $p < 0.01$, $p < 0.001$) 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. However, pretreatments with graded oral doses of the extract significantly ($p < 0.05$, $p < 0.01$, $p < 0.001$) 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 ($p < 0.05$, $p < 0.01$, $p < 0.001$) improved packed cell volume (PCV), hemoglobin (Hb), and total leucocyte count (TLC) levels but non-significant ($p > 0.05$) increase in the mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), and mean

corpuscular hemoglobin concentration (MCHC), in the repeated acetaminophen model. Thus, the overall results showed that *Harungana* extract protects against acetaminophen nephrotoxicity (Adeneye A.A et.al.2008).

Allium ascalonicum

The clinical use of an immunosuppressive cyclosporine A (CsA) is limited by its serious nephrotoxic effect. Evidences have suggested the role of oxidative stress in its pathogenesis. Shallot (*Allium ascalonicum* L.) has recently been shown to possess antioxidative and free radical scavenging abilities. The present study was undertaken to investigate 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, histopathology, tissue malondialdehyde (MDA) and glutathione (GSH) levels were evaluated 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 vacuolations and tubular necrosis. CsA also induced oxidative stress, as indicated by increased renal MDA and reduced GSH concentrations. Administration of shallot extract along with CsA counteracted the deleterious effects of CsA on renal dysfunction, oxidative stress markers, and morphological changes. These data indicate the protective potential of shallot extract against CsA nephrotoxicity and suggest a significant contribution of its antioxidant property to this beneficial effect (Wongmekiat O et.al.2008).

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 current investigation was undertaken to explore the protective effect of the aqueous-ethanol extract of cultured mycelium of *M. esculenta* against cisplatin and gentamicin induced acute renal toxicity in Swiss albino mice. Cisplatin and gentamicin when administered 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 su-

peroxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx), and reduced glutathione (GSH) in the kidneys consequent to cisplatin and gentamicin administration was significantly elevated. The enhanced renal antioxidant defense system also prevented the tissue lipid peroxidation. The experimental results suggest that aqueous-ethanol extract of morel mushroom, *M. esculenta* mycelium protected cisplatin and gentamicin induced nephrotoxicity possibly by enhancing renal antioxidant system. The findings thus suggest the potential therapeutic use of morel mushroom mycelium as a novel nephroprotective agent (Nitha B et.al.2008).

Pimpinella tirupatiensis

Pimpinella tirupatiensis (Apiaceae) isan herbaceous medicinal plant used to treat cough, stomach, liver problems, asthma, ulcer and tooth ache in India and other Asian countries. Acetaminophen (APAP) is a commonly used analgesic and antipyretic agent which, at high doses, causes liver and kidney necrosis in man and animals. The aim of the present study is to investigate 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. Biochemical studies show that 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. Apart from these, histopathological changes also reveal the protective nature of the *P.tirupatiensis* extract against acetaminophen induced necrotic damage of renal tissues. In conclusion, these data suggest that 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 S et. al.2009).

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 in animal models of acute renal failure. The present study was undertaken

to see whether 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. CP increased the activities of lactate dehydrogenase and acid phosphatase whereas, the activities of malate dehydrogenase, glucose-6-phosphatase, superoxide dismutase, catalase, and 32Pi transport significantly decreased. GT consumption increased the activities of the enzymes of carbohydrate metabolism, brush border membrane, oxidative stress, and 32Pi transport. GT ameliorated CP-induced nephrotoxic and other deleterious effects due to its intrinsic biochemical/antioxidant properties (Sara A. Khan et. al.2009).

Carica papaya

The dose related effect of the aqueous seed extract of *Carica papaya* Linn. extract (CPE) was evaluated by pre-treating three groups of rats (made up of six male rats per group) with 100– 400 mg/kg body weight per oral of the extract for 7 days before challenging with 1.5 ml/kg body weight of 20% carbon tetrachloride in olive oil in addition to the untreated control and model control rats. Also, the time-course effect of 400 mg/kg per oral of the extract were determined at 3 hr. pre-, 0 hr., 1 hr. post-, 3 hr. post-, and 6 hr. post-CCl₄ induction, respectively, in addition to the untreated control and model control groups. After 72 hours, serum levels of uric acid, urea and creatinine of all study groups were measured using standard procedures. Histological studies of rat kidneys of all study groups were also done. Results showed that intraperitoneal injection of CCl₄ caused a significant ($p < 0.001$) elevation in the serum levels of uric acid, urea and creatinine and induced histological features of severe tubulointerstitial necrosis. However, elevations in the measured biochemical parameters were significantly ($p < 0.05$, $p < 0.01$ and $p < 0.001$) attenuated in rats pre-treated with the graded oral doses of the extract, in dose related fashion. Maximum nephroprotection was offered by the extract at 400 mg/kg/day CPE which lasted up to 3 hours post-CCl₄ exposure and these biochemical evidences were corroborated by improvements in the renal histological lesions induced by CCl₄ intoxication. In conclusion, our study showed that CPE has nephroprotective

tive effect on CCl₄ renal injured rats, an effect which could be mediated by any of the phyto-components present in it via either antioxidant and/or free radical scavenging mechanism (Olagunjua J.A et.al.2009).

