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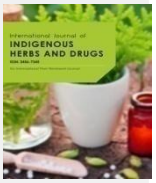

NEPHROPROTECTIVE HERBS: AN UPDATED REVIEW

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Abstract

Many natural products, medicinal plants, and food sources have been evaluated as possible nephroprotective agents. When developing an appropriate treatment to treat a range of kidney problems, medicinal plants can be a valuable source for new molecules with potential applications. Medicinal plants contain many complex molecules that impart their medicinal properties. Because medicinal plants have relatively high concentrations of phytoconstituents, bioactive compounds including, but not limited to, alkaloids, phenols, steroids, and flavonoids demonstrate significant nephroprotective properties to nephrotoxicity. The objective of the current review was to highlight a few of the contemporary medicinal herbs that have been evaluated for nephroprotective properties.

***Keywords*:** *Nephrotoxicity, herbal plants, medicinal uses, phytoconstituents, renal illness.*

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Introduction

Rapid decline in kidney function brought on by the harmful effects of drugs and chemicals is known as nephrotoxicity. There are several types, and certain medications may have multiple effects on renal function. It describes adverse consequences that impair the filtration, reabsorption, and excretion processes of the kidneys. Nephrotoxicity is the result of exogenous or endogenous toxicants damaging or destroying kidney function, which impairs kidney-specific detoxification and excretion. A kidney-specific condition known as nephrotoxicity occurs when hazardous chemicals or medications cause problems with excretion. Drugs are responsible for about 20% of nephrotoxicity, but as people age, the incidence of nephrotoxicity can rise to 66% due to medicine. Nephrotoxicity has hindered the use of anticancer medications and chemotherapy. A straightforward blood test can be used to diagnose nephrotoxicity. Blood tests that quantify blood urea nitrogen (BUN), serum creatinine concentration, glomerular filtration rate, and creatinine clearance are used to assess nephrotoxicity. However, only when the majority of kidney function is impaired can these evaluations of nephrotoxicity be made [1]. The urinary system of our body is vitally useful for the maintenance and control of operations related to our endocrine glands, blood pressure, acid-base balance, and erythropoiesis. Upon exposure to drugs or toxic agents, nephrotoxicity has been one of the primary causes for kidney deterioration, which includes acute and chronic renal failure, and can include such effects as anemia, disorders of the bone, cardiovascular disease risk, dyslipidemia, and nephritis. The kidneys have been regarded as one of the primary target organs for exogenous toxicants, as they are important organs required for many vital processes in the body, including homeostasis, regulation of the extracellular environment (involving detoxification), and excretion of toxic metabolites and drugs [2]. One of the eight leading causes of death is renal disease. In India, around 80,000 individuals develop chronic kidney failure each year and around 19 million adults suffer chronic kidney disease. Currently, renal replacement therapy is the only treatment for end-stage renal failure. If kidneys are not available, then dialysis is the only option, but unfortunately this is incredibly limited by many factors, particularly price. Exposure to an array of potent therapeutic medications,

including aminoglycoside antibiotics, NSAIDs, chemotherapeutic agents, and chemical agents such as ethylene glycol, carbon tetrachloride, sodium oxalate, and heavy metals underline acute renal failure (lead, mercury, cadmium, and arsenic), chronic interstitial nephritis, nephritic syndrome, or a rapid decline in renal function that results in abnormal retention of serum creatinine and blood urea that should be excreted [3]. Nephroprotective medicines are those that exhibit protective action against nephrotoxicity, which is brought on by medications like acetaminophen, gentamicin, and cisplatin, among others. Parts of plants such as leaves, stems, bark, roots, flowers, seeds, and fruits have been used in alternative and complementary medicine. Traditional medicines contain a wide range of active agents or phytochemicals, including flavonoids, alkaloids, saponins, terpenoids, isoprenoids, polyphenols and tannins found in medicinal herbs. Herbs rich in antioxidants also have nephroprotective properties [4].

