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*Traditional Medicine in Sri Lanka*

# South Asian medicinal plants and chronic kidney disease

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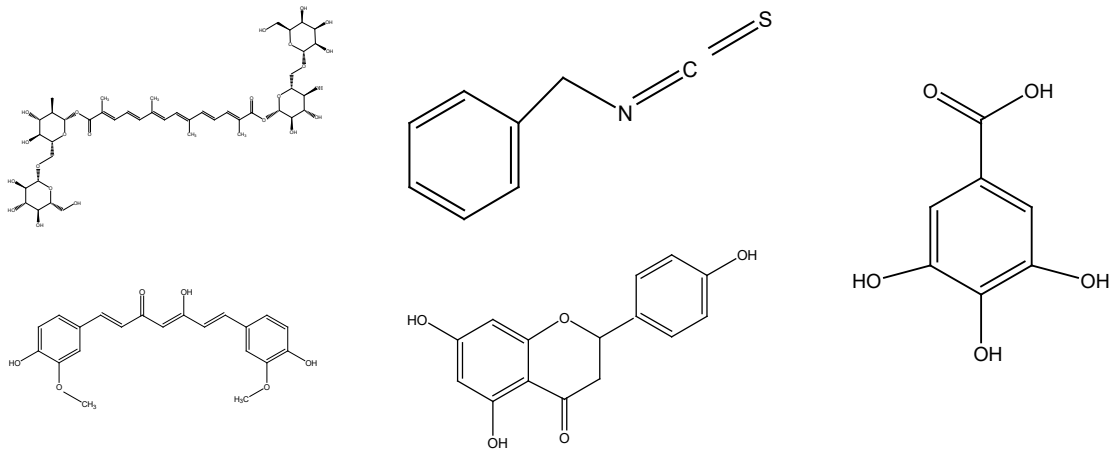
## Highlights

This review focuses on the use of South Asian medicinal plants in the therapy for kidney disease in traditional systems of medicine and on the nephroprotective activity of medicinal plant extracts in animal models.

## Traditionality

The potential threat to quality of life and the chronic nature of kidney disease have led many patients with chronic kidney disease to turn to complementary and alternative medicine practices to help them manage their disease. Several complementary and alternative medicine systems have been used in South Asian countries, including Ayurveda, Siddha, Unani, and Dhivehi beys. Ayurveda is the oldest system of medicine, originating in 1500 B.C.E.–2000 B.C.E. The classical Indian Ayurvedic texts, such as *Rigveda* (unknown author, written in 1500 B.C.E.–900 B.C.E.), *Atharvaveda* (unknown author, written in 600 B.C.E.), *Charak Samhita* (written by Charaka in 120 C.E–162 C.E.), and *Sushruta Samhit*a (written by Divodasa Dhanvantari, Susruta and Nagarjuna in 1500 B.C.E.–4$^{th}$ century C.E.), may have originated centuries ago as well and guide this approach to health. In 1997, the National Center for Complementary and Alternative Medicine of the National Institutes of Health in United States defined the complementary and alternative medicine as the practices that are not categorized as a part of the current conventional medical system for managing health and disease. The use of herbal therapeutics is the most common form of complementary and alternative medicine used by chronic kidney disease patients worldwide.



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## Abstract

Chronic kidney disease remains as one of the serious health issues in South Asia. The paucity of effective pharmacotherapy targeting the management of chronic kidney disease has led to a search for alternative pharmacologic therapies. The traditional knowledge of medicinal plants plays a key role in the discovery of novel nephroprotective agents. This review aims to present the use of such South Asian ethnomedicinal plants that have sufficient therapeutic potency for the management of kidney diseases. Medicinal plants are rich sources of bioactive compounds that have been reported to exert nephroprotective mechanisms, such as antioxidant, anti-inflammation, diuretic, and immunomodulation. Many South Asian medicinal plants have been detailed in traditional medicinal pharmacopoeias for the management of kidney-related diseases. Some have shown promising effects to address nephropathy in animal models and in vitro research. This information can be beneficial in the development of novel pharmaceutical agents targeting the management of kidney diseases and improvement of quality of life for chronic kidney disease patients by fulfilling the requirements for disease management unmet by modern allopathic medicine.
**Keywords:** Chronic kidney disease, Medicinal plants, Nephroprotective agents, South Asia, Antioxidant, Anti-inflammation

***Author contributions*:**

Sachinthi Sandaruwani Amarasiria contributed to the acquisition of data and writing the manuscript; Anoja Priyadarshani Attanayakeb contributed to conception of the manuscript, critical reviewing and revisions to the article; Kamani Ayoma Perera Wijewardana Jayatilakab and Lakmini Kumari Boralugoda Mudduwac contributed to revisions to the article.

***Competing interests*:**

The authors declare no conflicts of interest.

***Abbreviations*:**

AGE, aged garlic extract; CAM, complementary and alternative medicine; CKD, chronic kidney disease; CKDu, chronic kidney disease of unknown origin; ESRD, end stage renal disease.

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## Background

Reports on traditional systems of medicine provide several effective therapeutic approaches to address the diverse pathologic conditions related to kidney disease. In general, medicinal plants are the key element in most of the therapeutic remedies used in traditional systems of medicine. Ethnomedicinal plants used in the management of chronic kidney disease (CKD) are effective in diuresis and renal detoxification, and thus are beneficial to reduce the adverse effects of dialysis treatment [1, 2, 3, 4]. The ease of availability, low cost, efficacy, and safety of these plants available as herbal medicines to the general public make their use common in this population [5, 6, 7, 8]. Use of ethnomedicinal plants is further supported with the fact that they have shown promising effects in the treatment of diseases that allopathic systems of medicine have failed to manage [5, 9]. Therefore, these plants are of utmost importance to protect renal function and slow the occurrence and the progression of CKD, thus forestalling the need for end-stage treatment options such as renal replacement therapy [9].

Most of the South Asian population continue to rely on traditional systems of medicine, especially for the treatment of chronic diseases. Several systems of complementary and alternative medicine (CAM) are used in South Asia, with different approaches among the countries in the region, including Ayurveda, Siddha, Unani, and Dhivehi beys, for example. Ayurveda is the oldest system of medicine, originating in 1500–2000 B.C.E. The classical Indian Ayurvedic texts, such as the *Rigveda* (unknown author, written in 1500 B.C.E.–900 B.C.E.), *Atharvaveda* (unknown author, written in 600 B.C.E.), *Charak Samhita* (written by Charaka in 120 C.E–162 C.E.), and *Sushruta Samhit*a (written by Divodasa Dhanvantari, Susruta and Nagarjuna in 1500 B.C.E.–4$^{th}$ century C.E.), likewise may have originated thousands of years ago. In the modern era, in 1997, the National Center for Complementary and Alternative Medicine of the National Institutes of Health in United States (renamed the National Center for Complementary and Integrative Health in 2014) defined CAM as the practices that are not categorized as a part of the current conventional medical system for managing health and disease. The use of ethnomedicinal plants, also referred to as herbal therapeutics, is the most common form of CAM used by CKD patients worldwide.

Although several studies to date have focused on the nephroprotective medicinal plants used in traditional Indian medicine, there is no comprehensive review of the medicinal plants grown in other countries within the South Asia region, to the best knowledge of these authors [2, 3]. Therefore, this current review focuses on the use of ethnomedicinal plants of South Asian origin, with a potential therapeutic application in kidney disease.

## Disease burden in South Asia

CKD remains one of the leading public health issues worldwide [12, 13, 14]. It is characterized mainly by progressive loss of kidney function [15]. The complex nature and the risks associated with the progression of the disease to a severe state—called the end-stage renal disease (ESRD)—make the management of CKD quite critical [9]. The disease burden is massive in developing countries, as described later in text [12]. In addition, CKD is a major contributor to increased morbidity and mortality in South Asia, where the disease is most frequently present as ESRD [16]. Thus, CKD has become a devastating health problem in the South Asia, which directly affects the social and economic growth throughout the region [16].

Glomerular nephritis and interstitial disease have been considered to be the most common causes of ESRD in South Asia. Prevalent infections and environmental toxins are identified as the risk factors for glomerular nephritis and interstitial disease, respectively [12, 17]. However, diabetes mellitus and hypertension have drawn increasing research attention and are currently the leading causes of CKD [12, 18]. The oxidative stress associated with these two diseases leads to the progression of CKD. A high prevalence of diabetes mellitus and hypertension among the South Asian population may be the reason for an increase in the prevalence of CKD [1, 19, 20]. Furthermore, individuals with a positive family history of kidney disease are more prone to develop diabetic renal disease or glomerulonephritis associated with CKD [14]. However, the primary cause of CKD may vary depending on the socioeconomic status of patients and their environmental factors as well [18].

Chronic kidney disease of unknown origin (CKDu) is a condition in which the etiology and the exact prevalence of the disease remain unknown. This type of CKD has become a major health issue throughout South Asia, especially in countries such as Sri Lanka, where most CKDu patients are in the north central and north western provinces of the island, and in the Uva and Eastern provinces as well. Exposure to heavy metals (Cd, As, Pb), fluoride, pesticide residues, glyphosate from herbicides, and cyanogens from algae present in contaminated water sources have been identified as possible predisposing factors for CKDu [17, 18, 21].

The mean age of CKD patients in South Asian countries is lower compared with those in other countries globally. This age discrepancy may be the result of exposure to environmental toxins at a young age and poor access to health care, which delays diagnosis. In general, South Asian countries perform poorly on health care indices [16, 17]. Therefore, providing sufficient health care for patient with CKD is a major challenge within this region. Moreover,

although the prevalence of CKD is high among South Asian countries, no accurate data are currently available. Most of the reported data are hospital-based records or individual approximations [16]. Therefore, there is a large gap between the reported prevalence of CKD and the actual value because many patients with CKD never seek or receive medical attention [17]. Furthermore, CKD is often asymptomatic until the disease reaches its advanced stages; thus, these patients already have one or more disease complications or comorbidities by the time they seek medical attention [14]. Therefore, it is critical to implement a strategy so that measures can be taken for prevention as well as management of the disease before the progression to ESRD [17].

## Management strategies

Management of CKD is mainly based on early diagnosis, pharmacologic intervention, and strategies to preserve renal function [14]. Early diagnosis permits initiation of pharmacologic interventions early, resulting in a slower progression from CKD to ESRD. Early diagnosis of the disease may reduce the risks for cardiovascular events as well as the associated comorbidities and mortality [15].

However, pharmacologic management strategies in CKD are constrained by several limitations. First, no medication is available to cure CKD, and the available pharmacologic approaches mainly comprise measures to control the signs and symptoms and reduce the complications of disease [9, 22]. Second, although the management of hypertension would be beneficial in delaying the decline in renal function for patients with CKD, the therapeutic use of antihypertensive medications, such as angiotensin-converting enzyme inhibitors and angiotensin II receptor blockers, has been undermined because of their serious adverse effects, including neutropenia, proteinuria, angioneurotic edema, and hyperkalemia [14, 23, 24].

Management of ESRD is possible only with renal replacement therapy [23, 25, 26]. Dialysis and kidney transplantation are two main components of renal replacement therapy; however, their application may be limited because these approaches to management are highly sophisticated and expensive [23].

Although the use of pharmaceutical agents has been beneficial to some extent, the comorbidities and mortality associated with CKD have increased within the past few years. Patients with CKD are more likely to develop other systemic diseases, such as atherosclerosis and cardiovascular disease, which are a frequent cause of mortality [23, 25, 27]. Based on these factors of disease progression and the unavailability of extensive management options and renal replacement therapy facilities, the annual mortality rate for CKD patients is high in South Asian countries compared with other countries globally. Therefore, prevention of disease progression is a critical factor in the appropriate management of CKD [23].

The implementation of measures to preserve renal function is considered as one of the best options available to slow the progression of CKD and to delay the need of renal replacement therapy [28]. In this regard, the use of nephroprotective agents at the earlier stages of the disease play an important role in the management of CKD [14].