Orthosiphon stamineus

A study was undertaken to carry out the preliminary phytochemical screening and Nephroprotective activity of *orthosiphon stamineus*, family Lamiaceae (*Labiatae*). These studies 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. These observations made us to investigate the plant material for its nephroprotective activity in rats. Gentamycin is an extensively used aminoglycoside antibiotic. It has been reported to produce nephrotoxicity even at normal therapeutic dose level. The drug was administered intraperitoneally at a dose of 80mg/kg weight for 9 days. 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 *Orthosiphon stamineus* at both dose levels that is 100 and 200 mg/kg body weight in rats (Kannappan N.2010).

Paronychia argentea

Renal protection and antiurolithiasic effects of two extracts of *Paronychia argentea* (PA), a traditional Algerian plant commonly known as Algerian tea, were evaluated. This study was carried out to determine whether 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 administered 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 ($p < 0.01$) and blood urea levels ($p < 0.01$)

(nephroprotective effect). However, the increase in ALT (27%) and PAL (31–51%) serum levels and in the relative liver weights ($p < 0.01$) in the groups treated with doses of APA may indicate that this extract has not a hepatoprotective effect against oxalate toxicity. The data indicate that administration 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 Wistar rats (Bouanania et.al.2010).

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 non-enzymatic antioxidants along with lipid peroxidation were evaluated in various experimental groups. GM treatment induced significant elevation ($p < 0.05$) in plasma and urine urea, creatinine, renal lipid peroxidation along with significant decrement ($p < 0.05$) in renal enzymatic and non-enzymatic antioxidants. SR treatment to GM treated rats (GM+ SR) recorded significant decrement ($p < 0.05$) in plasma and urine urea and creatinine, renal lipid peroxidation along with significant increment ($p < 0.05$) in renal enzymatic and non-enzymatic antioxidants. SR leaf extract ameliorates GM induced nephrotoxicity and renal dysfunction and thus validates its ethno medicinal use (Menaka C et. al.2010).

Tecoma stans

A study was conducted to highlight the nephroprotective activity of ethyl acetate extract of dried flowers of *Tecoma Stans* for its protective effects on gentamicin-induced nephrotoxicity in albino rats. For studying acute toxicity study, single oral dose of 5 000 mg ethyl acetate floral extract/kg body weights was administered to albino rats (five females, five males). Nephrotoxicity was induced in albino rats by intraperitoneal administration of gentamicin 80 mg/kg/day for eight days. Effect of concurrent administration of ethyl acetate floral extract of *Tecoma 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. The study groups contained six rats in each group. 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. For acute toxicity testing both female and male rats administered with the extract at a dose of 5 000 mg/kg. The results showed no toxicity in terms of general behavior change, mortality, or change in gross appearance of internal organs ($LD_{50} > 5\ 000$ mg/kg). It was observed that the ethyl acetate floral extract of *Tecoma 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 ($P > 0.01$). The study indicates a very important role of reactive oxygen species (ROS) and the relation to renal dysfunction and point to the therapeutic potential of *Tecoma stans* in gentamicin induced nephrotoxicity (Raju S et. al.2011).