Plants are responsible for their nephroprotective activity. Some of the highlights include-

***Scholaris Alstonia Linn*:** Experimental rats received a single injection of gentamycin (80 mg/kg) and were divided into treatment groups in which two groups labeled gentamycin group (200 mg/kg dose and 400 mg/kg dose) and gentamycin treated group with Alstoniascholaris dichloromethane extract. There was considerately high serum urea, creatinine, uric acid, total protein, urine urea, uric acid and creatinine levels in animals treated with gentamycin so that they were susceptible to extreme nephrotoxicity. The animals treated with Alstoniascholarislinn extract or in this case showed a great magnitude of reduction creatinine, uric acid and urea levels in serum and urine samples as mentioned because the herb contain terpenoids or alkaloids or flavonoids [5].

Biophytum sensitivum (linn): The ethanol extract of the whole plant Biophytumsensitivum (linn) has nephroprotective properties, against nephrotoxicity induced by cisplatin in wistar albino rats. Urinary evaluation of total protein, salt, potassium, calcium, and magnesium assessments, as well as nephrotoxicity through various kidney functioning tests and markers of damage including water intake, urine volume, body weight, and urine pH. The ethnomedical application of the plant can be attributed to nephrotoxicity, since the coadministration of the whole plant extract showed increased body weight, urine pH, serum protein, calcium, and sodium levels; decreased urinary excretion of total protein and calcium, low serum BUN, and creatinine concentration [6].

***Corallocarpus epigaea*:** Ahydroalcoholic extract of Corallocarpusepigaea has renoprotective effects against cisplatin-induced nephrotoxicity at doses of 100, 200 and 400 mg/kg. In the Cisplatin group, blood creatinine and urea were elevated, and serum albumin was reduced. In the extract + vitamin E (100 mg/kg), a well-known nephroprotective agent, SOD was higher and malondialdehyde was lower. Histopathological examination shows resolution of tubular necrosis in the kidney caused by cisplatin [7].

Descurania sophia: The dicot annual weed Descuraniasophia is in the Brassiaceae (cruciferae) family. This wasp is used in Chinese medicine to treat a variety of diseases. The seeds are used to treat coughs, asthma, urinary retention, and diuretics. They have some pharmaceutical value because of their abundance of phytoconstituents.22 Descuraniasophiahydroalcoholic extract protects experimental rats from gentamicin-induced nephrotoxicity. The serum levels of BUN, creatinine, cholesterol, triglycerides, Na excretion, and rate of cell death (apoptosis) were all significantly and dose dependently reduced [8].

***Sphaeranthus amaranthoides burm f.*:** Sphaeranthus amaranthoidesb urm f. aqueous extract is effective in the treatment of acute kidney injury (AKI) and provides protection against gentamicin-induced nephrotoxicity. In animals that had been pre-treated with various concentrations of Sphaeranthusamaranthoides, levels of LDH, GGT, creatinine, BUN and electrolytes in serum and urine remain normal, while animals treated with gentamicin had elevated levels of all these parameters [9].

Combretum micranthum: The medicinal plant *combretum micranthum* is from the Combretaceae family. High glucose (100 mM) was related to nephrotoxicity in human embryonic kidney cells (HEK-293) as the in vitro model for diabetic nephropathy. The results showed that kidney cells incubated in the higher concentration of glucose for 72 hours decreased by a marked difference in cell viability resulting in morphological changes in kidney cells that included, cytoplasmic vacuolation, rounded cell shape, and shrinkage. There was a significantly improved cell viability ranging from 10 to 23% after treatment with CM extract at 10 and 25 µg/mL over high glucose control. The above three stages of research determines that C. micranthum may have nephroprotective features [10].

***Tamarindus indica Linn*:** *Tamarindus indica* is a significant medicine distributed mainly in tropical countries and belongs to the Fabaceae family. This medicine is used in the Unani system and has proven good antiseptic, stomachic, laxative, digestant, cardiac tonic, and dysentery treatment activity.30 In experimental rats, the ethanolic extract of Tamarindus indica Linn fruit pulp has nephroprotective effect against nephrotoxicity caused by cisplatin. Histopathological studies even demonstrate that it reverses kidney damage and restores the normal structure of kidney, This supports its nephrprotective activity from flavonoids. Renal parameters were evaluated in nephrotoxic rats treated with EETI and ultimately found significantly increased attenuated body weight, increased urine volume, increased creatinine clearance and significant decreased elevated serum creatinine levels.Danish TK [11].