### Complementary and alternative practices in South Asia

The potential threat to quality of life and the chronic nature of kidney disease have led many South Asian patients with CKD to turn to CAM practices to help them manage their disease [29]. In addition, the available treatment options in allopathic medicine for CKD are in most cases unaffordable for low- and middle-income patients in South Asia, and this cost factor further directs these patients toward the traditional systems of medicine [30]. Furthermore, in terms of the social context of South Asia, the region is known for a rich heritage of traditional systems of medicine that have been practiced for centuries [5].

More than 70% of the South Asian population relies on these nonallopathic systems of medicine that are based on knowledge generated from centuries of experience, observation, and investigation. Traditional systems of medicine served as the mainstay of treatment in most of the South Asian countries before colonization by West [5, 6]. Traditional medicines comprise a variety of therapeutic approaches, including food habits and the use of herbs, metals, minerals, and precious stones. The approaches may vary among the different countries within the region [6, 31, 32].

Several CAM systems of have been used in South Asia. For example, Bangladesh, India, Nepal, and Sri Lanka mainly practice Ayurveda, Siddha, and Unani medicine, whereas Maldivians practice their own unique system known as Dhivehi beys [5, 6]. As the oldest system of medicine, originating in 1500–2000 BC [5, 31] Ayurveda is not simply a system of medicine—rather it is the science of life [6, 31, 32]. Its objective is not just treating the diseased person, but also for the person to achieve physical, mental, social, and spiritual well-being [6, 31, 32]. Ayurveda is based on the individualized treatment approaches that promote healing mechanisms and self-repair processes in the body [5]. Thus, Ayurveda is effective in the management of common diseases as well as many chronic diseases [6]. The Siddha system of medicine has a striking similarity to Ayurveda, but is specialized with regard to iatrochemistry with the use of herbomineral products [6]. Moreover, this system uses extensive astrology and incantations during treatments [32]. The Unani system of medicine has its origins in Greece. Different modes of treatments including regimental therapy, diet modification, pharmacotherapy, and

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surgery are practiced in Unani [5, 31]. However, medicinal plants play a key role in all of these traditional systems of medicine [6].

**Nephroprotective role of natural products**

Herbs are the most common forms of CAM used by CKD patients [30, 33]. The traditional treatment approaches based on medicinal plants focus the cause as well as the outcomes of kidney diseases to forestall the need for hemodialysis and to reduce the adverse consequences of dialysis treatments [1, 2, 3, 4]. In addition, herbs are beneficial to relieve some of the associated symptoms of CKD comorbidities, including cutaneous pruritus, fatigue, depression, muscle cramps, and uremic bruising. [29, 30, 33]. These herbs may decrease the frequency of dialysis treatment as well. Therefore, over the past decade there has been a remarkable increase in the use of medicinal plant-derived herbal medicines by patients who undergo hemodialysis [33]. The diuretic properties of these herbal medicines are not only useful for patients on hemodialysis, but also for pre-dialysis patients by stimulating their declining kidney function and thus delaying the need for dialysis [34].

Since herbal medicines have been used for thousands of years, their use is popular among general public. Moreover, medicinal plants used in the traditional systems of medicine have been beneficial in the discovery of number of modern allopathic medicines. Examples include aspirin, atropine, ephedrine, digoxin, morphine, quinine, reserpine, and tubocurarine, all of which have been developed based on the observations of indigenous medicine [35]. It is estimated that nearly one-third of all newly approved compounds in modern pharmacology are derived from medicinal plants [36]. Therefore, the World Health Organization has also recommended promoting herbal medicine in order to fulfill the requirements for disease management unmet by modern allopathic medicine [5]. The literature supports a number of medicinal plants used in these traditional systems of medicine that show promising effects in renal failure [2, 37].

**Nephroprotection by suppression of oxidative stress and chronic inflammation**

Several mechanisms are suggested for the nephroprotective activity of medicinal plants. Among them the most common mechanism is through the antioxidant defense system [19, 37]. Antioxidants are the molecules that combat the oxidative stress developed from an imbalance between the rate of production and removal of produced oxidants. Oxidative stress is the causative factor for a wide variety of diseases, including CKD [19]. A key advantage to medicinal plants is that they are rich sources of antioxidants, mainly present in the form of phenolic compounds (flavonoids, phenolic acids, tocopherols, tocotrienols), ascorbic acid, and carotenoids. These substances work to prevent renal damage by reducing lipid peroxidation and increasing endogenous antioxidants [9, 19, 38, 39]. Therefore, supplementation with medicinal plant-derived antioxidants is of utmost importance in curtailing the free radical pathologies present in CKD [14]. However, the literature provides evidence for the capacity of natural whole products rather than single antioxidants or their combinations in preventing or managing kidney diseases [19].

Another important mechanism of nephroprotection is the anti-inflammatory effects of medicinal plants. The compounds such as curcumin and resveratrol found in medicinal plants have shown promising effects in nephroprotection by modulating inflammation processes [30]. Moreover, other pharmacologic characteristics, such as diuresis, immunomodulation, reduction in proteinuria, and stimulation of renal repair mechanisms, may contribute to slowing the progression from kidney-related disease conditions to later-stage disease [1, 36].

Polyphenols in medicinal plants play an important role in nephroprotection by acting as antioxidant, anti-inflammatory, and diuretic agents [1, 36]. The enormous value of these phytoconstituents mandates investigating the bioactivities of medicinal plants for the discovery of nephroprotective therapeutic agents. In this context, medicinal plants used in the management of kidney-related diseases in traditional systems of medicine have drawn increasingly more research attention.

Although a large number of medicinal plants are used in the therapy for kidney diseases in the indigenous and traditional systems of medicine, most have not been scientifically scrutinized for their therapeutic effects as well as for their safety. Therefore, it is important to validate the use of these plants through phytochemical analysis and investigation of their relevant pharmacologic activities [35]. In view of that goal, many research studies have been conducted in the fields of pharmacognosy, chemistry, pharmacology, and clinical therapeutics, on native medicinal plants through the approach of reverse pharmacology, facilitated by traditional knowledge [1, 3, 31, 40, 41, 42, 43, 44]. Table 1 summarizes an overview of such ethnomedicinal plants of South Asian origin, with potential for the treatment of kidney diseases.

**Nephroprotective activity of medicinal plant extracts on animal models**

A number of medicinal plants with nephroprotective activity have been effective in the treatment of kidney diseases as shown in animal models [36, 41, 72, 69, 88]. These plants have been useful in the management of glomerulonephritis, different forms of nephropathies, glomerulosclerosis, nephrotic syndrome, lupus, and tubulointerstitial nephritis, as well as in the treatment of kidney stones [36].

Different mechanisms of nephrotoxicity are used for

**Table 1 Overview of South Asian medicinal plants used in therapy for kidney diseases**

| | Botanical name | Family | Local name | Part used | Chemical constituents | References |
|---|---|---|---|---|---|---|
| 1. | *Abelmoschus esculentus* L. | Malvaceae | Bhendi | Fruit, seed, root | Carotene, folic acid, thiamine, riboflavin, tocopherol, palmitic acid, tannins, mucilages, flavonoids, leuco-anthocyanins, reducing compounds, sterols, terpenes. | [3, 45] |
| 2. | *Abrus precatorius* L. | Leguminosae | Gunja | Root, leaves | Glucoside, alkaloid, flavonoids, phenols, saponins, tannins, carbohydrate, terpenoids | [3, 46] |
| 3. | *Acacia arabica* (Willd) | Leguminosae | Babul | Leaves | Tannin, flavonoid | [3, 47, 48] |
| 4. | *Acacia catechu* L. | Mimosaceae | Khair | Bark | Flavonoid, tannin, phenol, saponins, carbohydrates, alkaloids, glycosides | [3, 49] |
| 5. | *Acacia sinuate* (Lour) Merrill | Mimosaceae | Cikakai | Bark, pods | Saponin, flavonoid, tannin | [3] |
| 6. | *Acer pensylvanicum* | Aceraceae | Striped maple | Bark | Flavonoids, tannins, phenylpropanoids, diarylheptanoids, terpenoids, benzoic acid derivatives | [1, 40] |
| 7. | *Achilla millefolium* L. | Compositae | Gandana | Whole plant | Alkaloid, essential oil, flavonoid, tannins, saponins | [3, 50, 51] |
| 8. | *Adiantum Lunulatum* Burm | Polypodiaceae | Hansraj | Leaves | Flavonoids, terpenoids, tannin, volatile oil, steroid, anthocyanin, alkaloids, anthraquinones | [3, 52] |
| 9. | *Alangium salvifolium* Wang | Alanglaceae | Ankol | Bark | Alkaloids, akoline lamarkine, steroids, saponin, flavonoids | [3, 53] |
| 10. | *Allium cepa* L. | Alliaceae | Onion | Bark | Essential oil, orgnic sulfide, flavonoid, phenolic acid, tannins, alkaloids | [3, 54, 55] |
| 11. | *Amaranthus spinosus* L. | Amaranthaceae | Katelichaulai | Root | Alkanes, quinoline,sterols, terpene, alkaloids, glycosides | [3, 56] |
| 12. | *Andropogon muricatus Retz.* | Graminae | Kalavala | Leaves, flower | Essential oil | [3] |
| 13. | *Anogeissus latifolia* (Roxb) | Combretaceae | Dhavara | Bark, root | Tannins, calcium, gum, qurecetin, phenolic compounds | [3, 57] |
| 14. | *Anona squamosa* L. | Annonaceae | Custard apple | Leaves, seed | Alkaloid, amino acids, camphor, anonaine, flavonoids, coumarins, terpenoids | [3, 58] |
| 15. | *Arachis hypogaea* L. | Fabaceae | Mung-phali | Seed | Vitamin E, flavonoid, tannins, alkaloid, fat, oils, lignins, saponins | [3, 59] |
| 16. | *Arctium lappa* L. | Compositae | Great burdock | Root | Flavonoid, hexasaccharide, tannin, volatile oil, lignans | [3, 60] |
| 17. | *Asclepias syriaca* L. | Asclepiadaceae | Mohari | Root | Asclepiadin, glucol | [3] |
| 18. | *Asparagus racemosus* Willd | Liliaceae | Shatavari | Root | Oil, saponin | [3, 31] |
| 19. | *Atropa belladona* L. | Solanaceae | Belladona | Root | Alkaloid, tannin, starch | [3, 61] |
| 20. | *Azadirachta indica* L. | Meliaceae | Nimb | Leaves | Alkaloid, flavonoid, steroid, glycosides, amino acid, reducing sugar, azardin, resin, tannin, saponins, phenols, fixed oils, | [3, 62] |

