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SHORT REVIEW

Nephroprotective Plants in *Ayurveda*: A Comprehensive Review

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Abstract

Renal diseases, particularly nephrotoxicity, pose a significant threat to human health, often stemming from exposure to medications or toxins. Acute renal failure, resulting from factors such as heart failure, hypoxia, antibiotics, chemotherapy, and non-steroidal anti-inflammatory drugs, presents a critical health challenge with a high mortality rate. This review involves the potential of medicinal plants, known for their antioxidant properties, in preventing and treating kidney disorders. This article provides a thorough exploration of nephroprotective plants, including insights into their mechanism of action, active phytoconstituents, sources, and potential utilizations. The aim is to contribute to a comprehensive understanding of traditional medicinal practices and their relevance in addressing the complexities of kidney-related issues.

Keywords: *Ayurveda*, Chronic Kidney Disease, Herbal Medicine, Nephroprotective, Traditional Knowledge

Abbreviations: BUN: Blood urea nitrogen; CAT: Catalase; EC: Epicatechin; ECG: Epigallocatechin; EEMOS: Ethanolic extract of *Moringa oleifera* seed; EGCG: Epigallocatechin gallate; GPx: Glutathione peroxidase; GSH: Glutathione; GST: Glutathione-S-transferases; IL-6: Interleukin-6; Kim-1: Kidney injury molecule-1; LPO: Lipid peroxidation; MDA: Malondialdehyde; MRP: Multidrug resistance protein; Nrf_2: Nuclear factor erythroid 2- related factor 2; OCT2: Organic cation transporter; PAH: Para-aminohippurate; ROS: Reactive oxygen species; SOD: Superoxide dismutase; TBARS: Thiobarbituric acid reactive compunds TNF-α: Tumor necrosis factor - α; VEGF: Vascular endothelial growth factor

1. Introduction

Throughout their daily activities and occupations, individuals are frequently unprotected from a variety of effectively hazardous situations and pollutants. The kidney is one of the most vital organs in the body of an individual. The kidneys perform several vital functions, such as preserving the acid-base balance, getting rid of dangerous substances and poisons, managing blood pressure, secreting hormones, and regulating osmolality[1,2]. Any irregularities in renal function carry a significant public health risk that can result in life-threatening consequences[3] and a significant burden on society[4]. The rapid deterioration in kidney functionality is referred to as acute renal disease, and it is usually curable with timely and effective therapy. Serum creatinine and plasma urea nitrogen concentrations rise in this situation, and the rate of glomerular filtration decreases as well[5]. If treatment is delayed, it may worsen and cause irreparable damage that may eventually cause chronic kidney dysfunction and end-stage renal failure. Every year, acute renal illness causes around 1.7 million deaths[6]. According to the World Health Organization's 2018 report, renal illness was a contributing factor in 1.2 million fatalities in 2015, which is a roughly 32% increase from 2005. In 2010, 2.62 million individuals globally underwent kidney transplantation; by 2030, that number is expected to increase to 3.4 million[7].

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An estimated 5 to 10 million fatalities worldwide are attributed to neurological illnesses each year. Inorganic metals, non-steroidal anti-inflammatory medicines, organic solvents, antitumor drugs, aminoglycoside antibiotics, and some antibacterial agents all interfere with the proper functioning of the kidneys[8]. Kidney-related issues can be linked to insufficient oxygen and nutrient supply, resulting from inadequate oxygen and nutrient delivery to the kidneys. Deficits in oxygen and nutrients can be attributed to low oxygen and delivery of nutrients to the kidneys as well as increased energy requirements brought on by oxidative stress[9,10]. The use of medicinal herbal medicines to treat acute and chronic renal diseases is becoming more and more popular worldwide[11]. Plant-based chemicals and herbal remedies are becoming more and more popular as safe and efficient treatment choices in today's healthcare environment. Several scientific studies have demonstrated the effectiveness of chemicals derived from plants and herbal remedies in treating a range of kidney problems. This review's main goal is to summarize and clarify important facets of the Indian medical care system concerning medicinal herbs and their use in treating nephrological issues. Additionally, the research explores the pharmacological properties of plant extracts and the phyto ingredients that are frequently utilized to treat kidney-related issues. The goal of this thorough examination is to determine which medicinal plant combinations are best for use in upcoming studies. We focused exclusively on investigating possible nephroprotective plants in the context of the conventional Indian medical system in our review.

2. Nephroprotective Plants used as Traditional Medicine

We systematically assessed peer-reviewed literature to identify various medicinal plants native to Indian traditional medicine that have been documented for their protective properties on kidney health are discussed in the following section.

2.1 *Adhatoda zeylanica*

Adhatoda zeylanica, commonly known as Malabar nut, it is a perennial shrub that belongs to the Acanthaceae family. It is native to the Indian subcontinent and Southeast Asia. The plant is characterized by lance-shaped leaves and white or purple flowers. It is rich in various bioactive compounds, with alkaloids being the major constituents responsible for its pharmacological effects. Key alkaloids found in *A. zeylanica* include vasicine and vasicinone, among others. These alkaloids have been studied for their potential therapeutic properties, including anti-inflammatory and antioxidant properties via neutralizing Reactive Oxygen Species (ROS), protecting kidney cells from oxidative stress-induced damage[12,13]. It may also have vasodilatory effects that help to regulate renal blood flow, contributing to kidney protection. It exhibits nephroprotective effects, especially against gentamicin-induced renal damage possibly relying on the capacity for neutralizing gentamicin-induced free radicals[14]. In Wistar albino rats, the foliage of adhatoda has shown a strong protective effect against renal damage caused by gentamicin. Rats given gentamicin (80 mg/kg/day) had higher quantities of blood creatinine, urea, and protein, all of which are signs of early-stage renal disease. The principal explanation for its kidney-protective action against drug-induced toxicity in Wistar rats is its capacity to counteract free radicals generated by gentamicin[12].