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 evaluated. ADR nephropathy rats were randomly treated with ARE (2.5 g/kg/d, n = 6, ARE group), or benazepril (10 mg/kg/d, n = 6, 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 NO_3^-/NO_2^- excretion were determined by chromatometry. Renal cortex cyclic guano sine monophosphate (cGMP) level was measured by enzyme immunoassay and eNOS expression was determined by immunohistochemistry. ARE and ACEI treatments could remarkably reduce more 24 h urinary protein excretion than that in ADR group (88.32 ± 9.96 mg, 81.78 ± 16.28 mg vs. 153.91 ± 28.63 mg, $P < 0.01$), 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 NO_3^-/NO_2^- excretion in ARE group was lower than ADR group. Renal cortex MDA content ($r = 0.895$, $P < 0.01$), cGMP content ($r = 0.666$, $P < 0.01$) and eNOS expression in glomerulus ($r = 0.910$, $P < 0.01$) were strongly positively associated with 24 h urinary protein excretion. And renal cortex SOD content was negatively associated with 24 h urinary protein excretion ($r = -0.861$, $P < 0.01$). ARE may ameliorate the proteinuria by suppressing the over expression of eNOS, and inhibiting the oxidative injury in ADR nephropathy rats (Huaizhou You 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 (CCl₄) induced nephrotoxicity was studied. Intraperitoneal dose of 20% CCl₄ (0.5 ml/kg b.w) was administered twice a week for 8 weeks to a 28 group of rat. Other groups were given CCl₄ and various fractions of *C. opaca* fruit (200 mg/kg bw). CCl₄ 29 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), H₂O₂, DNA injuries and 31 histopathological lesions were observed in CCl₄ test group. CCl₄ increased RBCs, WBCs, urea, urobilinogen 32 and creatinine in urine while BUN, creatinine, urobilinogen, direct and total bilirubin, and nitrite in 33 serum. Treatment of various fractions attenuates the toxicity of CCl₄ and weight of body and kidneys 34 reversed towards the normal level. HPLC analysis showed the presence of myricetin, isoquercetin, apige- 35 nin and orientin in CFC, AFC and MFC with evident protective effects for the studied parameters indicating that *C. opaca* fruit is a useful functional food for preventing kidney disorders (Muhammad Rashid Khan et al.2011).

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 present study was carried out to investigate the effect of *Smilax china* L. on hyperuricemia and renal dysfunction in induced hyperuricemic animals. Materials and methods: Five fractions (petroleum ether, chloroform, ethyl acetate, n-butanol and resid-

ual ethanol fraction) of *Smilax china* L. were orally administered 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 administered to 10% fructose-induced peruricemic 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, with the IC₅₀ values of 42.60, 37.53, 42.20 and 40.69 μ M, respectively, and exhibited competitive or mixed inhibitory actions. Moreover, EAF (125, 250 and 500 mg/kg) markedly reversed the serum uric acid level ($p < 0.05$, $p < 0.01$ and $p < 0.001$, respectively), fractional excretion of urate ($p < 0.05$, $p < 0.01$ and $p < 0.01$, respectively) and blood urea nitrogen ($p < 0.05$, $p < 0.01$ and $p < 0.01$, respectively) 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 (Lvyi Chena et.al. 2011).

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 *Moringa oleifera* leaves (150 and 300 mg/kg) was evaluated against gentamicin-induced (80 mg/kg) renal injury in rabbits. Serum urea and creatinine levels were evaluated as the markers of renal nephrotoxicity. At the end of the experiment, the kidneys of rabbits were excised for histological examinations and determination of lipid peroxidation levels. Serum urea and creatinine levels were reduced in the *M. oleifera* (150 and 300 mg/kg) plus gentamicin treated groups. On histological examinations, kidney of intoxicated rabbits groups which received *M. oleifera* extract showed reparative tendencies. A highly significant ($p < 0.01$) 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 ($p < 0.01$) depletion in LPO. The present study indicates that aqueous-ethanolic extract of *M. oleifera* leaves attenuates renal injury in rabbits treated with gentamicin, possibly by inhibiting lipid peroxidation (Moustapha Ouédraogo C et.al.2011).

Croton zambesicus

A study was conducted to evaluate the kidney protective effect of ethanolic root extract of *Croton zambesicus* (*C. zambesicus*) against gentamicin-induced kidney injury in rats. The root extract (27-81 mg/kg) was administered to rats for eight days with concurrent administration of gentamicin (100 mg/kg) daily for the same period of time. Protective effect of the extract was evaluated in serum levels of creatinine, urea, and uric acid as well as some ions like sodium, potassium and chloride. Histological examination of the kidneys from different treatment groups were also carried out. Administration 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 ($P < 0.01$) 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 (Jude E Okokon et. al.2011).

Vernonia cinerea

Effect of petroleum ether, ethyl acetate, and alcoholic extracts of aerial parts of *Vernonia cinerea* on Cisplatin induced nephrotoxicity was studied in albino rats. The nephroprotective activity of the plant was assessed in prophylactic and curative models by estimating blood urea nitrogen, serum creatinine, serum total proteins, urinary proteins, creatinine clearance and urine to serum creatinine ratio. Cisplatin elevated blood urea nitrogen, serum creatinine, serum total proteins, increased excretion of urinary protein, decreased the creatinine clearance. 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).