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**Table 1 Overview of South Asian medicinal plants used in therapy for kidney diseases (*continued*)**

| | Botanical name | Family | Local name | Part used | Chemical constituents | References |
|---|---|---|---|---|---|---|
| 21. | *Bacopa monnieri* L. | Scrophulariacea | Brahmmi | Leaves | Essential oil, alkaloid | [3, 31] |
| 22. | *Balanites roxburghii* L. | Balanitaceae | Hingol | Root, fruit | Saponins, amino acid, carbohydrate, alkaloid, flavonoids, tannins, phenolic compounds | [3, 63] |
| 23. | *Baliospermum montanum* Willd | Euphorbiaceae | Danti | Leaves, root | Alkaloids, graminae, cardiac glycoside, phorbol esters, terpenoid, tannin, saponins, hydrocarbon, sitoserol, D-glucoside | [3, 64] |
| 24. | *Bambusa arundinacea* Von | Graminae | Bamboo | Leaves | Flavonoid, phenols, steroids, tannins, quinones, cholin, betain, nuclease, urease | [3, 65] |
| 25. | *Bambusa nutans* L. | Arundinacea | Bamboo | Leaves | Cholin, betain, nuclease, urease | [3] |
| 26. | *Barleria prionitis* Linn. | Aceanthaceae | Kate-Koranti | Leaves, flowers | Alkaloid, phenolic compounds, tannins, saponins, essential oil, flavonoid glycoside, β-sitosterol | [3, 66] |
| 27. | *Basella alba* L. | Basellaceae | Indian spinach | Leaves | Alkaloid, saponnins, iodine, fiuorine, carotenoids, flavonoid, diterpenes, phenols, tannin | [3, 67] |
| 28. | *Benincasa hispida* (Thunb) Cogn | Cucurbitaceae | White gourd | Fruit, seed | Alkaloid, glycoside, flavonoids, phenolic compounds, glucoge, mannitol, β-sitosterol, protene | [3, 68] |
| 29. | *Bombax ceiba* L. | Bombacaceae | Salmali | Fruit | Tannins, β–sitosterol, D-glucoside | [3] |
| 30. | *Boswellia serrata* roxb | Burseraceae | Dhupali, Salai | Gum | Tanins, pentosans, lignin, holocellulose, β–sitosterol | [3, 31] |
| 31. | *Brassica oleracea* L. | Brasscaceae | Cabbage | Leaves | Essentinl, amino acid, alkaloid, tannins, flavonoids, glycosides, terpenes | [3, 69] |
| 32. | *Butea monosperma* Lam | Fabaceae | Palash | leaves | Glucoside, butine, proteolytic lipolytic enzyme, flavonoid | [3, 31] |
| 33. | *Cajanus cajan* L. | Fabaceae | Millsp, Tuvar | Leaves, seed | Amino acid, galactoside, tannins, saponins, alkaloids, flavonoids, phenols | [3, 70] |
| 34. | *Carica papaya* L. | Caricaceae | Papaya | Fruit | Alkaloid, papain enzymes | [3, 4, 41] |
| 35. | *Cassia absus* L. | Caesalpiniaceae | Ran Kulith | Leaves, seed | Alkaloid, sitosterol, glucoside, flavonoid | [3, 71] |
| 36. | *Cassia fistula* L. | Caesalpiniaceae | Bahava | Leaves, pods | Glycoside, tannin, flavonoid | [3, 31] |
| 37. | *Chelidonium jajus* L. | Papaveraceae | Celandine | Flowers | Alkaloids, flavonoids | [3] |
| 38. | *Clitoria terneata* L. | Papilionaceae | Aparajita | Root | Teraxeron, glucoside, oligosaccharide | [42] |
| 39. | *Cocos nucitera* L. | Arecaceae | Coconut | Leaves, seed, fruit | Saccharose, sorbitol alcohol, ketones, alkaloid, tannins, saponins, steroid, glycosides, terpenoids | [3, 72] |
| 40. | *Commiphora mukul* Engl | Burseraceae | Guggal | Gum | Guggulsterone, flavonoid | [3] |
| 41. | *Cornus canadensis* | Cornaceae | Bunchberry | Whole plant | Antioxidant phenolics | [1] |

**Table 1 Overview of South Asian medicinal plants used in therapy for kidney diseases (*continued*)**

| | Botanical name | Family | Local name | Part used | Chemical constituents | References |
|---|---|---|---|---|---|---|
| 42. | *Cordia dichotoma* Forst | Boraginaceae | Bhoker | Fruit | Alkaloid, tannin, coumarins, flavonoids, saponins, terpenes, sterols | [3, 73] |
| 43. | *Crataeva Religoea* Buch, Ham | Capparidaceae | Varun | Bark, leaves | Linalool, linalyl acetate, thymol, β-caryphyllene, α-pinene borneol, limonene, B-pheliandrene, citranellol | [3] |
| 44. | *Curculigo orchioides* Gaertn | Amaryllidaceae | Kalimusli | Root | Saponins, curculigo, phenolicglycoside, alkaloids, steroids | [3, 74] |
| 45. | *Cynodon dactylon* Pers | Gramineae | Durva | Root | β-ionone, 2-propionic4-hydroxybenzoic, tannins, saponins, phenols, flavonoids | [3, 75] |
| 46. | *Cyperus rotundus* | Cyperaceae | Nagermotha | Root | Essential oil, cyperene, cyperol, starch, β-sitosterol, phenolic compounds, steroids, flavonoids, glycosides | [3, 76] |
| 47. | *Datura metal* L. | Solanaceae | Datura | Leaves, flowers | Alkaloid, scopolamine, hyposcymine, atropin, vitamin C, saponins, flavonoids, phenols, alkaloids, glycosides, steroids | [3, 77] |
| 48. | *Daucus carota* L. | Umbelliferae | Carrot | Root | Oil, carotol, essential oil, flavones, phenolic compounds | [3, 78] |
| 49. | *Demostachya bipinnata* L. | Compositae | Kush | Root | Alkaloid, terpenoid | [3, 79] |
| 50. | *Desmodium gangeticum* L. | Fabaceae | Salpan | Root | Alkaloids | [3, 31] |
| 51. | *Digitalis Purpurea* L. | Scrophulariacea | Hrutpatri | Leaves | Glycosides, flavonoids, saponin, volatile oil, fatty matter, starch, gum, sugars | [3, 80] |
| 52. | *Dolichos biflorus* L. | Leguminosae | Kulith | Seed | Urease, lectin, carbohydrate, glycosides, tannins, saponin | [3, 81] |
| 53. | *Elettaria cardamomum* Maton. | Zingiberaceae | Chhoti elaichi | Seed | Palmitic acid, phenols, starch, tannins, terpinoids, flavonoids, proteins, sterols | [3, 82] |
| 54. | *Foeniculum vulgare* Mill | Apiaceae | Saunf | Seed, flowers | Methyl chavicol, limonene, essential oil, terpinoids, flavonoids, sterols, tannins, reducing sugars | [3, 83] |
| 55. | *Gmeliana arborea* (Roxb) | Verbenaceae | Jivanti | Fruit, leaves | Volatile oil, sugar, glycosides, tannins, alkaloids, flavonoids, sterols, steroid, phenolic compounds | [3, 84] |
| 56. | *Gossypium arboreum* L. l | Malvaceae | Cotton | Leaves | Betaine, choline, salicylic acid, tannins, reducing sugars, steroid, flavonoids, terpenoid | [3, 85] |
| 57. | *Gymnema sylvestrer* (Retz) R. Br | Asclepiadaceae | Gudmar | Leaves, whole plant | Saponine, I-V, gymnemic acid | [3, 31] |
| 58. | *Haldina cordifolia* (Roxb) | Rubiaceae | Haldu | Bark, fruit | Oleoresin, essential oil, cellulose, β-sitosterol, alkaloids, flavonoids | [3, 86] |
| 59. | *Helianthus annus* L. | Compositae | Sunflower | Seed, root | Albumin, globulin, glutelin, βsitosterol | [3] |
| 60. | *Hibiscus sabdariffa* L. | Malvaceae | China rose | Leaves | Organic acid, anthocyanin vitamin, saponins, steroids, flavonoids, tannins. | [3, 87] |

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**Table 1 Overview of South Asian medicinal plants used in therapy for kidney diseases (*continued*)**

| | Botanical name | Family | Local name | Part used | Chemical constituents | References |
|---|---|---|---|---|---|---|
| 61. | *Holarrhena antidysentrica* L. | Apocynaceae | Kala-Kuda | Bark, seed | Alkaloids, tannin, triterpene | [3, 31] |
| 62. | *Humulus lupulus* L. | Cannabidaceae | Hop | Fruit | Volatile oil, polyphenolic, tannin, aspargin | [3] |
| 63. | *Hygrophila auriculata* K.Schum. | Acanthaceae | Neermali | Root, leaves | Fatty oil, alkaloid, saponins, steroids, tannins, flavonoids, Triterpenoids | [3, 88] |
| 64. | *Jasmium grandiflorum* L. | Oleaceae | Chameli | Leaves | Alkaloid, salicylic acid, essencial oil, ascorbic acid, glycoside | [3] |
| 65. | *Larix laricina* | Pinaceae | Tamarack | Gum | β-glucosides, *p*-coumaric acid, α-glucoside | [1] |
| 66. | *Lawsonia inermis* L. | Lythraceae | Mehandi | Seed, root, leaves | 2-hydroxy-1,4naphthquinoneFlavonoid, βsitosterol, alkaloid, saponins, steroids, tannins, flavonoids, glycoside | [3, 89] |
| 67. | *Leptadenia reticulata* W. & A | Asclepiadaceae | Jivanti | Root | Stigma sterol, tocopherol | [3, 31] |
| 68. | *Linum usitatissimum* L. | Linaceae | Aalsi | Seed, root | Fixed oil, protene wax, resin, sugar glycoside | [3] |
| 69. | *Mangiifera indica* L. | Anacardiaceae | Mango plant | Leaves | Flavonoid, phenolic acid, Vitamin A, B, C, D, alkaloid, tannins | [3, 90] |
| 70. | *Menta arvensis* L. | Labiatae | Podina | Leaves | Essential oil, carvones, flavonoids, saponin, alkaloids, tannins, terpenoids, cardiac glycosides | [3, 91] |
| 71. | *Mesua ferrea* L. | Guttiferae | Nagkesarah | Seed | Palmitic, stearic, oleic, linoleic | [3] |
| 72. | *Michelia champaca* L. | Magnoliaceae | Champa | Leaves, whole plant | Essential oil, fatty oil, flavonoids, saponin, alkaloids, tannins, sterol, carbohydrate, amino acid | [3, 92] |
| 73. | *Mimosa pudica* L. | Leguminosae | Lajalu | Leaves, root | Alkaloids, mimosine, terpenoids, flavonoids, glycosides, quinines, phenols, tannins, saponins, coumarin | [3, 93] |
| 74. | *Momordica dioica* Roxb ex willd | Cucurbitaceae | Jangali karelaa | Root | Glycoside, saponin, alkaloids, steroids, triterpenoids, flavonoids, triterpenes | [3, 94] |
| 75. | *Mucana pruriens* L. | Leguminosae | Khaj-kuiri | Root, seed | Calcium, phosphorus, iron, sulfur, alkaloids | [3, 31] |
| 76. | *Mucuna adans* L. | Leguminosae | Khaj-kuiri | Root, seed | Calcium, glucoside, alkaloids, β-sitosterol | [3] |
| 77. | *Musa paradiciaea* L | Scistaminaceae | Banana | Seed | Albumin, globulin, glutelin, proteoses | [3, 95] |
| 78. | *Nelumbium nucifera* gaertn | Nelumbonaceae | Lotus | Seed, leaves, fruit, rhizome | Alkaloids, nuciferine, protene sugar, vitamin, cardiac glycosides, flavonoids, saponin, tannin, phlobatanins, phenolic compounds | [3, 96] |
| 79. | *Nerium indicum* Mill | Apocynaceae | Kaner | Leaves, root | Glycoside, digitoxigenin, tannins, terpenoids, alkaloids, flavonoids, carbohydrates | [3, 97] |