P. amboinicus The aqueous leaf extract of P. amboinicus has a powerful nephroprotective potential against the acute nephrotoxicity of Adriamycin. The 400 mg/kg of the aqueous leaf extract of P. amboinicus was given simultaneously with the ADR treatment of the nephrotoxic

group. At the conclusion of the experiment, the serum creatinine concentration of the extract treated group was much less than in the nephrotoxic control group. The plant extract treated group compared to the ADR induced control group has reduced acute tubular necrosis as noted histopathologically in the kidney tissue [12].

Aegle marmelos Aeglemarmelos (L.) (AM), often called bael, is in the Rutaceae family and is used in Ayurvedic medicine for multiple conditions. Methanolic extract of AM significantly reduces renal damage in rats from cisplatin. The cisplatin-generated nephrotoxicity is due to decrease antioxidants and antioxidant enzymes generation of reactive oxygen species (ROS) metabolites and lipid peroxidation. Antioxidants appear to protect against adverse consequences. AM has strong antioxidant activity in vitro and in vivo. Different doses of extracts decreased malondialdehyde significantly but increased GSH, SOD and catalase significantlly. The histology of kidney tissue (600mg/kg) confirmed recovery of tubular casts, glomerular damage, and desquamation. There are many phytochemicals in AM, especially polyphenols which are responsible for nephroprotection [13].

Adhatoda zeylanica: One of the major drugs in the Ayurvedic medical system, Adhatodazeylanica (Syn. A. vasica Linn) (AZ), which belongs to the Acanthaceae family, is used predominantly in the treatment of symptoms of cough and infection of the respiratory tract. In Wistar albino rats, AZ leaves confer a significant nephroprotective effect against gentamicin-induced renal damage. Treatment of rats with gentamicin (80 mg/kg/day) increases serum creatinine, urea and protein levels, representing a progressive renal disease marker. The most important factor in AZ's nephroprotective effect against drug-induced toxicity is that it scavenges the free radicals produced by gentamicin in Wistar rats [14].

Aerva lanata: The shrub Aervalanata (L.) A. L. Juss. exSchultes (AL) occurs throughout India. In Ayurveda it is known as Paashaanabheda. The nephroprotective ability of an ethanol extract of the entire AL plant was studied in acute renal damage induced by gentamicin and cisplatin. Blood urea and serum creatinine levels decreased in a dose-dependent manner with the extract at 75, 150, and 300 mg/kg in the curative regimen, and histological changes returned to normal upon treatment. In addition, rats given 300 mg/kg of ethanol extract exhibited similar improvement in the gentamicin paradigm. Due to AL ethanol extract's substantial nephroprotective capacity and low toxicity, it may serve as an important treatment modality in the attenuation of the nephrotoxic effect of nephrotoxins - gentamicin and cisplatin - in acute renal damage [15].

***Allium sativum*:** The aromatic herbaceous plant Allium sativum L. (AS), from the Amaryllidaceae family, is consumed and utilized as traditional medicine around the world. In diabetic rats, garlic is found to protect nephropathy induced by diabetes. Diabetic rats treated with 45 mg/kg body weight of streptozotocin (STZ) have significant biochemical changes in their urine and serum relative to non-diabetic control rats. Diabetic rats were found to have thickening of the mesangium and thickened basement membranes, histologically, while it appears their urine and serum biochemistry were experientially altered when treated with 500 mg/kg body weight of garlic extract. Moreover, diabetic rats treated with garlic supplements were seen to have a significant decline in VEGF and ERK-1, which resulted in decreased glomerulo-sclerosis and mesangial proliferation [16].

***Boerhavia diffusa*:** The restorative properties of Boerhaviadiffusa L. (BD), specifically relating to the urinary tract, are well established. The aqueous root extract of BD was found to protect rats against gentamicin nephrotoxicity. The rats had a weight gain and decrease in creatinine and BUN in their blood after getting various daily doses of 200 mg/kg and 400 mg/kg of the BD root extract. In the BD root extract groups, the levels of MDA and GSH were nearly normal while the usual levels showed a significant increase. The presence of extremely active antioxidants in the BD root extract could account for this. The treatment provides protection against gentamicin-induced acute tubular necrosis, even in the lower doses of BD. Increased renal blood flow is caused by better elimination of para aminohippurate (PAH) and both doses of BD improved PAH clearance in the groups [17].