2.2 *Aegle marmelos*

It is commonly known as Bael or Bael fruit and is a medical plant belonging to the Rutaceae family. The active constituents present include mamelon, umbelliferone, flavonoids, alkaloids such as skimmianine, and essential oils which show potential for antioxidant, and anti-inflammatory and influence renal blood flow which contributes to neuroprotective effects. The methanol-based extract of *Aegle marmelos* effectively decreases the impact of cisplatin-induced renal impairment in rats. Cisplatin can cause nephrotoxicity by reducing antioxidants and enzymes, leading to an elevated release of ROS radicals and lipid peroxidation. In rats, an ethyl acetate extract of *A. marmelos* demonstrated superior nephroprotection against cisplatin-induced toxicity compared to hydroalcoholic extract[15,16]. The treatment with acetate from ethyl acetate extract decreased creatinine in the serum and blood urea levels, reduced LPO levels, and enhanced SOD, GSH, and CAT[17]. It also decreases lipid peroxidation levels.

2.3 *Andrographis paniculata*

It is commonly known as King of Bitters or Kalmegh, and is a medicinal plant belonging to the Acanthaceae family. The primary bioactive constituents responsible for the nephroprotective actions are andrographolides and neoandrographolides. These diterpenoid lactones are known for their diverse pharmacological activities, including anti-inflammatory, antioxidant, and immunomodulatory properties. Free radicals may be produced as a result of gentamicin-induced nephrotoxicity, which suggests oxidative damage to the renal cortex's cells. Wistar albino rats treated with gentamicin show notable hepatoprotective benefits from the water-soluble extract of *Andrographis paniculata*. Its antioxidant and free radical neutralization qualities are thought to be responsible for its renoprotective qualities[18]. Furthermore, following cisplatin treatment, ethanolic extracts of *A. paniculata* leaves show a reduction in oxidative stress indicators, such as urine protein and blood creatinine levels. Rats given the extract before treatment exhibited less severe glomerular deterioration and the presence of inflammatory cells in their kidney tissue, suggesting that the extract inhibits the Kim-1 and Nrf_2 mechanisms in cisplatin-induced kidney damage[19].

2.4 *Allium sativum*

It is commonly known as garlic and is a bulbous plant belonging to the family Alliaceae. It is widely cultivated and has been used for culinary and medicinal purposes across various cultures for centuries. Allicin is one of the primary bioactive compounds in garlic responsible for its medicinal properties. Other sulfur-containing chemicals, including diallyl sulfide, diallyl disulfide, and diallyl trisulfide, are responsible for garlic's medicinal properties. These compounds are released when garlic is crushed or chopped. Diabetes caused by streptozotocin in rats, garlic extract has protective benefits against diabetes-induced nephropathy. After receiving 500 mg/kg body weight of garlic extract, diabetic rats exhibit notable changes in their urine and serum biochemistry. Histological improvements include reduced basement membrane hypertrophy and mesangial enlargement. In diabetic rats, supplementing with garlic also significantly lowers the expression of VEGF and ERK-1, which helps to prevent mesangial growth and glomerulosclerosis[20]. Additionally, rats treated with a water-soluble extract of garlic show protection against kidney damage caused by gentamicin. Garlic treatment reverses oxidative stress and lessens gentamicin-induced histological alterations in kidney tissue homogenates by reducing the production of inflammatory markers such as TNF-α, IL-6, and INF-γ[21].

2.5 *Aerva lanata*

It is commonly known as Mountain Knotgrass or Kapok Bush and is a medicinal plant belonging to the family Amaranthaceae. It is indigenous to various regions of Asia, Africa, and Australia, where it grows as a perennial herb. The bioactive constituents responsible for the nephroprotective actions include flavonoids (e.g., quercetin, kaempferol), tannins, phenolic acids, saponins, and alkaloids. These compounds have a wide range of pharmacological activities, including anti-inflammatory, antioxidant, and diuretic characteristics. Nephroprotective efficacy was established by an extract from ethanol of the entire plant that is used in acute renal injury caused by cisplatin and gentamicin. When the extract was given in the curative regime at 75, 150, and 300 mg/kg, both serum creatinine and blood urea levels decreased in a dose-dependent manner, and the histological alterations returned to normal. In the gentamicin experiment, rats given 300 mg/kg of the ethanol extract also showed encouraging results. Significant nephroprotective efficacy and low toxicity are displayed by its ethanol extract, which may help to mitigate the effects of renal hazardous material such as gentamicin and cisplatin on acute renal damage[22]. Renal function impairment is the main purpose of *Sirupeelai Kudineer*, a decoction of the complete *Aerva lanata* plant, in the Siddha medical system. Blood urea and serum creatinine levels significantly decreased after ten days of therapy with its dosage of 500 mg/kg/body weight in a rat model of gentamicin-induced nephrotoxicity. Renal cell healing is attributed to its strong antioxidant capabilities, as shown by histopathological investigation of the kidneys[23]. The methanol-based extract of *A. lanata* flowers showed very significant kidney-protective properties (97.04%) at 20 µg/mL doses in an *in vitro* investigation employing HEK 293 cell lines exposed to cisplatin, which is equivalent to the common nephroprotective medication quercetin

(8 µg/mL)[24]. Reduced OCT_2 expression, elevated MRP, decreased apoptosis, and reduced inflammation are linked to the nephroprotective actions of flavonoids in *A. lanata*[25].

2.6 *Azima tetracantha*

It is commonly known as Linga mooli or Thoothuvalai is a medicinal plant belonging to the Salvadoraceae family. The primary constituents available are flavonoids (quercetin), alkaloids (azimine), saponins, phenolic compounds, and terpenoids, and show potential for various pharmacological activities including antioxidant, anti-inflammatory, and diuretic effects. An ethanolic extract from *Azima tetracantha* roots showed improved protection against glycerol-induced kidney injury in Wistar albino mice. The ethanolic extracts demonstrated strong antioxidant qualities *in vivo* and *in vitro*, with a dose-associated increase in antioxidant levels. This defense mechanism was essential in preventing glycerol-induced oxidative damage to the renal parenchyma. The vasodilation activity of tannins and terpenoids can improve the production of urine and the rate of glomerular filtration by opening the renal artery[26]. *A. tetracantha* root extract was reported to protect the kidneys of Wistar rats against adenine damage. The ethanolic root extract was provided at a dosage of 250 mg/kg body weight, which improved the intake of food, aggregate protein, albumin, and the production of urine. The medication also significantly reduced the dimensions and quantity of kidney oxalate crystals, as well as plasma creatinine and blood nitrogen in the form of urea levels. Its leaf powder improves antioxidant activity decreases lipid oxidation, and preserves cellular membranes, all of which have an ameliorating impact against the effects of ferrous sulfate[27].