**Table 1 Overview of South Asian medicinal plants used in therapy for kidney diseases (*continued*)**

| | Botanical name | Family | Local name | Part used | Chemical constituents | References |
|---|---|---|---|---|---|---|
| 80. | *Nyctanthus arbortristis* L. | Oleaceae | Parijat | Leaves | Oil, manitol, tannin, βsitosterol, tannins, terpenoids, saponins, steroids, carbohydrates, cardiac glycosides, alkaloids, proteins | [3, 98] |
| 81. | *Ocimum basillicum* L. | Labiatae | Sweet basil | Leaves, root, seed | Essential oil, methylcinnamate, eugenol, alkaloid, Flavonoid | [3] |
| 82. | *Ocimum canum* L. | Labiatae | Sathra | Seed | Essential oil, eugenol, βsitosterol, flavonoids, carbohydrates, phytosterols, tannins | [3, 99] |
| 83. | *Ocimum Sanctum* L. | Labiatae | Tulasi | Leaves, root | Eugenol, methol, ether, carvacol | [3, 31] |
| 84. | *Orchis latifolia* L. | Orchidaceae | Salam | Whole plant | Volatile oil, loroglosin, glucoside | [3] |
| 85. | *Orza sativa* L. | Gramineae | Chawal | Seed | Alkaloid, oriline, protene, fat, carbohydrate, flavonoid, terpenoids, tannins, phytosterols | [3, 100] |
| 86. | *Ougeinia oojeinensis* (Roxb) Hochr | Fabaceae | Dandan | Bark | Dimethoxy, isoflavone, homoferreiri, saponin, alkaloids, tannins, glycosides, carbohydrate, flavonoid | [3, 101] |
| 87. | *Paederia foetida* L. | Rubiaceae | Hirenwel | Leaves, root | Essential oil, alkaloids, foetida, iridoid glycosides, sitosterol, stigmasterol, carbohydrates, protein, amino acid | [3, 102] |
| 88. | *Pandanus odoratissimus* L. | Pandanaceae | Ketek | Leaves | Essential oil, methyl ether, phenyl ethyl alcohol, alkaloid, flavonoid | [3, 103] |
| 89. | *Phaseolus mungo* L. | Leguminoseae | Green gram | Seed | Oil | [3] |
| 90. | *Phyllanthus niruri* L. | Euphorbiaceae | Bhui awala | Seed | Alkaloid, flavonoids, phyllanthin, hypophyiianthin, terpenoids, cardiac glycoside, saponins, tannins, cyanogenic glycosides | [3, 104] |
| 91. | *Phyllanthus urinaria* L | Euphorbiaceae | Valaitisaunf, Muhuri | Seed | Alkaloid, flavonoid-quercetin, astragalin, carboxylic acids, tannins, coumarins, lignans | [3, 105] |
| 92. | *Phyllanthus reticulates* Pair | Euphorbiaceae | Jarmala | Leaves | Tannic acid, steroid, tannin, quinone, phenol | [3, 106] |
| 93. | *Pimpinella anisum* L. | Umbelliferae | Rajanigandh | Leaves | Volatile oil, flavonoid, sterol | [3] |
| 94. | *Pinus strobus* | Pinaceae | White pine | Bark, twig | Diterpenes, strobol, strobal, manoyl oxide, *cis*- and *trans*-abienols | [1, 43] |
| 95. | *Piper nigrum* L. | Pipereceae | Blak piper | Seed | Piperin, piredin alkaloid, chavicine essential, oil | [3, 31] |
| 96. | *Saccharum officinarum* L. | Poaceae | Suger cane | Seed, root | Phenol, glycolic acid | [3] |
| 97. | *Santalum album* L. | Santalaeae | Safed chandan | Weed | Santalbic acid,palmitic acid, olic acid | [3] |
| 98. | *Saraca indica* L. | Leguminosae | Ashok tree | Leaves, seed, bark | Tannin, atechol, sterol, glycocide, steroid, saponin, tannin, phenolic compounds | [3, 107] |
| 99. | *Sarracenia purpurea* | Sarraceniaceae | Purple pitcher plant | Root | Quercetin, taxifolin compounds, betulinic acid, ursolic acid | [1, 44] |

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**Table 1 Overview of South Asian medicinal plants used in therapy for kidney diseases (*continued*)**

| | Botanical name | Family | Local name | Part used | Chemical constituents | References |
|---|---|---|---|---|---|---|
| 100. | *Securinega leucopyrus* Muell-Arg | Euphorbiaceae | Hartto | Leaves | Alkaloids, freetriterpens, steroids, tannin | [3] |
| 101. | *Solanum indicum* L. | Solanaceae | Dorli | Whole plant | Alkaloid, enzymes, steroidal glycoside, sesquiterpenoids, hydroxycoumarins, phenolic compounds, coumarins, alkaloids, saponin, fatty acid, polysaccharide, triterpenes | [3, 108] |
| 102. | *Solanum surattense* burn | Solanaceae | Katali Kattay | Fruit, flower | Gluco alkaloid, solasodine, solasonine | [3] |
| 103. | *Solanum xantocarpum* schrad & Wendell | Solanaceae | Kateringani | Root | Carpesterol, glucoside, alkaloid, solanocarpine | [3, 31, 42] |
| 104. | *Solena amplexicaulis* Lam | Umbelliferae | Gomathi Tawgaula | Root | Alkaloid, glycoside, steroid | [3] |
| 105. | *Tectona grandis* L. | Verbenaceae | Teak | Whole plant | Calcium, phosphate, silica ammonium | [3, 41, 42] |
| 106. | *Tephrosia purpurpa* L. | Fabaceae | Sarphomka | Leaves | Tephrosin, rotenone | [3, 42] |
| 107. | *Terminalia chebula* Retz | Combrataceae | Hirda | Seed | Palmitic, stearic, oleic, linoleic, astrigent, tannic acid | [3, 31] |
| 108. | *Urtica dioica* L. | Urticaceae | Guelder rose | Root | Flavonoids, amines, steroids, phenols, phytosterols, saponins, tannins, amino acids | [3, 109] |
| 109. | *Vernonia antheimintica* Willid | Asteraceae | Kalijira | Fruit | Amino acid, linoleic, myristic, oleic, palmitic, sterols, alkaloid, flavanoids | [3, 110] |
| 110. | *Vitis vinifera* L. | Vitaceae | Wine grape | Fruit | Thiamine, niacin, biotin, tocoferol, coumarins, flavanoids | [3, 111] |
| 111. | *Zingiber officinale* (Rose) | Scitaminaceae | Ginger | Rhizome | Essential oil, volatile oil | [3, 42] |
| 112. | *Zizyphus xylopyrus* L. | Rhamnaceae | Kath ber | Leaves | Alkaloid, zizipine, flavonoids, saponins, tannins | [3, 112] |

the scientific investigation of nephroprotective activity of the medicinal plants in animal models. Several different nephrotoxic agents, including therapeutic drugs, diagnostic agents, and chemicals, have been used to induce nephrotoxicity in animal models. The most common among them is the use of various antineoplastic agents including the following: cisplatin, cyclophosphamide, streptozotocin, carmustine, lomustine, semustine, mitomycin, mithramycin, and doxorubicin. Moreover, aminoglycosides, such as gentamycin, amikacin, kanamycin, and streptomycin, and antimicrobial agents, such as tetracycline, acyclovir, pentamidine, sulfadiazine, trimethoprim, and rifampicin are widely used as nephrotoxic agents. Furthermore, the literature supports the use of heavy metals such as Hg, As, Pb, and Bi as nephrotoxic agents [113, 114].

These toxins may directly affect the membrane permeability of renal tubular cells, thereby causing potential injury. Further, they involve in remodeling of the cellular surface changing the area available for ion transportation. These changes may result in accumulation of intracellular calcium and loss of enzymes and nucleotides. An increase in calcium in the renal cortex and mitochondria may lead to features of cellular necrosis and renal failure [114]. Further, intracellular metabolism of these toxic drugs lead to the formation of reactive metabolites, such as free radicals, which are toxic for cells. The superoxide ions formed during oxidation of hydroxyl radicals in turn leads to lipid peroxidation. This effect may result in oxidative deterioration of polyunsaturated lipids of membranes, causing modification of the structure and function. Moreover, these nephrotoxins may reduce the concentration of antioxidants, superoxide dismutase, glutathione, catalase, vitamin E, and ascorbic acid, all of which are protective against free radical injury. In addition, these toxins might induce changes in the integrity of renal tubular cells, thereby causing several lethal changes such as development of abnormally

enlarged lysosomes and myeloid bodies, loss of brush border membrane, and vacuolization and dilation of the endoplasmic reticulum. Free radical-induced renal damage has been demonstrated in several in vivo and in vitro studies that have shown the development of glomerular dysfunction and proteinuria because of altered glomerular permselectivity by chemical infusion of reactive oxygen species [114].

Table 2 details the nephroprotective medicinal plants for which the protective activity was investigated in animal models. The nephroprotective activity was evaluated using changes in renal function parameters as follows: serum creatinine, blood urea, serum protein, serum albumin, urine creatinine, urinary protein, albumin, uric acid, and urinary osmolality [113, 118, 121, 124, 129, 143]. Furthermore, plasma concentrations of malondialdehyde, superoxide dismutase, reduced glutathione, and total antioxidants were investigated in several studies [120, 121, 125, 131, 132, 136, 139]. Assessment of histopathology in hematoxylin and eosin-stained kidney sections for the features of glomerular congestion, tubular casts, peritubular congestion, epithelial desquamation, blood vessel congestion, and presence of inflammatory cells have also been conducted for the evaluation of the nephroprotective effects of these medicinal plants in selected animal models [114, 115, 116].

In addition to these medicinal plants, the nephroprotective activity of a polyherbal mixture composed of *Bauhinia racemosa* (Caesalpiniaceae; stem bark), *Dolichos biflorus* (Fabaceae; seed), *Sphaeranthus indicus* (Asteraceae; flower), *Tectona grandis* (Verbenaceae; saag seed), *Tephrosia purpurea* (Fabaceae; leaves) and *Tribulus terrestris* (Zygophyllaceae; fruit) have been investigated for nephroprotective effect by Chopda et al. [8].

**Table 2 South Asian medicinal plants investigated for nephroprotective activity in animal models**

| | Botanical name | Family | Local name | Part used | Screening method | Chemical constituents | Reported bioactivities | References |
|---|---|---|---|---|---|---|---|---|
| 1. | *Abutilon indicum* | Malvaceae | Atibalaa | Whole plant | Cisplatin (ethanol extract-pretreatment) | Asparagines, mucilage, tannin, alkaloids | Antioxidants | [113, 73, 3] |
| 2. | *Achyranthes aspera* Linn | Amaranthaceae | Apamarga | Whole plant | Deprived of water for eighteen hours for investigation of diuretic acivity (methanolic extract) | Alkaloids, saponin, tannin oil | Diuretic, spermicidal, anti-allergic, cardiovascular, nephroprotective, antiparasitic, hypoglyceamic, analgesic, and antipyretic | [119, 3] |
| 3. | *Acorus calamus* L. | Araceae | Bach, Ugragandha | Aerial part | Acetaminophen (ethanol extract-pretreatment) | Monoterpene, sesquiterpene, phenylpropanoid, flavonoid, quinone | Antidiabetes, antiproliferative, immunosuppressive, antidiarrhoeal, hypolipidemic, antioxidant | [120] |
| 4. | *Aegle marmelos* Linn | Rutacae | Bael | Leaves | Gentamicin (aqueous extract-pretreatment) | Aegeline, aegelinine, rutin, lupeol, sterol, tannins, flavanoids, quercetin β-sitostersol, β-D-glucoside, marmesinine, phlobatannins, umbelliferone, volatile oils | Cardiotonic effect, antifungal, analgesic and antioxidant activities, cellular anti-inflammatory activity | [41, 113, 121] |
| 5. | *Aerva javanica* Juss. | Amaranthaceae | Pasanabheda | Roots | Cisplatin (aqueous extract-posttreatment) | Isoquercetin, 5 methylmellein, 2hydroxy -3-O-β primeveroside naphthalene-1, 4dione, apigenin 7oglucoronide, kaempferol | Antioxidant and free radical scavenging properties, anthelmintic, diuretic, demulcent | [113, 122, 123] |