Bauhinia variegata

The nephroprotective effect of ethanolic extract of *Bauhinia variegata* whole stem against cisplatin induced nephropathy was investigated by *in vivo* method in rats. The statistically processed results suggested the protective action of the plant against cisplatin induced nephropathy (Saumya R Pani et.al.2011).

Aegle marmelos

An investigation was carried out to evaluate the Nephroprotective activity of an aqueous

extract of the leaves of *Aegle marmelos* in wistar rats. The aqueous extract of the plant was administered 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 nephroprotective effect (Kore K. J et. al.2011).

Ficus racemosa

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

Plant formulations as Nephroprotective agents

Shi-quan-da-bu-tant

A poly herbal Chinese formulation *Shi-quan-da-bu-tant* was studied for its protective effect on ddY mice administered with 3 mg/kg of cisplatin. Among the ingredients of the formulation, *Angelica radix* was more effective and it showed the strongest protective effect against the toxicity. The effectiveness of *Angelica radix* was found to be due to its constituent l-malate which was isolated and tested for nephroprotective activity (Sugiyama.1981).

Tong Fu Xie Zhuo

Chinese traditional medicine "Tong Fu Xie Zhuo" was tested for uremia. The results indicated that 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).

Jian-pi-qili-shu,

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

Tripterygium wilfordii* and *Salviae miltiorrhizae

Tripterygium wilfordii polyoglucoiside mg/kg combined with radix *Salviae miltiorrhizae* (6-

15g) for treating purpuric nephritis (Group-A) was compared with the control group of using *T.wilfordii* polyglucoside treatment only (Group-B). The average time of edema disappearing and blood pressure resuming to normal range was observed to be 8 days in Group-A, which was much better than those in Group-B. It indicates that the effect of Group-A was much better (Yu.1992).

Chai-ling-tang

A Chinese poly herbal formulation was administered 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. 32 children with SDNS treated with prednisone and cyclophosphamide served as control. Results showed that short-and long-term relapse and average prednisone dose were similar in the two groups. It is considered that 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).

Moringa oleifera* and *Tinospora cordifolia

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

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 (i.p.) 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, administration of *Crocus sativus* and *Nigella sativa* together with cisplatin partially reversed many of the kidney enzymes changes induced by cisplatin. The results of this study indicate a possible way of counteracting the toxicity by introducing protective agents. 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).

Ekongsan

Ekongsan (containing plants like *Ginseng radix*, *Atractylis rhizome*, *Glycyrrhiza radix* and *Aurantii nobilispercarpium*) 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 administration of Ekongsan significantly inhibited the loss in body weight of cisplatin injected rats. These findings suggest that Ekongsan is an active prescription in protection against nephrotoxicity of cisplatin (Lee et. al.1998).

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 administration of gentamicin (Anwar. 1999).

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*, *Boerhaavia diffusa*, *Saccharum officinarum*, *Butea frondosa*) were administered to male albino 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).

GINSENOID-Rd

Ginsenoside-Rd has been proved to decrease the severity of renal injury induced by cisplatin, in which proximal uriniferous 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. In addition, it was

demonstrated that ginsenoside-Rd affected cultured proximal tubule cells exposed to Cisplatin (Yokozava T et. al.2000).

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*, *Embllica officinalis*, *Withania somnifera*, *Ocimum sanctum* and *Boerhaavia diffusa*. On the basis of results obtained, it can be suggested that 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).

Tribulus terrestris and *Crataeva nurvula*

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

Liver-kidney care

A clinical study was conducted to study 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).

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 investigated for its diuretic activity by measuring total urine output and nephroprotection, studied in gentamicin model. JZS showed significant diuretic activity (Afzal. 2004).

Seeds of Papaya and Pumpkin Fruit

A study was focused on the Nephroprotective evaluation of ethanolic extract of the Papaya seed, PaSE (Biological name- *Carica papaya*, family – Caricaceae) and pumpkin seed, PuSE (Biological name - *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 PaSE & PuSE exhibited protection against cisplatin-induced nephrotoxicity, which were proved by the gross behavioral studies, histopathological, renal function and biochemical studies. Antioxidant studies like nitric oxide

scavenging activity, lipid peroxidation in kidney also supporting the nephroprotective activity of these seeds. This nephroprotective study also compared with chloroform extract of the dried Zinger roots, ZE (*Zingiber officinale* Rosc, Family- Zingiberaceae) and methimazole (MZL) which is already evaluated. Histopathological investigation of the kidney like glomerular congestion, blood vessel congestion, intestinal edema, inflammatory cells, necrosis, tubular casts were also observed for control, test and reference groups (Subal Debnath et.al.2010).

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