2.7 *Boerhavia diffusa*

It is also known as *Punarnava* or Red Spiderling is a medicinal plant belonging to the family Nyctaginaceae. It is native to India and other parts of Asia, as well as Africa and the Americas. The bioactive constituents responsible for the nephroprotective action include flavonoids (quercetin, kaempferol), alkaloids (punarnavine), saponins, phenolic compounds, and terpenoids. These chemicals have a variety of therapeutic actions, comprising diuretic medication, antioxidant, and anti-inflammatory properties. Aqueous root extract of *Boerhavia diffusa* has been shown to protect rats from nephrotoxicity caused by gentamicin. Weight increase, lower serum creatinine, and blood urea nitrogen (BUN) levels, and near-normal levels of reduced glutathione (GSH) and malondialdehyde (MDA) were seen after daily dosages of 200 and 400 mg/kg of its root extract. Treatment with Boerhavia prevents acute tubular necrosis caused by gentamicin, even at lower dosages. Improved renal blood flow is shown by the enhanced clearance of para-aminohippurate (PAH), especially in the groups who received both doses of *B. diffusa*[28]. In rats, methotrexate-induced nephrotoxicity has been demonstrated to be reduced by a standardized polyherbal combination that includes *B. diffusa* together with three other potential ayurvedic herbs (*R. emodi, N. nucifera,* and *C. nurvala*). In combination significantly repaired oxidative markers, such as the oxidation of lipids[29], and decreased TNF-alpha levels, as compared to the intoxicated group. The synergistic effects of the controlled polyherbal mixture are effective for its nephroprotective characteristics. Acetyl-para-amino benzoquinoneimine, an exceptionally reactive acetaminophen metabolite that arylates proteins in the proximal tubule, causes nephrotoxicity. In rats, its root aqueous extract showed promise in treating acetaminophen-induced nephrotoxicity. The kidneys' glutathione reserves were restored, MDA levels were lowered, and antioxidant defense enzymes (CAT and SOD) were increased by the extract therapy. Its high concentration of secondary metabolites is considered to be attributed to its antioxidant properties and nephroprotective characteristics[30]. Additionally, it shows preventative treatment and effectiveness in shielding the kidneys from the adverse consequences of cisplatin. At a higher dosage of 200 mg/kg, it preserved kidney function from cisplatin-induced damage by reducing antioxidant enzymes (SOD, GSH), lowering MDA levels, and decreasing pro-inflammatory cytokines (IL-1beta, IL-6), as well as apoptotic indicators (caspase-3)[31].

2.8 *Camellia sinensis*

It is also known as the tea plant and is the biological source of various types of tea, constitute green tea, black tea, white tea, and oolong tea. It belongs to the family Theaceae. The primary chemical constituents

responsible for the nephroprotective actions of *Camellia sinensis*, particularly in green tea, include catechins such as epicatechin (EC), epicatechin gallate (ECG), epigallocatechin (EGC), and epigallocatechin gallate (EGCG). Its antioxidant, anti-inflammatory, and potential blood pressure-regulating properties, attributed to catechins, may contribute to kidney health. It has been demonstrated that green tea extracts lower nonenzymatic kidney indicators like creatinine and urea. The catechins in green tea help scavenge free radicals created by ROS, and vitamins C and E also contribute to this nephroprotective action. Green tea extract's antioxidant properties are primarily responsible for its nephroprotective advantages[32]. Green tea extract has shown protective properties against kidney damage caused by smoking along with gentamicin-induced nephrotoxicity. Green tea extract pretreatment was associated with lower serum and renal malondialdehyde (MDA), as well as decreased levels of urea, creatinine, and uric acid. Notably, this pretreatment increased the level of activity of antioxidant-producing enzymes including SOD, CAT, and GPx, and markedly increased the amounts of vitamin E and C in blood and kidney tissue. These doses of green tea showed strong nephroprotection as demonstrated by a marked reduction in oxidative stress[33]. Additionally, its nephroprotective function has lessened the effects of lead acetate-induced kidney injury, which is defined by changes in renal parameters. Reduced oxidation of lipids in tissues and a rise in antioxidant activity are caused by its prevention of radical generation and decrease in oxidative stress[34].

2.9 *Clitoria ternatea*

It is also known as the Butterfly pea or blue pea flower and is a flowering plant belonging to the family Fabaceae. It is native to Southeast Asia but is also found in other tropical regions. The plant is known for its striking blue flowers and has been used traditionally in *Ayurveda* and other traditional medicine systems. The bioactive constituents are anthocyanins, flavonols, alkaloids, terpenoids, and phenolic compounds. Anthocyanins are remarkable for their antioxidant abilities and bright blue pigmentation. Excessive consumption of acetaminophen, despite its analgesic and antipyretic properties, the liver and kidneys to suffer from adverse effects. Acetaminophen is hazardous because it is converted by the enzymes in CYP creating an intensely reactive quinoline imine referred to as N-acetyl-p-benzoquinone imine. In rats, ethanolic extracts of *Clitoria ternatea* have demonstrated nephroprotective effects against acetaminophen-induced toxicity. Moreover, histological investigation revealed the recovery of renal tissue from acetaminophen-induced necrosis. Its hepatoprotective properties are most likely due to the antioxidant activity of its phytoconstituents[35].

2.10 *Cassia auriculata*

It is also known as Tanner's Cassia or *Avaram Senna* and is a flowering plant belonging to the family Fabaceae. It is native to India and is commonly found in tropical regions of Asia. Traditionally, several plant components, including leaves, flowers, and seeds, are used for their medicinal properties. The bioactive constituents responsible for the nephroprotective actions include flavonoids (kaempferol, quercetin), phenolic acids (gallic acid, ellagic acid), tannins, saponins, and alkaloids[36]. The study evaluated the preventive effect of alcoholic extract from the roots of *Cassia auriculata* on rats that were suffering from chronic renal damage caused by cisplatin and gentamicin. With its nitric oxide-scavenging and antioxidant qualities, the ethanolic root extract shows promise as a nephroprotective agent against kidney damage caused by gentamicin and cisplatin. Hydroalcoholic extracts from its aerial parts are shown to have adverse impacts on the development of diabetic nephropathy[37].