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**Table 2 South Asian medicinal plants investigated for nephroprotective activity in animal models (*continued*)**

| | Botanical name | Family | Local name | Part used | Screening method | Chemical constituents | Reported bioactivities | References |
|---|---|---|---|---|---|---|---|---|
| 6. | *Aerva lanata* L. Juss | Amaranthaceae | Pasanabheda, Chaya, Gorakhganja | Whole plant | Cisplatin (ethanol extract-posttreatment) Gentamicin (ethanol extract-pretreatment) | flavonoides, glycoside, botulin, β-sitostersol, amyrin, campesterol, kaempferol,propionic acid, aervoside, aervolanine | Diuretic, hepato protective, antidiabetic, antimicrobial, anthelmintic and demulcent activity | [41, 113, 114] |
| 7. | | | | | Gentamicin (aqueous extract-pretreatment) | | Antioxidant and free radical scavenging activity, anti-inflammatory, antiviral, antitumor, moisturizing, anti-aging effect, antiseptic, enhance immune system, hypoglycemic, cytotoxic, antiulcer and antidiabetic effects, antibacterial effect, antioxidant, cardiovascular effect | |
| 8. | *Aloe barbadensis* | Xanthorrhoeaceae | Aloe vera | Leaves | Cisplatin (aqueous extract-pretreatment) | Anthraquinones, tannin, saponin, flavonoids, terpenoids | | [42, 113, 124] |
| 9. | *Azima tetracantha* | Salvadoraceae | Wel dehi, Katuniyanda | Root | Glycerol (ethanol extract) | Flavonoids, terpinoids, alkaloids, tannins, saponins, glucosinolates | Antimicrobial, antifungal, anti-inflammatory, analgesic, antioxidant, antiulcer, anticancer, anti-snake venom, diuretic and hepatoprotective activity, vasodilatory activity | [10, 125] |
| 10. | *Bauhinia Variegata* Linn. | Caesalpiniaceae | Koboleela, Kovidara | Root | Gentamicin (ethanol and aqueous extracts-post treatment) | Flavonoids, tannins, steroids, saponins, triterpenes, quercetin, rutin, apigenin, apigenin 7-O-glucoside | Antitumour, antimicrobial, anti-inflammatory, antioxidant, hepatoprotective, antihyperlipidemic, immunomodulatory activities. | [10, 41, 127] |
| 11. | *Boerhaavia diffusa* | Nyctaginaceae | Punarnava | Roots | Acetaminophen (aqueous extract-pretreatment) | Flavanoids, alkaloids, triterpenoids, proteins, carbohydrates, glycosides, lipids, lignins, glycoprotiens, steroids, lignins, | Diuretic, anti-inflammatory, antiarthritic | [31, 41, 113, 114, 123] |
| 12. | *Bridelia retusa* | Euphorbiaceae | Kajja | Stem bark | CCL4 (ethanolic and aqueous extracts-post treatment) | Glycosides, steroids, tannins, terpenoids | Antiviral, anticancer, hypotensive properties | [11, 128] |

**Table 2 South Asian medicinal plants investigated for nephroprotective activity in animal models (*continued*)**

| | Botanical name | Family | Local name | Part used | Screening method | Chemical constituents | Reported bioactivities | References |
|---|---|---|---|---|---|---|---|---|
| 13. | *Cardiospermum halicacabum* Linn. | Sapindaceae | Kanphuti | Whole plant | Acetaminophen (methanol and petroleum ether extracts-pretreatment) | Flavone, aglycones, triterpinoids, glycosides, carbohydrates, fatty acids, volatile ester sterol, saponins, flavonoids, tannin | Antimalarial, antifilarial, antiparasitic, antipyretic, anti-inflammatory, antianxiety, antiulcer activity, antihyperglycemic activity | [114, 129] |
| 14. | *Cassia auriculata* | Fabaceae | Ranawara, Avartaki, Adaari | Roots | Cisplatin (ethanol extract-post treatment) Gentamicin (ethanol extract-both pre and post treatment) | Tannins, Di-(2 ethyl) hexyl phthalate, alkaloids, resins, $Ca^{2+}$ and phosphorous | Antioxidant and free radical scavenging property | [10, 41, 42, 114] |
| 15. | | | | Fruits | Gentamicin (aqueous extract-post treatment) | | | |
| 16. | *Crataeva nurvala* | Capparidaceae | Varuna | Stem bark | Cisplatin (ethanol extract-pretreatment) | Kaemferol-3-O-a-D-glucoside, quercitin3-O-a-D-glucoside, flavanoids, glucosinolates, steroids, lupeol, tannins | Diuretic, anti-inflammatory, antioxidant, cardio-protective, hepatoprotective, lithonotriptic, anti-rheumatic, anti-periodic, contraceptive, antiprotozoal, rubifacient, vesicant | [113, 114, 130] |
| 17. | *Indigofera barberi* Linn. | Fabaceae | Thummajalari | Whole plant | Paracetamol (ethanol extract) | Glycosides, carbohydrates, flavonoids, tannins & phenols, steroids, triterpenoids, tannins, phenols. | Nephroprotective, hepatoprotective activity | [113, 134, 135] |
| 18. | *Ficus religiosa* | Moraceae | Pepal | Bark | Cisplatin (methyl alcohol extract-both pre and post treatment) | tannin, saponin, gluanol acetate, βsitosterol, leucopelargonidin-3-O -β-D-glucopyranoside, leucopelargonidin-3-O-α-L-rhamnopyranoside, lupeol, ceryl behenate, lupeol acetate, α-amyrin acetate, leucoanthocyanidin, leucoanthocyanin | Antitumor activity, anthelmintic activity, antimicrobial activity | [113, 114, 132] |
| 19. | *Ginkgo biloba* | Ginkgoceae | Maidenhair tree | Whole plant | Gentamicin (aqueous extract-concurrent administration) | Flavanoids, bilobalide, gingkolide A, gingkolide B, gingkolide C, biflanoide | Antioxidant effect | [41, 114] |

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**Table 2 South Asian medicinal plants investigated for nephroprotective activity in animal models (*continued*)**

| | Botanical name | Family | Local name | Part used | Screening method | Chemical constituents | Reported bioactivities | References |
|---|---|---|---|---|---|---|---|---|
| 20. | *Hemidesmus indicus* Linn. | Asclepiadaceae | Anantmool | Root | Gentamicin (aqueous extract-concurrent administration) | 2-hydroxy 4-methoxy benzaldehyde, fatty acids, saponin, tannins, resinal fractions, resin acids, sterols, β-sitosterol, stigmasterol, sarsapic acid, lupeol, vanillin, rutin | Anticancer, chemopreventive, immunomodulatory activity, wound healing activity, antiulcer activity, antioxidant and free radical scavenging activity, hepatoprotective activity, anti-inflammatory effect, diuretic, antihypergycemic effect, antimicrobial activity | [1, 116, 133] |
| 21. | *Eruca sativa* | Brassicaceae | Arugula | Seed | $HgCl_2$ (ethanolic extract-pretreated) | Glucosinolate, flavanoids, caratenoids | Antioxidant, astringent, diuretic, digestive | [113, 131] |
| 22. | *Murraya koenigii* | Rutaceae | Curry leaf plan | Leaves | Cyclophosphamide (methanol and aqueous extracts-concurrent administration) | Carbohydrates, flavonoids, tannins, alkaloids, glycosides, protein, steroid | Antioxidant and free radical scavenging activity, hypoglycemic, anti-cancer, hepatoprotectve | [136] |
| 23. | *Moringa oleifera* M. | Moringaceae | Malunggay | Seed | Sodium fluoride (aqueous extract-concurrent administration) | Carotene, nicotic acid, ascorbic acid, amino acid | Hypotensive, anticancer, antibacterial activities | [3] |
| 24. | *Nigella sativa* | Ranunculaceae | Black seed | Seed | Gentamicin (oil-post treatment) | Alanine, L-spinasterol, arabic acid, arginine, aminoacid, aspargine, aspartic acid, carvone, cystine, cholesterol, glutamic acid, linoleic acid, melanthin, myristic acid, oleic acid, tannins | Diuretic, antihypertensive, antidiabetic, anticancer and immunomodulatory, analgesic, antimicrobial, anthelmintics, analgesics and anti-inflammatory, spasmolytic, bronchodilator, gastroprotective, hepatoprotective, renal protective, and antioxidant properties. | [41, 114, 137] |
| 25. | *Orthosiphon stamineus* | Lamiaceae | Cat's whiskers | Leaves | Gentamicin (methanol extract-post treatment) | Flavonoids, polyphenols, carbohydrates, steroids, tannins, glycosides, terpins, saponins | Anti-inflammatory, anti- bacterial, diuretic, hypoglycemic activity, antihypertensive activities | [41, 115, 117, 138, 139] |

**Table 2 South Asian medicinal plants investigated for nephroprotective activity in animal models (*continued*)**

| | Botanical name | Family | Local name | Part used | Screening method | Chemical constituents | Reported bioactivities | References |
|---|---|---|---|---|---|---|---|---|
| 26. | *Paeonia emodi* Royle | Paeoniaceae | Ood-saleeb | Root | Streptozotozin (alcohol and hydroalcohol extracts-post treatment) | Monoterpene glycosides, monoterpene galactosides, triterpene, 1,5-dihydroxy-3-methyl-anthraquinone, ethylgallate, methyl grevillate | b-glucouronidase inhibitory activity, lipoxygenase inhibiting activity, hydroxyl radical scavenging activity, neuroprotection, anticonvulsant activity | [117] |
| 27. | *Pedalium murex* Linn | Pedaliaceae | Gokhru | Fruit | Cisplatin (ethanol extract-post treatment) | Flavanoids, flavones, alkaloids, titerpenoids, carbohydrates, glycosides, saponins | Diuretic, analgesic and antipyretic activities, antioxidant activity | [41, 140, 141] |
| 28. | *Pongamia pinnata* | Papilionaceae | Magul karanda, Indian beach | Flower | Cisplatin (ethanol extract-post treated) | Flavonoids, pongamol, protien, alkaloids, tannins, sugar, resin, fatty oil | Antioxidant | [4, 41, 114, 126] |
| 29. | *Salviae radix* | Lamiaceae | Red sage | Whole plant | Cisplatin (methanol extract-post treatment) | Salvianolic acid –G, rosmarinic acid, lithospermic acid, isoferulic acid, tanshinone I, IIA, IIB | Antioxidant | [4, 41, 114, 142] |
| 30. | *Sesamum indicum* Linn. | Pedaliaceae | Sesame | Seed | Streptozotocin induced diabetic rats-ethanol extract-post treated | Tocopherols, phytosterols, resveratrol, flavonoids, lignans sesamin, and sesamolin. | Laxative, emollient and demulcent, protect the liver from oxidative damage, antibacterial, anti-fungal, antiviral and anti-inflammatory, analgesic activity | [1, 143, 144] |
| 31. | *Tectona grandis* Linn. | Verbenaceae | Teak | Bark | Alloxan induced diabetes (ethanol extract-post treatment) | Calcium, phosphate, silica ammonium | Antiulcer, antimicrobial, wound healing, anticancer activity | [145] |
| 32. | *Tribulus terrestris* | Zygophyllaceae | Gokshura | Fruits | Gentamicin (aqueous extract-post treatment) | Saponine, diosgenine, gitogenine, flaonoids, alkaloid | Diuretic | [46, 50, 117] |
| 33. | *Withania somnifera* | Solanaceae | Ashwagandha | Root | Gentamicin (aqueous extract-concurrent administration) | Alkaloids, withaminon, wasamin, sugars, glycosides, aminoacids, essential oils, withaniol, phytosterol, oils | Antioxidant activity | [1, 41, 116] |

Gentamicin was administered to induce renal toxicity. Coadministration of the polyherbal mixture at three selected doses resulted in reverting changes in biochemical parameters. The protective effect was found increased with the increased dose of the mixture. Assessment of histopathology revealed the features of tubular necrosis, increased urinary space, loss of epithelial lining, and inconspicuous nucleoli in the nephrotoxic control group. However, the highest dose of the polyherbal mixture resulted in restoration of the changes induced by gentamicin in the animal model. Further, the polyherbal preparation has shown relatively

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high antioxidant activity in the kidney tissues [8].