Camellia sinensis: Green tea is a traditional beverage with many health benefits. Green tea protects the kidney from the nephrotoxic effects of gentamicin. Green tea extract significantly decreases the increase in creatinine (0.617±0.167 mg/dL) and the increase in urea (43.83±3.45 mg/dL), two classic nonenzymatic markers of kidney insult. Free radicals arise from reactive oxygen species that glucuronic acid, catechins, and vitamins C and E, which are found in green tea extract, destroy. Antioxidant properties of green tea extract are solely responsible for its nephroprotection [18].

Cichorium intybus: Aqueous and methanolic seed extracts of Cichoriumintybus L. (CI) can protect rats from gentamicin-mediated nephrotoxicity. Blood creatinine and urea levels increase after gentamicin administration from the renal injury caused by gentamicin. CI seed extracts (500 mg/kg body weight/day) have been shown to decrease blood urea and creatinine levels in mice with kidney disease. In contrast to the methanolic extract, CI aqueous extract provides significantly better protection from gentamicin-mediated nephrotoxicity [19].

Clitoria ternatea: Though acetaminophen is an analgesic and antipyretic, acetaminophen overdose can lead to kidney and liver injuries. The toxicity of acetaminophen is caused by the presence of a reactive quinone imine known as N-acetyl-p-benzoquinone imine formed by CYP enzymes. Ethanolic extracts of the root of Clitoriaternatea L. (CT) has been shown to protect rats from acetaminophen-induced kidney damage. CT therapy with two different doses of extracts demonstrated significant reduction of blood urea and creatinine levels (250 and 500 mg/kg body weight). Additionally, normal renal tissue was confirmed by histopathology revealing complete recovery from acetaminophen-induced necrosis. The nephroprotective effect can be attributed to the

antioxidant properties of CT phytocompounds [20].

Curcuma longa: Turmeric is cultivated widely as a spice in India. Administering aqueous extracts of Curcuma longa L. (CL) and Matricaria chamomile orally can protect against nephrotoxicity induced by tetracycline. Mild nephrotoxicity and damage to the renal tubules caused by tetracycline toxicity can result in a rise in urinary levels of creatinine and urea. In the present study, blood urea, creatinine, sodium and potassium levels were statistically significantly lower in rats treated with aqueous extracts. Histology showed less interstitial septa thickness, decreased deposition of collagen, reduced tubule thickening, minor collagen deposition, and reduced cellular infiltrates, resulting in a large increase in total protein in rats treated with aqueous extract compared to the untreated group. Thus, CL may protect kidney health by scavenging free radical or acting in antioxidant capacity [21].

Eclipta alba: The elimination of oxidative stress promotes nephroprotection. Antioxidants in Ecliptaalba (L.) Hassk. (EA) leaf extract protect rats from nephrotoxicity caused by gentamicin. Eclipta alba is high in flavonoids, specifically wedelolactone and has been shown to exhibit good antioxidant activity . The extract has the ability to scavenge free radicals, and reduce iron (III), which could impart some nephroprotection against gentamicin toxicity. In vivo experimentation with rats has demonstrated that EA ethanolic extracts (100, 200, and 400 mg/kg, via oral route, based on body weight) lessened kidney injury caused by gentamicin. All parts of progress (total protein, uric acid, serum urea, and serum creatinine) decreased in a dose-dependent manner following treatment with the ethanol extract. Eclipta is rich with various polyphenolic compounds that reduce free radicals. It is probable that these properties led to the nephroprotective effects of EA [22].

Glycyrrhiza glabra: In mice, a hydroalcoholic extract of Glycyrrhizaglabra L. (GG) roots (200 mg/kg) protects renal tubular cells from inflammation induced by gentamicin. In order to reduce IL-1β and IL-6, GG therapy induced Gpx and SOD levels, leading to induction of expression of Nrf2 and subsequently inhibit Cox-2 levels. Moreover, GG's antioxidant and renoprotective effects are closely tied, explains its ability to produce high levels of phenolics [23].

Homonoiar iparia: The methanol extract and its various fractions from the whole plant of HomonoiaripariaLour. (HR) displayed nephroprotective activity in vitro, against cisplatin induced damage using the HEK 293 cell line. The HR n-butanol and aqueous fractions displayed the highest activity at 200 g/mL concentration: 293.09% and 345.07%, respectively. The nephroprotective and antioxidant properties of the fractions can be attributed to their significant concentrations of polyphenolic substances [24].