2.11 *Commiphora mukul*

It is commonly known as guggul or Indian bdellium, and is a smaller tree or shrub indigenous to India, Bangladesh, and Pakistan. It belongs to the family Burseraceae. The main active ingredients present in *Commiphora mukul* include guggulsterone (E and Z isomers), flavonoids, terpenoids, lignans, and steroids. Guggulsterones are responsible for their anti-inflammatory and antioxidant properties. Guggulsterones prevent the synthesis of proinflammatory cytokines and enzymes, thereby reducing inflammation in the kidneys. By attenuating inflammation, it helps in preserving renal function and preventing further damage. Chronic kidney injury often leads to the deposition of extracellular matrix proteins and the development of renal fibrosis, which impairs kidney function. It may have anti-fibrotic

properties by suppressing fibroblast activation and the production of collagen and other enlargement proteins. The potentially hazardous group of rats received 25 mg/kg guggulsterone for eight days, resulting in reduced creatinine and urea levels. Moreover, there was a decline in the kidney index, a considerable rise in the catalase enzyme's antioxidant capacity, and an elevation in NF-kB levels at the renal level. Histopathological examination revealed a small region of apoptosis and deterioration in the kidney's proximal tubules[38].

2.12 *Cichorium intybus*

It is commonly known as chicory and is a perennial herbaceous plant belonging to the Asteraceae family. Chicory contains bioactive constituents such as flavonoids such as quercetin and kaempferol, phenolic compounds and sesquiterpene lactones such as lactucin and lactucopicrin also show anti-inflammatory properties. Water soluble and methanolic seed extracts of Chicory have shown preventive properties against nephrotoxicity produced by gentamicin in rats. Elevated blood creatinine and urea levels are indicative of renal impairment caused by gentamicin. In rats with renal illness, supplementation of chicory seed extracts at a dose of 500 mg/kg body weight per day possibly reduced the elevated creatinine and blood urea levels. Similarly, compared to the methanolic extract, administration with the aqueous extract of this offered better protection[39]. Chicory roots are given in Unani medicine to increase urine flow, shield the kidneys from toxins, and improve the kidneys. Renal structural abnormalities were rectified and blood concentrations of urea and creatinine were recovered by both methanolic and aqueous preparations of its roots. These extracts may have a nephroprotective impact because of the presence of a high number of flavonoids, which are renowned for their antioxidant qualities[40]. The polyherbal extract was administered, and the results showed improvements in proximal reabsorptive markers, glomerular function, and glucose management. Furthermore, it resulted in the restoration of elevated pro-inflammatory cytokine concentrations and an altered redox state, indicating that the polyherbal extract's anti-inflammatory and antioxidant qualities are responsible for the nephroprotective action[41]. Cichoric acid is abundant in the aerial portion of *Cichorium intybus*. Serum creatinine, urine creatinine, and urine urea were all reduced after taking a tincture of chicory in a reversal concentration-dependent way. The lower overall oxidative damage, oxidative stress index, total nitrite, and nitrate levels in the pretreatment animal group indicated that the chicory tincture reduced oxidative stress. The inclusion of polyphenols, which may have oxidative and pro-inflammatory properties even in small amounts, has been suggested as a component of the nephroprotective benefits[42].

2.13 *Cucumis sativus*

It is also known as cucumber and is a widely cultivated plant species belonging to the family Cucurbitaceae. It is native to South Asia but is now cultivated globally for its edible fruits. Cucumber has been used traditionally in various cultures for its culinary and medicinal properties. Bioactive constituents present in *Cucumis sativus* are quercetin, kaempferol, cucurbitacins, particularly cucurbitacin E shows potential for antioxidant and anti-inflammatory properties. When given as a hydroalcoholic seed extract, which is frequently used in Indian cooking, has protective benefits against nephrotoxicity produced by gentamicin and cisplatin in a rat model. Two different doses of the extract of hydro alcohol were demonstrated to reduce excessive quantities of blood urea nitrogen, total urine protein, total serum protein, serum creatinine, and lipid peroxidation in rats suffering toxicity caused by cisplatin and gentamicin. Moreover, the hydroalcoholic extract raised the levels of catalase, glutathione (GSH), superoxide dismutase, and creatinine clearance in rats. These results were confirmed by histological investigations, which showed that its seeds are effective in alleviating drug-induced nephrotoxicity. The physiologically active components in cucumber juice have the ability to chelate lead, avoiding lead accumulation in body tissues. This effect might be is due to ionic interactions produced with the chelation process of sulfur-containing molecules in cucumber juice with lead nitrate[43].

2.14 *Crataeva nurvala*

It also known as Varuna or three-leaved caper, is a medicinal plant native to India and other parts of Southeast Asia. It belongs to the Capparaceae family. Traditionally, various components of the plant, such

as the outer layer of bark, branches, and roots, were utilized for medicinal purposes. They contain bioactive components such as lupeol, flavonoids, tannins, terpenoids and exhibit diuretic, anti-inflammatory, and antioxidant properties. The alcoholic extracts offer protection against cisplatin-induced nephrotoxicity, a condition linked to oxidative stress and free radical generation caused by drugs. The ability to eliminate free radicals and exhibit antioxidant activity is responsible for its nephroprotective action[44]. In numerous research studies, the triterpenoid lupeol extracted from its stem bark exhibited benefits against nephrotoxicity produced by cisplatin in mice. When lupeol was given to animals who were suffering toxicity, it was found to be helpful in reducing blood creatinine and urea levels at two distinct dosages. Treatment with lupeol reduced the concentrations of TBARS (thiobarbituric acid reactive compounds) and increased glutathione and the activity of catalase in the renal cortex. Lupeol's capacity to eliminate free radicals and possess antioxidant qualities is associated with its nephroprotective mechanism[45].