Moreover, the protective role of the aged garlic extract (AGE), which works as an antioxidant, has been investigated on gentamicin induced nephrotoxicity in male Wistar rats. Pretreatment with the AGE at a dose of 1.2 mL/kg every 12 hours ameliorated the changes in biochemical parameters and histopathology induced by gentamicin, suggesting the use of AGE for the prevention of gentamicin induced nephrotoxicity [114].

Similar studies have been used for evaluation of the nephroprotective effect of compounds isolated from medicinal plants, and increasingly more attention has been given to the use of phytochemicals as a protective strategy against nephrotoxicity [146]. A major turning point was the demonstration of nephroprotective potential for phenolic compounds, including flavonoids [146]. Table 3 depicts such phytoconstituents/ compounds isolated from South Asian medicinal plants with proven nephroprotective effects against nephrotoxicity tested in animal models.

**In vitro assessment of nephroprotective activity**

Based on the ethical concerns and the "3R" principle: reduction, replacement, and refinement, more attention

**Table 3 Nephroprotective secondary metabolites from South Asian medicinal plants against nephrotoxicity in animal models**

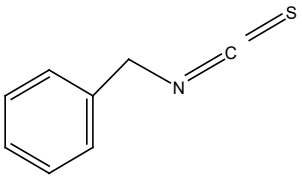
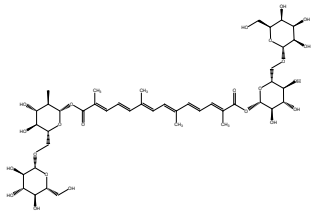
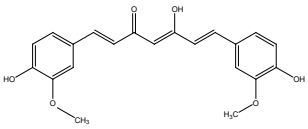
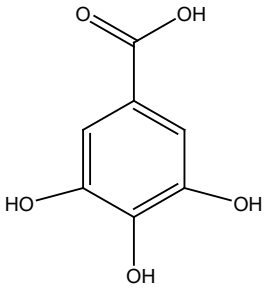
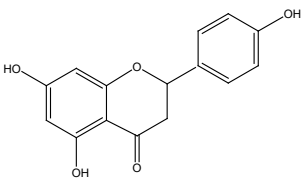
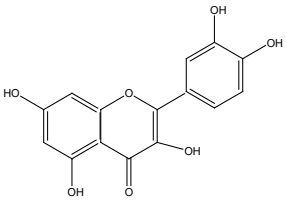
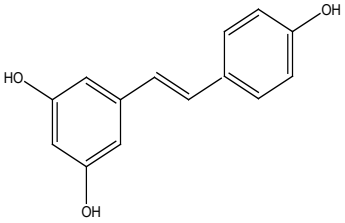
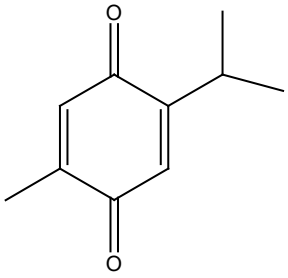
| | Secondary metabolite | Chemical name (IUPAC name) | Plant source | Animal model | Chemical structure | References |
|---|---|---|---|---|---|---|
| 1 | Benzyl isothiocyanate | (Isothiocyanatomethyl) benzene | Cruciferous vegetables | Cisplatin induced nephrotoxicity in Swiss Albino mice |  | [147] |
| 2 | Crocin (carotenoid pigment) | Bis [(2S, 3R, 4S, 5S, 6R) 3, 4, 5 trihydroxy-6 ({[(2R,3R,4S,5S,6R) 3,4,5-trihydroxy6 (hydroxymethyl) tetrahydro-2H-pyran-2yl]oxy} methyl) tetrahydro-2Hpyran-2-yl] (2E, 4E, 6E, 8E, 10E, 12E, 14E) 2, 6, 11, 15-tetramethyl2, 4, 6, 8, 10, 12, 14hexadeca heptaenedioate | *Crocus sativus* L. | Cisplatin induced nephrotoxicity in Wistar albino rats |  | [148, 149] |
| 3 | Curcumin | (1E, 6E)-1, 7-Bis (4hydroxy-3methoxyphenyl)-1, 6heptadiene-3, 5-dione | *Curcuma longa* | Adriamycin induced nephrotoxicity in Wistar rats |  | [148, 150] |
| 4 | Gallic acid | 3, 4, 5-trihydroxybenzoic acid | *Peltiphyllum peltatum* | NaF-intoxicated Wistar rats |  | [151] |
| 5 | Naringenin (bioactive flavonoid) | 5, 7-dihydroxy-2-(4-hydroxyphenyl) chroman-4-one | Citrus fruits | Low-dose streptozotocin induced damage in mice |  | [152] |

**Table 3 Nephroprotective secondary metabolites from South Asian medicinal plants against nephrotoxicity in animal models (*continued*)**

| | Secondary metabolite | Chemical name (IUPAC name) | Plant source | Animal model | Chemical structure | References |
|---|---|---|---|---|---|---|
| 6 | Quercetin (polyphenolic flavonoid) | 2-(3, 4-dihydroxyphenyl) 3, 5, 7-trihydroxy-4Hchromen-4-one | *Cassia auriculata*, *Phoenix dactylifera* L., *Ramulus mori* | Gentamicin induced nephrotoxicity in Wistar albino rats |  | [148, 153] |
| 7 | Resveratrol (polyphenolic phytoalexin) | 5-[(E)-2-(4hydroxyphenyl) ethenyl] benzene-1, 3diol | Grapes and berries | Cisplatin induced nephrotoxicity in Swiss Albino mice |  | [147, 148] |
| 8 | Thymoquinone | 2-Isopropyl-5methylbenzo-1, 4-quinone | *Nigella sativa* | Cisplatin and gentamicin induced nephrotoxicity in rats |  | [137, 148] |

has been recently directed toward in vitro cell-based studies for the discovery of new therapeutic candidates. Accordingly, a number of studies have been conducted on the therapeutic efficacy of medicinal plants in kidney diseases using different cell lines such as human renal proximal tubule cells HK-2, pig kidney epithelial cells LLC-PK1, and human embryonic kidney cells HEK293, in different nephrotoxicity models [154]. The nephroprotective effect was assessed by the measurement of cell viability through 3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium bromide (MTT) bioassay in most of the studies [146]. *Scoparia dulcis* Linn. (Scrophulariaceae) is one such South Asian medicinal plant for which nephroprotective activity was determined by MTT assay in HEK 293 against gentamycin-induced nephrotoxicity [155]. However, sparse evidence is available for the in vitro assessment of nephroprotective medicinal plants of South Asian origin.

## Conclusion

Medicinal plants used in traditional systems of medicine have become valuable sources of knowledge for modern medicine. This plant-based knowledge serves as a powerful search engine as well as a facilitator for the discovery of novel drugs. Accordingly, a large number of research studies are being conducted on medicinal plants native to the South Asian region, in combination with modern technology for the discovery of nephroprotective agents. The discoveries will be beneficial in the near future in the clinical arsenal of medicine, especially for patients with limited access to use expensive Western systems of medicine. Further, these findings will be advantageous for developing nutraceuticals with high nephroprotective effects in the management of CKD.

## References

1. Chand MG, Chand T. A Critical review on commonly used herbal drugs in CKD. J Med Plants Stud 2015, 3: 44–47.
2. Srivastava AK, Kaushik D, Shrivastava AK, et al. Nephroprotective ethno-medicinal action of selected Indian medicinal plants. Int J Pharm Sci Drug Res 2017, 8: 11–24.
3. Talele BD, Mahajan RT, Chopda MZ, et al. Nephroprotective plants: a review. Int J Pharm Pharm Sci 2012, 4: 8–16.
4. Gaikwad K, Dagle P, Choughule P, et al. A review on some nephroprotective medicinal plants. Int J Pharml Sci Res 2012, 3: 2451–2454.
5. Gogtay NJ, Bhatt HA, Dalvi SS, et al. The use and

TMR
doi: 10.12032/TMR20200603189

safety of non-allopathic Indian medicines. Drug Saf 2002, 25: 1005–1019.
6. World Health Organization [Internet]. Traditional medicine in Asia [cited 11 March 2020]. Available from: http://origin.searo.who.int/entity/medicines/documents/traditional_medicines_in_asia.pdf.
7. Sheehan HE, Hussain SJ. Unani tibb: history, theory, and contemporary practice in south Asia. Ann Am Acad Political Soc Sci 2002, 583: 122–135.
8. Chopda MZ, Talele D, Mahajan NG, et al. Nephroprotective study of polyherbal formulation in drug induced nephrotoxic rats. Int J Appl Res 2017, 3: 243–246.
9. Ahmad QZ, Jahan N, Ahmad G. An appraisal of nephroprotection and the scope of natural products in combating renal disorders. J Nephrol Ther 2014, 4: 4–10.
10. Jayaweera DMA. Medicinal plants (indigenous and exotic) used in Ceylon. Monog Collect 1980, 3:110–111.
11. Institute of Ayurveda and Alternative Medicine [Internet]. Ayurvedic medicinal plants of Sri Lanka [cited 11 March 2020]. Available from: http://www.instituteofayurveda.org/plants/plants_search.php.
12. Ene-iordache B, Perico N, Bikbov B, et al. Chronic kidney disease and cardiovascular risk in six regions of the world (ISN-KDDC): a cross-sectional study. Lancet Glob Health 2016, 4: 307–319.
13. Pugsley D, Norris KC, Garcia-garcia G, et al. Global approaches for understanding the disproportionate burden of chronic kidney disease. Ethnic Dis 2009, 19: S1-1–S1-2.
14. Gomes M, Mastroianni G. Chronic kidney disease: importance of early diagnosis, immediate referral and structured interdisciplinary approach to improve outcomes in patients not yet on dialysis. Braz J Nephrol 2011, 33: 74–87.
15. Rukhaimi M Al, Sahow A Al, Boobes Y, et al. Adaptation and implementation of the "kidney disease: improving global outcomes (KDIGO)" guidelines for evaluation and management of mineral and bone disorders in chronic kidney disease for practice in the middle east countries. Saudi J Kid Di Transpl 2014, 25: 133–148.
16. Mishra SR, Adhikari S, Sigdel MR, et al. Chronic kidney disease in south Asia. Lancet Glob Health 2016, 4: e523.
17. Jha V. Current status of chronic kidney disease care in Southeast Asia. Semi Nephrol 2009, 29: 487–496.
18. Abraham G, Varughese S, Thandavan T, et al. Chronic kidney disease hot spots in developing countries in South Asia. Clin Kidney J 2016, 9: 135–141.
19. Rafieian-kopaei M. Medicinal plants for renal injury prevention. J Renal Injury Prev 2013, 2: 63–65.
20. Oluyombo R, Ayodele OE, Akinwusi PO, et al. Awareness, knowledge and perception of chronic kidney disease in a rural community of South-West Nigeria. Nigerian J Clin Pract 2016, 19: 161–169.
21. Wijetunge S, Ratnatunga NVI, Abeysekera TDJ, et al. Endemic chronic kidney disease of unknown etiology in Sri Lanka: correlation of pathology with clinical stages. Indian J Nephrol 2015, 25: 274–280.
22. Das S, Vasudeva N, Sharma S. Kidney disorders and management through herbs: a review. J Phytochem 2019, 8: 21–27.
23. Cerbo AD, Iannitti T, Guidetti G, et al. A nutraceutical diet based on *Lespedeza spp*., *Vaccinium macrocarpon* and *Taraxacum officinale* improves spontaneous feline chronic kidney disease. Physiol Rep 2018, 6: e13737.
24. Ash S, Campbell KL, Bogard J, et al. Nutrition prescription to achieve positive outcomes in chronic kidney disease: a systematic review. Nutrients 2014, 6: 416–451.
25. Levin A, Stevens PE, Bilous RW, et al. Kidney disease: improving global outcomes (KDIGO) CKD work group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney Int Supp 2013, 3: 1–150.
26. Nikolaidou B, Katsiki N, Lazaridis A, et al. The effects of nutraceuticals in patients with or without chronic kidney disease: classification matters. Open Hypertens J 2013, 5: 35.
27. Riccio E, Nuzzi AD, Pisani A. Nutritional treatment in chronic kidney disease: the concept of nephroprotection. Clin Exp Nephrol 2015, 19: 161–167.
28. Medscape [Internet]. 2018. Chronic kidney disease treatment and management [cited 11 March 2020]. Available from: https://emedicine.medscape.com/article/238798.
29. Akyol AD, Yildirim Y, Toker E, et al. The use of complementary and alternative medicine among chronic renal failure patients. J Clin Nurs 2011, 20: 1035–1043.
30. Shamsuddin N, Gnanasan S, Karuppanan M, et al. Complementary and alternative medicine (CAM) in chronic kidney disease (CKD): more evidence needed. Altern Integr Med 2016, 5:4–5.
31. Ravishankar B, Shukla VJ. Indian systems of medicine: a brief profile. Afr J Tradit Complement Altern Med 2007, 4: 319–337.
32. Chaudhary A, Singh N. Contribution of World Health Organization in the global acceptance of Ayurveda. J Ayurveda Int Med 2011, 2: 179–186.
33. Zyoud SH, Al-jabi SW, Sweileh WM, et al. Use of complementary and alternative medicines in haemodialysis patients: a cross-sectional study