Momordica tuberosa Hydroalcoholic extract of MomordicatuberosaCogn (MT) tuber (40 mg/kg, BW, p.o.) easily reduced renal damage caused by paracetamol, gentamicin, and cisplatin. The hydroalcoholic extract contains a notable quantity of triterpenes and saponins according to a phytochemical screening. Animals treated with MT hydroalcoholic extract show increased body weight, decreased levels of creatinine and urea; as well as improved nitric oxide scavenging. In addition, it protected tissues from both glutathione (GSH) depletion and from lipid peroxidation. MT has a paramount role due to its antioxidant properties in relation to the remedy for acute renal injury resulted from a variety of nephrotoxins [25].

Plectranthus amboinicus: Ethanol extracts of *Plectranthus amboinicus* Roxb. (PA) aerial parts protect rats against acetaminophen-induced toxicity. Seven days of doses of 250 and 500 mg/kg with the ethanol extracts have decreased serum urea, creatinine, malondialdehyde, superoxide dismutase, catalase and glutathione-S-transferase more than extract without treatment, while superoxide dismutase, catalase, and glutathione-S-transferase activity increased. The ethanol extract diminished the impact of toxin-induced depletion of GSH. Glomeruli, Bowman's capsule, and larger renal tubules preservation were seen in rats treated with ethanol extract of (PA), supporting studies that the phytochemicals present in the plant have antioxidant properties that influence nephroprotective activity [26].

Solanum xanthocarpum: Mice with gentamicin poisoning had nephroprotective effects by an alcoholic preparation of the fruit of SolanumxanthocarpumSchrad. &Wendl (SX). When given the extract at 200 and 400 mg/kg/BW there was a significant reduction in high urea and creatinine levels, and protection against a rise in kidney weight ratio. Also, SX was tested on kidney antioxidants and was found to protect against loss of SOD, CAT, and GSH activity. The control standard and the nephroprotection (400 mg/kg) are very similar. Histopathological examination showed that 200 mg/kg caused minimal degenerative and necrotic tubular changes but 400 mg/kg allowed for tubular epithelial cells to regenerate [27].

***Tribulus terrestris*:** Oxidative stress caused by mercury causes damage to the kidneys through the generation of free radicals. Tribulusterrestris L. (TT) has been shown to be a potent antioxidant and anti-inflamatory compound. TT hydroalcoholic extract at doses of 100, 200, and 300 mg/kg (BW) was found to elevate GSH, SOD, and GPx and decrease elevated BUN, serum creatinine, MDA, liver fatty acid-binding protein, and KIM-1. Moreover, administration of the highest dose of TT (300 mg/kg) was associated with nephoprotective properties. TT proptied significant protection against mercuric chloride-induced kidney damage due to TT's anti-inflammatory and antioxidant properties and ability to reduced mercury accumulation in the kidney [28].

***Vitex negundo*:** Ethanolic extracts of Vitexnegundo L. (VN) leaves protect rats against nephrotoxicity mediated by thioacetamide. Thioacetamide (0.03 percent w/v in drinking water) administration for twelve weeks, two independent doses of ethanolic extracts of VN (100 and 300 mg/kg), decreased blood urea, serum creatinine, and renal MDA levels while increasing CAT and SOD activity. VN extract at a higher dose (300 mg/kg) significantly reduced renal microscopic abnormalities and nearly

normalized the renal histological architecture. The VN extracts' nephroprotective effectiveness is dependent on radical scavenging activity and is most likely due to their higher flavonoids and alkaloids content [29].

Conclusion

Clearly, medicinal plants offer a basic form different from pharmaceutical products in the prevention of various diseases. Many medicinal plants and plant extracts have been shown to be remarkably nephroprotective in animal models. All of the few medicinal plants that we know of have flavanoids and this could be responsible for its nephroprotective action. Compared to plants obtained from pharmaceutical therapies, natural therapies of plant sources are probably safer. Both developing countries and more affluent nations have nephrological issues. The Indian traditional medical system uses many medicinal plants regarding renal problems. Many medicinal plants and their phytoconstituents have less side effects than chemical products and offer significant assistance in the improvement of nephrological problems. The article outlined some compelling evidence that herbal plants and their components have nephroprotective effects against different forms of nephrotoxic agents.

Conflicts of Interest

There are no conflicts of interest.

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