2.15 *Curcuma longa*

It is commonly known as turmeric and is a perennial herbaceous plant belonging to the ginger family, Zingiberaceae. It is native to Southeast Asia and is cultivated for its rhizomes, which are used both as a spice and in traditional medicine. The bioactive constituents responsible for the nephroprotective actions are curcumin, turmerones, and curcuminoids. Administering aqueous extracts of turmeric and Matricaria chamomile orally provides defense against tetracycline-induced nephrotoxicity. Urinary creatinine and urea levels can rise as a result of damage to the renal tubules and early-onset renal impairment caused by tetracycline poisoning. Blood urea, creatinine, salt, and potassium levels were suggestively lower in the group treated with aqueous extracts, but total protein levels were higher. A histopathological examination showed thin interstitial septa, minor collagen depositions, decreased renal tubular thickness, and a reduction in cellular infiltrates. It has been proposed that it functions as an antioxidant or a reactive oxygen species quencher to protect the kidneys[46]. The usage of essential oils of ginger, as well as turmeric (50 mg/kg BW), avoided a rise in urea, creatinine, and BUN levels in the setting of cadmium poisoning, which involves many processes such as cell death, inflammation, and oxidative stress, in comparison to the control group[47]. When combined with the non-selective beta-blocker carvedilol, it showed anti nephrotoxic effects in the setting of cisplatin-induced renal damage. This combination, probably as a result of its antioxidant qualities and ability to scavenge free radicals, together with the aqueous and methanolic extracts, decreased abnormalities and mortality caused by cisplatin. Carvedilol metabolites include flavonoids, alkaloid molecules, saponin glycosides, and a carbazole group are examples of secondary metabolites found in curcumin that contribute to its antioxidant activity[48]. Curcumin enhanced renal function, decreased oxidative stress, inflammation, and tubular cell death, and prevented renal tubular cell apoptosis caused by cisplatin. The protective mechanisms include lower cisplatin accumulation by modification of OCT-2 and CTR-1 transporters, decreased apoptosis-related proteins (Fas, Fas-L, p53), and suppression of NF-Kβ and pro-inflammatory cytokines. Additionally, curcumin reduced the elevation of Bax/Bcl-2, inhibited ERK1/2 phosphorylation, and inhibited NF-kβ expression. These activities lowered the invasion of inflammatory cells and renal necrosis[49].

2.16 *Eclipta alba*

It is also known as False Daisy or Bhringraj is a medicinal plant belonging to the Asteraceae family. The bioactive constituents responsible for the nephroprotective actions are wedelolactone, and flavonoids such as apigenin, luteolin, and alkaloids. Leaf extract, which has been demonstrated to have antioxidant characteristics, shields rats against gentamicin-induced nephrotoxicity[50]. Bhringraj has a high concentration of flavonoids, particularly wedelolactone, and it has powerful antioxidant effects. The extract may have renal protective advantages against gentamicin toxicity because of its ability to remove free radicals and reduce iron (III) levels. The nephroprotective benefits shown are probably due in part to the polyphenolic chemicals found in bhringraj, which are recognized for their capacity to scavenge free radicals[51].

2.17 *Moringa oleifera*

The drumstick tree, sometimes known as the tree that produces horseradish, is a tree that grows rapidly

and is resistant to drought endemic to the Indian subcontinent. It belongs to the family Moringaceae and is cultivated in various tropical and subtropical regions worldwide. Moringa is valued for its nutritional and medicinal properties, with various components of the plant, especially the seeds, leaves, and roots, utilized for their medicinal properties. Moringa leaves are rich in vitamins C and E, quercetin, kaempferol, and rutin contributing to its antioxidant and anti-inflammatory effects and benzyl isothiocyanate found in seeds. The seeds of *M. oleifera* contain a concentrated extract of ethanol (EEMOS) containing numerous essential fatty acids, especially oleic and linoleic. The nephrotoxic effects of gentamicin are closely linked to oxidative stress, which is caused by an overabundance of ROS production. The antioxidant characteristics of oleic and linoleic acids have a major role in the lowering of plasma creatinine and urea levels. Following EEMOS treatment, there is a considerable improvement in creatinine clearance, indicating an increased rate of glomerular filtration due to improved blood circulation in the kidneys and function. The anti-inflammatory impact of EEMOS counteracts inflammation and renal edema, resulting in a significant reduction in comparative kidney weight as contrasted with kidneys treated with toxins. The electrolyte imbalances caused by gentamicin were counteracted by the impact of EEMOS on membrane stability[52].

The prior medication with ethanol-water (80:20) extracts of its leaves protects rabbit kidneys against toxicity. The nephroprotective activity of leaves is thought to be due to their capacity to reduce reactive chemicals such as thiobarbituric acid, restore decreased glutathione contents in rabbit cells of the kidney, and lower increased levels of blood urea as well as creatinine levels are dosage dependant. Histopathological analysis demonstrates enhanced renal kidney function after therapy; this improvement may be related to rapid tubular cell regeneration[52]. After receiving a 400 mg/kg methanol extract of its leaves, female rats exhibit substantial reductions in body weight, blood urea nitrogen, and creatinine values after four weeks. While the methanol extract does not appear to be dangerous for the kidneys, prolonged use may be detrimental to the liver. The moringa ethanolic extract of the leaf has a significant antioxidant effect, which raises blood levels of albumin, globulin, and total protein. This extract also lowers malondialdehyde levels while raising those of TNF-α, IL-6, glutathione peroxidase, catalase, and superoxide dismutase in male Wistar rats with diabetes caused by streptozotocin[53]. Ethanolic leaf extract and magnesium nanoparticles made from its leaves mitigate melamine-induced kidney failure in rat kidneys via reducing oxidative stresses, apoptosis, and renal function impairments. When it is administered at two different doses, serum blood urea nitrogen, and creatinine concentrations are lowered while GPx and GST activity are increased. According to histological investigations, this treatment lowers nitric oxide and hydrogen peroxide levels in the kidneys and significantly minimizes renal tissue damage.

2.18 *Solanum xanthocarpum*

It is also known as yellow-berried nightshade or Kantakari is a medicinal plant belonging to the Solanaceae family. The bioactive constituents responsible for the nephroprotective actions are solasonine, solamargine, solasodine, and various alkaloids and flavonoids. These compounds contribute to the plant's pharmacological activities, including its anti-inflammatory and antioxidant effects. The boiled roots have traditionally been utilized as an antipyretic, diuretic, and expectorant. Seeds are effective as expectorants and asthma treatments. Respiratory problems, thymitis, gastrointestinal diseases, hemorrhoids, and dysuria can all be treated with entire plants and fruits. An in-vivo investigation on gentamicin-induced mice demonstrated a nephroprotective effect. Extracts of this are protected towards elevated renal weight ratio. At 400 mg/kg, it effectively protects renal organs and increases urine production. Additionally, Urine and plasma levels of urea and creatinine decreased significantly. The study found that *Solanum xanthocarpum* can prevent reduced activity of SOD, CAT, and GSH in renal antioxidants[54].