from Palestine. BMC Complement Altern Med 2016, 16: 204.
34. Combest W, Newton M, Combest A, et al. Effects of herbal supplements on the kidney. Urol Nurs 2005, 25: 381–387.
35. Rahmatullah M, Jahan R, Khatun MA, et al. A pharmacological evaluation of medicinal plants used by folk medicinal practitioners. Am Eurasian J Sustain Agric 2010, 4: 170–195.
36. Ghayur MN, Janssen LJ. Nephroprotective drugs from traditionally used Aboriginal medicinal plants. Kidney Int 2010, 77: 470–471.
37. Swathi N, Sreedevi A, Bharathi K. Evaluation of nephroprotective activity of fruits of Ficus hispida on cisplatin-induced nephrotoxicity. Pharmacogn J 2011, 3: 62–68.
38. Vaidya ADB, Devasagayam TPA. Current status of herbal drugs in India: An overview. J Cli Biochem Nutr 2007, 41: 1–11.
39. Ali SS, Kasoju N, Luthra A, et al. Indian medicinal herbs as sources of antioxidants. Food Res Int 2008, 41: 1–15.
40. Bi W, Gao Y, Shen J, et al. Traditional uses, phytochemistry, and pharmacology of the genus Acer (maple): a review. J Ethnopharmacol 2016, 189: 31–60.
41. Jose S, Sreedevi A. A review on medicinal plants possessing nephroprotector activity. Int J Pharm 2015, 4: 191–196.
42. Swati P, Rajashekhar I. Role of pants as nephroprotective agents—a review. Int J Ther Appl 2015, 26: 6–14.
43. Zinkel DF, Evans BB, Service F. Terpenoids of *Pinus strobus cortex* tissue. Phytochemistry 1972, 11: 3387–3389.
44. Muhammad A, Haddad PS, Durst T, et al. Phytochemical constituents of *Sarracenia purpurea* L. (pitcher plant). Phytochemistry 2013, 94: 238–242.
45. Reine GBS, Houndékon BP, Marcelline G, et al. Phytochemical composition and antioxydant capacity of *Abelmoschus esculentus* L. fresh immature fruits. Am J Food Sci Food Sci Technol 2018, 6: 223–227.
46. Hussain AZ, Kumaresan S. Phytochemical and antimicrobial evaluation of *Abrus precatorius* L. Asian Pac J Cancer Prev 2014, 4: 10–14.
47. Roqaiya M, Begum W, Jahufe R. *Acacia arabica* (Babool)-a review on ethnobotanical and Unani traditional uses as well as phytochemical and pharmacological properties. Int J Pharm Phytopharmacol Res 2015, 4: 315–321.
48. Farzana MUZN, Tharique IAL, Sultana A. A review of ethnomedicine, phytochemical and pharmacological activities of Acacia nilotica (Linn) willd. J Pharmacogn Phytochem 2014, 3: 84–90.
49. Lakshmi T, Aravind Kumar S. Preliminary phytochemical analysis and in vitro antibacterial activity of *Acacia catechu willd bark* against *Streptococcus* mitis, *Streptococcus* sanguis and *Lactobacillus* acidophilus. Int J Phytomedicine 2011, 3: 579–584.
50. Georgieva L, Gadjalova A, Mihaylova D, et al. *Achillea millefolium* L.—phytochemical profile and in vitro antioxidant activity. Int Food Res J 2015, 22: 1347–1352.
51. Souza TM, Rangel VLBI, Pietro RCLRr, et al. Phytochemical screening of Achillea millefolium harvested at Araraquara—SP. Braz J Med Plants 2006, 8: 151–154.
52. Mengane SK. Phytochemical analysis of *Adiantum lunulatum*. Int J Curr Microbiol Appl Sci 2016, 5: 351–356.
53. Venkateshwarlu R, Raju AB, Yerragunta VG. Phytochemistry and pharmacology of *Alangium salvifolium*: a review. J Pharm Res 2011, 4: 1423–1425.
54. Dalhat MH, Adefolake FA, Musa M. Nutritional composition and phytochemical analysis of aqueous extract of *Allium cepa* (onion) and *Allium sativum* (garlic). Asian Food Sci J 2018, 3: 1–9.
55. Ogbonna OJ, Udia PM, Abe PN, et al. Phytochemical and proximate analysis, mineral and vitamin compositions of *Allium Cepa bulb extract*. Adv Biomed pharma 2016, 3: 181–186.
56. Jhade D, Ahirwar D, Jain R, et al. Pharmacognostic standardization, physico-and phytochemical evaluation of *Amaranthus spinosus* Linn. root. J Young Pharm 2011, 3: 221–225.
57. Dubey R, Shaikh S, Dhande S, et al. Anogeissus latifolia-an overview. Res J Pharmacogn Phytochem 2012, 4: 287–290.
58. Biba VS, Lakshmi S, Dhanya GS, et al. Phytochemical analysis of *Annona squamosa seed extracts*. Int Res J Pharm Appl Sci 2013, 3: 29–31.
59. Marka R, Talari S, Penchala S, et al. Preliminary phytochemical analysis of leaf, stem, root and seed extracts of *Arachis hypogaea* L. Int J Pharm Sci Rev Res 2013, 20: 134–139.
60. Al-Snafi AE. The pharmacological importance and chemical constituents of *Arctium lappa*. A review. Int J Pharm Res Scholars 2014, 3: 663–670.
61. Asha Rani NS, Prasad MP. Comparison studies on callus induction of fresh and reused explants of *Atropa belladonna*. Asian J Plant Sci Res 2014, 4: 50–53.
62. Ramadass N, Subramanian N. Study of phytochemical screening of neem (*Azadirachta indica*). Int J Zoo Stud 2018, 3: 209–212.
63. Singh V, Patel JR, Tyagi LK, et al. Antimicrobial activity and phytochemical analysis of stem bark of *Balanites roxburghii* Planch. Acad J Plant Sci 2009, 2: 109–112.
64. Bijekar SR, Gayatri MC, Rajanna L. Phytochemical profile of *Baliospermum*

TMR
doi: 10.12032/TMR20200603189

*montanum* (Wild.) Muell. Arg. Int J Innov Sci Res 2014, 12: 37–42.
65. Thamizharasan S, Umamaheswari S, Rajeswari Hari, et al. Quantitative phytochemical analysis of *Bambusa arundinacea* seeds. Int J Pharmacogn Phytochem Res 2015, 7: 980–983.
66. Kapoor A, Shukla S, Kaur R, et al. Preliminary phytochemical screening and antioxidant activity of whole plant of *Barleria prionitis* Linn. Int J Adv Pharm Biol Chem 2014, 3: 410–419.
67. Tongco JVV, Añis AD, Tamayo JP. Nutritional analysis, phytochemical screening, and total phenolic content of *Basella alba* leaves from the Philippines. Int J Pharmacogn Phytochem Resh 2015, 7: 1031–1033.
68. Rana S, Suttee A. Phytochemical investigation and evaluation of free radical scavenging potential of *Benincasa hispida peel* extracts. Int J Curr Pharml Res 2012, 3: 43–46.
69. Ahmed MF, A. Rao S, Ahemad SR, et al. Phytochemical studies and antioxidant activities of *Brassica oleracea* L. var. capitata. Int J Pharm Pharm Sci 2012, 4: 374–378.
70. Sahu M, Verma D, Harris KK. Phytochemical analysis of the leaf, stem and seed extracts of *Cajanus cajan* L (dicotyledoneae: Fabaceae). World J Pharm Pharmaceut Sci 2014, 3: 694–733.
71. Nancy P, Ashlesha V. Pharmacognostic and phytochemical studies of *Cassia absus seed extracts*. Int J Pharm Pharm Sci 2016, 8: 325–332.
72. Joshua OO, Elijah P, Nkechi EJ. Phytochemical analyses of *Cocos nucifera* L. Arch Pharm Sci Res 2009, 1: 87–96.
73. Jamkhande PG, Barde SR, Patwekar SL, et al. Plant profile, phytochemistry and pharmacology of *Cordia dichotoma* (Indian cherry): a review. Asian Pac J Trop Biomed 2013, 3: 1009–1012.
74. Agrahari AK, Panda SK, Meher A, et al. Phytochemical screening of *Curculigo orchioides* Gaertn. root tubers. J Chem Pharm Res 2010, 2: 107–111.
75. Deore SR, Namdeo AG. Pharmacognostic investigation of *Cynodon dactylon* Pers roots. Pharmacogn J 2014, 6: 1–6.
76. Sivapalan SR, Jeyadevan P. Physio–chemical and phyto-chemical study of rhizome of *Cyperus rotundus* Linn. Int J Pharm Pharm Technol 2012, 1: 42–46.
77. Muthusamy A, Punitha M, Beslin LG. Phytochemical screening of *Datura metel* Linn and its antimicrobial activity on selected human pathogens. Int J Bioassays 2014, 3: 3474–3478.
78. Chatatikun M, Chiabchalard A. Phytochemical screening and free radical scavenging activities of orange baby carrot and carrot (*Daucus carota* Linn.) root crude extracts. J Chem Pharm Res 2013, 5: 97–102.
79. Shakila R, Arul Antony S, Gopakumar K. Phytochemical studies on *Desmostachya bipinnata* rootstock. Int J pharm bio sci 2015, 6: 305–310.
80. Al-Snafi AE. Phytochemical constituents and medicinal properties of *Digitalis lanata* and *Digitalis purpurea*—a review. Indo Ame J Pharm Sci 2017, 4: 225–234.
81. Alok S, Jain SK, Verma A, et al. Pharmacognostic and phytochemical evaluation of *Dolichos biflorus* Linn. Asian Pac J Trop Dis 2014, 4: 97–101.
82. Rajan A, Rajan AR, Philip D. Elettaria cardamomum seed mediated rapid synthesis of gold nanoparticles and its biological activities. Open Nano 2017, 2: 1–8.
83. Ahmed ZM, Eltayeb IM, Hamad AEH. Phytochemical screening and contractile activity of *Foeniculum vulgare* seeds on rat intestinal and uterine muscles. J Pharm Phytochem 2017, 6: 346–350.
84. Nayak BS, Rath AK, Pattnaik SC. Traditional use, toxicity study and phytochemical screening of *Gmelina arborea* roxb fruits. Int J Phytopharm Res 2015; 6: 78–81.
85. Kazeem MI, Abimbola SG, Ashafa AOT. Inhibitory potential of *Gossypium arboreum leaf extracts* on diabetes key enzymes, α-amylase and α-glucosidase. Bangladesh J Pharmacol 2013, 8: 149–155.
86. Dash PP, Mishra A, Chaturvedi D, et al. Search for an herbal medicine: anti-inflammatory activity of methanolic extract of *Haldina cordifolia*. J Pharm Phytochem 2015, 3: 79–82.
87. Adamu H, Ngwu RO. Phytochemical screening and antibacterial activities of *Hibiscus sabdariffa* L. leaf extracts. Nige J Chem Res 2015, 20: 46–52.
88. Hussain MS, Fareed S, Ali M. *Hygrophila auriculata* (K. Schum) Heine: ethnobotany, phytochemistry and pharmacology. Asian J Tradit Med 2010, 5:122–131.
89. Rao NB, SitaKumari O, Rajesh Goud G. Phytochemical analysis and antimicrobial activity of *Lawsonia inermis* (Henna). J Plant Sci Res 2016, 3: 158.
90. Rakholiya K, Kaneria M, Chanda S. Physicochemical and phytochemical analysis of different parts of Indian Kesar mango—a unique variety from Saurashtra region of Gujarat. Pharm J 2016, 8: 502–506.
91. Patil DB, Palshikar N, Patil SB, et al. Phytochemical investigation and antimicrobial activity of *Mentha arvensis* L. [Pudina]. World J Pharm Res 2015, 4: 1829–1834.
92. Ganesh I, Suhas P, Yash G, et al. Phytochemical screening and investigation of antibacterial and anticancer potential of *Michelia champaca* L. flowers. International Conference on Plant Research and Resource Management and 25th APSI Silver Jubilee Scientist Meet 2016, 345–353.
93. Ranjan RK, Kumar MS, Seethalakshmi I, et al.