2.19 *Zingiber officinale*

It is commonly known as ginger, is a flowering plant and rhizome belongs to the family Zingiberaceae. It is native to Southeast Asia but is now cultivated in many tropical and subtropical regions worldwide. Ginger is well-known for its culinary uses as a spice and its medicinal properties in traditional medicine systems. It contains bioactive compounds such as zingerone,

gingerol, shogaol, and paradol efficient for antioxidant and anti-inflammatory compounds. Ginger may exert vasodilatory effects on renal blood vessels, leading to improved renal blood flow and oxygen delivery to the kidneys. This vasodilation supports kidney function and may aid in the repair of damaged renal tissues. In rat models, gingerone showed protective effects against cisplatin-induced nephrotoxicity. Combining zingerone with cisplatin treatment effectively reduced tissue malondialdehyde levels, blood urea nitrogen, serum creatinine concentrations, and the activity of the enzyme lactate dehydrogenase. Furthermore, it maintained the activity of catalase-related enzymes and glutathione peroxidase, unlike the group associated with toxins. Gingerone inhibited tumor necrosis factor and halted the reduction of glutathione concentrations in kidney tissue to minimize the inflammatory reactions caused by cisplatin. Additionally, zygote stimulation increased glomerular diameters and red blood cell movements[54]. A ginger extract supplemented with 6-gingerols protected rats against the hematotoxicity and hepatotoxicity caused by carbendazim. Concurrently receiving the 6-gingerol-rich fraction, rats' livers and kidneys demonstrated an enhanced antioxidant state, decreased damage from oxidative stress, and avoided hepatotoxicity from cabendazim[55].

3. Conclusion

Natural medications made from therapeutic plants are thought to be safer than medications made from other sources. Problems related to the kidneys are common in both industrialized and underdeveloped nations. Many medicinal plants are used to treat nephrological issues in the ancient Indian medical system. This research suggests that, in comparison to manufactured medications, a variety of medicinal herbs and their natural constituents significantly contribute to the relief of nephrological issues with fewer adverse effects. In particular, for human usage, these plants must be carefully examined to guarantee their safety and effectiveness. As a result, for nephrological issues, these medicinal herbs may be suggested either on their own or in conjunction with currently prescribed pharmaceuticals. It is possible to create combinations of contemporary drugs and botanicals through synergistic research. One of the most notable roles that medicinal plants have in nephroprotection is antioxidant activity, and the active ingredients in these plants are crucial to their nephroprotective qualities. New treatments for kidney illness might be greatly aided by network pharmacological techniques and in silico study of absorption, distribution, metabolism, and excretion, as well as mode of action and safety. Experimental research helps improve formulations and forms the basis for upcoming clinical trials. As a result, many patients with nephrological difficulties may benefit from the use of medicinal plants from the ancient Indian medical system and their active ingredients.

4. References

1. Al-Snafi AE, Talab TA. A review of medicinal plants with nephroprotective effects. GSC Biol Pharm Sci. 2019; 8(1):114-22. https://doi.org/10.30574/gscbps.2019.8.1.0108
2. Molaei E, Molaei A, Abedi F, Hayes AW, Karimi G. Nephroprotective activity of natural products against chemical toxicants: The role of Nrf2/ARE signaling pathway. Food Sci Nutr. 2021; 9(6):3362-84. https://doi.org/10.1002/fsn3.2320
3. Dhondup T, Qian Q. Acid-base and electrolyte disorders in patients with and without chronic kidney disease: an update. Kidney Diseases. 2017; 3(4):136-48. https://doi.org/10.1159/000479968
4. Basist P, Parveen B, Zahiruddin S, Gautam G, Parveen R, Khan MA, *et al*. Potential nephroprotective phytochemicals: Mechanism and future prospects. J Ethnopharmacol. 2022; 283:114743. https://doi.org/10.1016/j.jep.2021.114743
5. Konda VR, Arunachalam R, Eerike M, Radhakrishnan AK, Raghuraman LP, Meti V, *et al*. Nephroprotective effect of ethanolic extract of *Azima tetracantha* root in glycerol induced acute renal failure in Wistar albino rats. J Tradit Complement Med. 2016; 6(4):347-54. https://doi.org/10.1016/j.jtcme.2015.05.001
6. Yang C, Yang B. Acute kidney injury in China: A neglected truth and perspective. Asian J Urol. 2016; 3(1):4. https://doi.org/10.1016/j.ajur.2015.11.001
7. Luyckx VA, Tonelli M, Stanifer JW. The global burden of kidney disease and the sustainable development goals. Bull World Health Organ. 2018; 96(6):414. https://doi.org/10.2471/BLT.17.206441
8. Negi K, Mirza A. Nephroprotective and therapeutic potential of traditional medicinal plants in renal diseases. J Drug Res Ayurvedic Sciences. 2020; 5(3):177-85. https://doi.org/10.5005/jdras-10059-0079
9. Makris K, Spanou L. Acute kidney injury: definition, pathophysiology, and clinical phenotypes. Clin Biochem Rev. 2016; 37(2):85.

10. Sujana D, Saptarini NM, Sumiwi SA, Levita J. Nephroprotective activity of medicinal plants: A review on *in silico*-, *in vitro*-, and *in vivo*-based studies. J Appl Pharm Sci. 2021; 11(10):113-27. https://doi.org/10.7324/JAPS.2021.1101016
11. Srinivasan N, Dhanalakshmi S, Pandian P. Encouraging leads from marine sources for cancer therapy a review approach. Pharmacogn J. 2020; 12(6). https://doi.org/10.5530/pj.2020.12.202
12. Kumar A, D'Souza P, Bhargavan D. Evaluation of renal protective activity of *Adhatoda zeylanica* (medic) leaves extract in Wistar rats. JHAS NU. 2013; 3(04):045-56. https://doi.org/10.1055/s-0040-1703701
13. D'souza PS, Holla R, Swamy G. Effect of *Adhatoda zeylanica* ethanolic extract on attenuated kidney in streptozotocin-induced diabetic rats. J Health Allied Sci NU. 2021; 11(02):073-9. https://doi.org/10.1055/s-0040-1722801
14. Mossoba ME, Flynn TJ, Vohra SN, Wiesenfeld PL, Sprando RL. *In vitro* exposure of *Adhatoda zeylanica* to human renal cells lacks acute toxicity. Toxicol. 2016; 3:15-20. https://doi.org/10.1016/j.toxrep.2015.11.005
15. Ojha S, Venkataraman B, Kurdi A, Mahgoub E, Sadek B, Rajesh M. Plant-derived agents for counteracting cisplatin-induced nephrotoxicity. Oxid Med Cell Longev. 2016; 1-27. https://doi.org/10.1155/2016/4320374
16. Ahmad R, Mujeeb M, Ahmad A, Anwar F. Ameliorative effect of *Aegle marmelos* leaves extract against cisplatin-induced nephrotoxicity and oxidative stress. Bangladesh J Pharmacol. 2016; 11(1):101-09. https://doi.org/10.3329/bjp.v11i1.24004
17. Dwivedi J, Singh M, Sharma S, Sharma S. Antioxidant and nephroprotective potential of *Aegle marmelos* leaves extract. J Herbs, Spices, and Med Plants. 2017; 23(4):363-77. https://doi.org/10.1080/10496475.2017.1345029
18. Singh P, Srivastava MM, Khemani LD. Renoprotective effects of *Andrographis paniculata* (Burm. f.) Nees in rats. Upsala J Med Sci. 2009; 114(3):136-9. https://doi.org/10.1080/03009730903174321
19. Adeoye BO, Oyagbemi AA, Asenuga ER, Omobowale TO, Adedapo AA. The ethanol leaf extract of *Andrographis paniculata* blunts acute renal failure in cisplatin-induced injury in rats through inhibition of Kim-1 and upregulation of the Nrf2 pathway. J Basic Clin Physiol Pharmacol. 2018; 30(2):205-17. https://doi.org/10.1515/jbcpp-2017-0120
20. Shiju TM, Rajkumar R, Rajesh NG, Viswanathan P. Aqueous extract of *Allium sativum* L bulbs offer nephroprotection by attenuating vascular endothelial growth factor and extracellular signal-regulated kinase-1 expression in diabetic rats. 2013.
21. Galal HM, Abd el-Rady NM. Aqueous garlic extract suppresses experimental gentamicin-induced renal pathophysiology mediated by oxidative stress, inflammation, and Kim-1. Pathophysiology. 2019; 26(3-4):271-9. https://doi.org/10.1016/j.pathophys.2019.07.002
22. Shirwaikar A, Issac D, Malini S. Effect of *Aerva lanata* on cisplatin and gentamicin models of acute renal failure. J Ethnopharmacol. 2004; 90(1):81-6. https://doi.org/10.1016/j.jep.2003.09.033
23. Lekha GS. Evaluation of the nephroprotective activity of sirupeelai kudineer (*Aerva lanata* decoction) in rats. J Chem Pharm Res. 2015; 7(10):522-30.
24. Narayanan M, Krishnan L, Natarajan D, Kandasamy S, El Askary A, Elfasakhany A, *et al*. Evaluation of antibacterial, antioxidant, and nephroprotective proficiency of methanol extract of *Aerva lanata*. Process Biochem. 2021; 109:98-103. https://doi.org/10.1016/j.procbio.2021.07.004
25. Ma X, Yan L, Zhu Q, Shao F. Puerarin attenuates cisplatin-induced rat nephrotoxicity: The involvement of TLR4/NF-κB signaling pathway. PLoS One. 2017; 12(2):e0171612. https://doi.org/10.1371/journal.pone.0171612
26. Arunachalam R, Konda VGR, Eerike M, Radhakrishnan AK, Devi S. Nephroprotective effects of ethanolic root extract of *Azima tetracantha* lam in adenine-induced chronic kidney failure in Wistar rats. Indian J Pharmacol. 2021; 53(3):198. https://doi.org/10.4103/ijp.IJP_552_19
27. Manikandaselvi S, Ramya D, Ravikumar R, Thinagarbabu R. Evaluation of antinephrotoxic potential of *Azima tetracantha* Lam. and *Tribulus terrestris* Linn. Int J Pharm Pharm Sci. 2012; 4:566-8.
28. Sawardekar SB, Patel TC. Evaluation of the effect of *Boerhavia diffusa* on gentamicin-induced nephrotoxicity in rats. J Ayurveda Integr Med. 2015; 6(2):95. https://doi.org/10.4103/0975-9476.146545
29. Sharma S, Baboota S, Amin S, Mir SR. Ameliorative effect of a standardized polyherbal combination in methotrexate-induced nephrotoxicity in the rat. Pharm Biol. 2020; 58(1):184-99. https://doi.org/10.1080/13880209.2020.1717549
30. Pareta SK, Patra KC, Harwansh R, Kumar M, Meena KP. Protective effects of *Boerhaavia diffusa* against acetaminophen-induced nephrotoxicity in rats. Pharmacologyonline. 2011; 2:698-706.
31. Karwasra R, Kalra P, Nag TC, Gupta YK, Singh S, Panwar A. Safety assessment and attenuation of cisplatin-induced nephrotoxicity by tuberous roots of *Boerhaavia diffusa*. Regul Toxicol Pharmacol. 2016; 81:341-52. https://doi.org/10.1016/j.yrtph.2016.09.020
32. Ibrahim A, Noman Albadani R. Evaluation of the potential nephroprotective and antimicrobial effect of Camellia sinensis leaves versus Hibiscus sabdariffa (*in vivo* and *in vitro* studies). Adv Pharmacol Pharm Sci. 2014; 2014. https://doi.org/10.1155/2014/389834
33. Ben Saad A, Ncib S, Rjeibi I, Saidi I, Zouari N. Nephroprotective and antioxidant effect of green tea

(*Camellia sinensis*) against nicotine-induced nephrotoxicity in rats and characterization of its bioactive compounds by HPLC–DAD. Appl Physiol Nutr Metab. 2019; 44(11):1134-40. https://doi.org/10.1139/apnm-2017-0834

34. Ramya S, Prasanna G. Nephroprotective effect of *Camellia sinensis* L. on lead acetate induced male albino rats. Int J Pharmtech Res. 2013; 5(2):511-15.
35. Sarumathy K, Rajan MSD, Vijay T, Jayakanthi J. Evaluation of phytoconstituents, nephroprotective and antioxidant activities of *Clitoria ternatea*. J Appl Pharm Sci. 2011; 164-72.
36. Annie S, Rajagopal PL, Malini S. Effect of *Cassia auriculata* Linn. root extract on cisplatin and gentamicin-induced renal injury. Phytomedicine. 2005; 12(8):555-60. https://doi.org/10.1016/j.phymed.2003.11.010
37. Bandawane DD, Mhetre NK. Study of Antihyperglycemic, Antihyperlipidemic, and Nephroprotective Activity of *Cassia auriculata* L. Extract in Streptozotocin-Induced Diabetic Rats. Dnyanamay. 2015; 43-9.
38. Al-joda AM, Zalzala MH. Inhibition of NF-kB Pathway by Gggulsterone in the Protective Effects of Cyclophosphamide-Induced Renal Toxicity. Iraqi J Pharm Sci. 2019; 28(2):180-5. https://doi.org/10.31351/vol28iss2pp180-185
39. Tahir M, Sadiq N, Ahmed S, Ali A, Rajpoot NN, Riaz U. Effects of aqueous and methanolic extracts of *Cichorium intybus* seeds on gentamicin induced nephrotoxicity in rats. J Islam (JIIMC). 2018; 13(4):184-8.
40. Zaman R, Alam A, Jafri MA, Sofi G, Ahmad G. Nephroprotective effect of Beekh Kasni (Roots of *Cichorium intybus*) in the form of methanolic and aqueous extract in Gentamycin induced rat models. J Pharmacogn Phytochem. 2017; 6(3):337-41.
41. Kausar MA, Parveen K, Siddiqui WA, Anwar S, Zahra A, Ali A, *et al*. Nephroprotective effects of polyherbal extract via attenuation of the severity of kidney dysfunction and oxidative damage in the diabetic experimental model. Cell Mol Biol. 2021; 67(4):42-55. https://doi.org/10.14715/cmb/2021.67.4.6
42. Epure A, Pârvu AE, Vlase L, Benedec D, Hanganu D, Gheldiu A-M, *et al*. Phytochemical profile, antioxidant, cardioprotective, and nephroprotective activity of Romanian chicory extract. Plants. 2020; 10(1):64. https://doi.org/10.3390/plants10010064
43. Bajpai VK, Kim J-E, Kang SC. Protective effect of heat-treated cucumber (*Cucumis sativus* L.) juice against lead-induced detoxification in rat model. Indian J Pharma Edu Res. 2017; 51:59-69. https://doi.org/10.5530/ijper.51.1.9
44. Shirwaikar A, Manjunath SM, Bommu P, Krishnanand B. Ethanol extract of *Crataeva nurvala* stem bark reverses cisplatin-induced nephrotoxicity. Pharm Biol. 2004; 42(7):559-64. https://doi.org/10.3109/13880200490901249
45. Shirwaikar A, Setty MM, Bommu P, Krishnanand B. Effect of lupeol isolated from *Crataeva nurvala* Buch.-Ham. stem bark extract against free radical-induced nephrotoxicity in rats. Indian J Exp Biol. 2004; 42:686-90. https://doi.org/10.1080/13880200490901249
46. Thuwaini MM, Kadhem HS, Al-Dierawi KH. The nephroprotective activity of *Matricaria chamomile* and *Curcuma longa* aqueous extracts on tetracyclines-induced nephrotoxicity in albino rats. Inter J Pharm Ther. 2016; 7(4):161-7.
47. Akinyemi AJ, Faboya OL, Paul AA, Olayide I, Faboya OA, Oluwasola TA. Nephroprotective effect of essential oils from ginger (*Zingiber officinale*) and turmeric (*Curcuma longa*) rhizomes against cadmium-induced nephrotoxicity in rats. J Oleo Sci. 2018; 67(10):1339-45. https://doi.org/10.5650/jos.ess18115
48. Pathak NN, Rajurkar SR, Tarekh S, Badgire VV. Nephroprotective effects of carvedilol and *Curcuma longa* against cisplatin-induced nephrotoxicity in rats. Asian J Med Sci. 2014; 5(2):91-8. https://doi.org/10.3126/ajms.v5i2.5483
49. Topcu-Tarladacalisir Y, Sapmaz-Metin M, Karaca T. Curcumin counteracts cisplatin-induced nephrotoxicity by preventing renal tubular cell apoptosis. Renal Failure. 2016; 38(10):1741-8. https://doi.org/10.1080/0886022X.2016.1229996
50. Soetikno V, Sari SDP, Maknun LU, Sumbung NK, Rahmi DNI, Pandhita BAW, *et al*. Pre-treatment with *Curcumin ameliorates* cisplatin-induced kidney damage by suppressing kidney inflammation and apoptosis in rats. Drug Res. 2019; 69(02):75-82. https://doi.org/10.1055/a-0641-5148
51. Chan C-F, Huang W-Y, Guo H-Y, Wang BR. Potent antioxidative and UVB protective effect of water extract of *Eclipta prostrata* L. TSWJ. 2014; 2014. https://doi.org/10.1155/2014/759039
52. Dungca NTP. Protective effect of the methanolic leaf extract of *Eclipta alba* (L.) Hassk. (Asteraceae) against gentamicin-induced nephrotoxicity in Sprague Dawley rats. J Ethnopharmacol. 2016; 184:18-21. https://doi.org/10.1016/j.jep.2016.03.002
53. Thomas P, Gururaja MP, Joshi H, Prasannashama K, D'Souza U, Chacko N, *et al*. Ameliorative potential of *Eclipta alba* on gentamycin induced renal toxicity in rats. Res J Pharm Technol. 2019; 12(1):192-6. https://doi.org/10.5958/0974-360X.2019.00035.0
54. Alibakhshi T, Khodayar MJ, Khorsandi L, Rashno M, Zeidooni L. Protective effects of zingerone on oxidative stress and inflammation in cisplatin-induced rat nephrotoxicity. Biomed. Pharmacother. 2018; 105:225-32. https://doi.org/10.1016/j.biopha.2018.05.085
55. Salihu M, Ajayi BO, Adedara IA, Farombi EO. A 6-Gingerol-rich fraction from *Zingiber officinale* prevents hematotoxicity and oxidative damage in the kidney and liver of rats exposed to carbendazim. J Diet Suppl. 2016; 13(4):433-48. https://doi.org/10.3109/19390211.2015.1107802