Phytochemical analysis of leaves and roots of *Mimosa pudica* collected from Kalingavaram, Tamil Nadu. J Che Pharm Res 2013, 5: 53–55.
94. Bawara B, Dixit M, Chauhan NS, et al. Phyto-pharmacology of *Momordica dioica* Roxb. ex. Willd: a review. Int J Phytomed 2010, 2: 1–9.
95. Imam MZ, Akter S. *Musa paradisiaca* L. and *Musa sapientum* L.: a phytochemical and pharmacological review. J Appl Pharml Sci 2011, 1: 14–20.
96. Ullah H, Khan R, Shah GM, et al. Ethnomedicinal, phytochemical and nutritional analysis of *Nelumbium nucifera* Gaertn rhizome. MOJ Food Process Technol 2018, 6: 122–127.
97. Chetwani K, Agnihotri RK, Chaturvedi P. Aqueous, acetone and ethanolic extract of *Nerium indicum* L. as potential antibacterial agent against *Pseudomonosa* aeruginosa. Int J Appl Environ Sci 2017, 12: 1721–1732.
98. Paikara D, Singh S, Pandey B. Phytochemical analysis of leave extract of *Nyctanthes arbortristis*. IOSR J Environ Sci Toxicol Food Technol 2015, 1: 39–42.
99. Rai S, Ghosh H, Basheer M. Phytochemical characterization and antioxidative property of *Ocimum canum*: effect of ethanolic extract of leaves and seeds on basic immunologic and metabolic status of male rats. J Immunobiology 2016, 1: 1–7.
100. Mannan MA, Sarker TC, Rahman MM, et al. Screening of phytochemical compounds and antioxidant properties in local and HYV of Bangladeshi rice (*Oryza sativa* L.). Int J Biosci 2013, 3: 151–160.
101. Gunasekaran R, Usha M, Arunachalam G. Pharmacognostical and phytochemical evaluation of *Ougeinia oojeinensis* (Roxb) Hochr. bark. Int J Pharm Sci Res 2011, 2: 706–712.
102. Khushbu C, Anar P, Mayuree P, et al. *Paederia foetida* Linn. as a potential medicinal plant: a review. J Pharm Res 2010, 3: 3135–3137.
103. Kumar D, Kumar S, Kumar S, et al. Antimicrobial and preliminary phytochemical screening of crude leaf extract of *Pandanus odoratissimus* L. Pharmacologyonline 2010, 2: 600–610.
104. Danladi S, Idris MA, Umar II. Review on pharmacological activities and phytochemical constituents of *Phyllanthus niruri* (Amarus). J Phytopharmacol 2018, 7: 341–348.
105. Guankui Du, Xiao M, Yu S, et al. *Phyllanthus urinaria*: a potential phytopharmacological source of natural medicine. Int J Clin Exp Med 2018, 11: 6509–6520.
106. Gopinath SM, Rakesh CK, Murthy TPN, et al. Preliminary phytochemical evaluation of leaf extracts of *Gymnema sylvestre*, *Phyllanthus amarus*, *Phyllanthus reticulatus* of Siddarabetta, Tumkur district, Karnataka. Int J Pharm Phytochem Res 2012, 4: 109–111.
107. Nataraj HR, Hiremath SK. Pharmacognostic and phytochemical analysis of different market samples of Ashoka (*Saraca indica* Linn). Anc Sci Life 2009, 29: 7–11.
108. Sharma V, Hem K, Seth A, et al. *Solanum indicum* Linn.: an ethnopharmacological, phytochemical and pharmacological review. Curr Res J Pharm All Sci 2017, 1: 1–9.
109. Joshi BC, Mukhija M, Kalia AN. Pharmacognostical review of *Urtica dioica* L. Int J Green Pharm 2014, 201–209.
110. Manva MN, Desai TR. *Vernonia anthelmintica* Willd.: an overview on phytopharmacological properties. Invent Rapid Ethnopharmacol 2012, 4: 1–4.
111. Saad KJ. Phytochemical investigation of fruits and seeds of grape (*Vitis vinifera* L.) grown in Iraq. Int J Pharm Sci Rev Res 2017, 42: 65–66.
112. Sharma VK, Tiwari M, Chauhan NS, et al. Phytochemical investigation on the ethanolic extract on the leaves of *Zizyphus xylopyrus* (Retz.) Willd. In J Agron Plant Pro 2012, 3: 26–37.
113. Chatterjee P, Chakraborty B, Nandy S. Review on nephroprotective activity study by different plant extract. Adv J Pharm Life Sci Res 2014, 2: 24–40.
114. Vaya RK, Sharma A, Singhvi IJ, et al. Nephroprotective Plants: a review. Bio Sci Technol 2017, 8: 801–812.
115. Padhye MR, Jogdand SD, Bhattacharjee J. Evaluation and comparison of nephroprotective effect of *Hemidesmus indicus* Linn. and *Withania somnifera* Linn. on gentamicin induced nephrotoxicity in Albino rats. Int J Basic Clin Pharm 2018, 7:691–695.
116. Kannappan N, Madhukar A, Sindhura PU, et al. Evaluation of nephroprotective activity of *Orthosiphon stamineus benth extract* using rat model. Int J Pharm Tech Res 2010, 2: 209–215.
117. Sarshar S, Brandt S, Asadi Karam MR, et al. Aqueous extract from *Orthosiphon stamineus* leaves prevents bladder and kidney infection in mice. Phytomedicine 2017, 15: 1–9.
118. Lakshmi MS, Reddy UT, Kumar ACK, et al. Protective effect of *Abutilon indicum* L. (Malvaceae) against cisplatin induced nephrotoxicity in rats. Inn J Life Sci 2013, 1: 35–39.
119. Srivastav S, Singh P, Jha KK, et al. Diuretic activity of whole plant extract of *Achyranthes aspera* Linn. Inn J Life Sci 2011, 1: 97–102.
120. Palani S, Raja S, Praveen Kumar R, et al. Therapeutic efficacy of *Acorus calamus* on acetaminophen induced nephrotoxicity and oxidative stress in male albino rats. Acta Pharm Sci 2010, 52: 89–100.
121. Kore KJ, Shete RV, Jadhav PJ. RP-HPLC method of simultaneous nephroprotective role of A.

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doi: 10.12032/TMR20200603189

marmelos extract. Int J Res Pharm Chem 2011, 1: 617–623.
122. Movaliya V, Khamar D, Setty MM. Nephroprotective activity of aqueous extracts of *Aerva javanica* roots in cisplatin induced renal toxicity in rats. Pharmacologyonline 2011, 1: 68–74.
123. Asif M. A review on various medicinal plants with for nephroprotective activity. Int J Rec Adv Bio Nanotechnol 2018, 1: 1–29.
124. Chatterjee P, Mukherjee A, Nandy S. Protective effects of the aqueous leaf extract of *Aloe barbadensis* on gentamicin and cisplatin-induced nephrotoxic rats. Asian Pac J Trop Bio 2012, S1754–S1763.
125. Rao V, Arunachalam R, Eerike M, 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: 347–354.
126. Sharma RK, Rajani GP, Sharma V, et al. Effect of ethanolic and aqueous extracts of *Bauhinia variegata* Linn. on gentamicin-induced nephrotoxicity in rats. Indian J Pharm Educ Res 2011, 45: 192–198.
127. Cordeiro MC, Kaliwal BB. Hepatoprotective and nephroprotective activity of bark extract of *Bridelia retusa* Spreng in CCL4 treated female mice. Int J Mol Bio 2011, 2: 22–30.
128. Tatiya A, Saluja A, Kalaskar M, et al. Phytochemical characterization and anti-inflammatory activity of *Bridelia retusa* bark Spreng. in acute and chronic inflammatory conditions: a possible mechanism of action. Eur J Pharm Med Res 2017, 4: 686–696.
129. Parameshappa B, Basha SA, Sen S, et al. Acetaminophen-induced nephrotoxicity in rats: protective role of *Cardiospermum halicacabum*. Pharml Bio 2012, 50: 247–253.
130. Shelkea TT, Bhaskarb VH, Adkara PP, et al. Nephroprotective activity of ethanolic extract of stem barks of *Crataeva nurvula* Buch Hum. Int J Pharm Sci Res 2011, 2: 2712–2717.
131. Alam MS, Kaur G, Jabbar Z, et al. Eruca sativa seeds possess antioxidant activity and exert a protective effect on mercuric chloride induced renal toxicity. Food Chem Toxicol 2007, 45: 910–920.
132. Yadav YC, Srivastava DN, Saini V, et al. Experimental studies of *Ficus religiosa* (L) latex for preventive and curative effect against cisplatin induced nephrotoxicity in Wistar rats. J Chem Pharm Res 2011, 3: 621–627.
133. Banerjee A, Ganguly S. Medicinal importance of *Hemidesmus indicus*: a review on its utilities from ancient ayurveda to 20th century. Adv Biores 2014, 5: 208–213.
134. Reddy JSV, Rao DG. Evaluation of in vitro & in vivo antioxidant studies of whole plant of 70 % ethanolic extracts of *Indigofera barberi* Gah mbles. Int J Innov Pharm Sci Res 2014, 5: 378–388.
135. Srinivasan N, Sathyanarayana D. Pharmacognostical investigation of *Indigofera barberi* Gamble (Fabaceae)—a threatened medicinal herb. Hygeia J Drugs Med 2014, 6: 45–56.
136. Mahipal P, Pawar RS. Nephroprotective effect of *Murraya koenigii* on cyclophosphamide induced nephrotoxicity in rats. Asian Pac J Trop Med 2017, 10: 808–812.
137. Ahmad A, Husain A, Mujeeb M, et al. Review on therapeutic potential of *Nigella sativa*: a miracle herb. Asian Pac J Trop Biomed 2013, 3: 337–352.
138. Ramesh K, Manohar S, Rajeshkumar S. Nephroprotective activity of ethanolic extract of *Orthosiphon stamineus* leaves on ethylene glycol induced urolithiasis in Albino rats. Int J Pharm Tech Res 2014, 6: 403–408.
139. Kishore L, Kaur N, Singh R. Nephroprotective effect of Paeonia emodi via inhibition of advanced glycation end products and oxidative stress in streptozotocin-nicotinamide induced diabetic nephropathy. J Food Drug Anal 2016, 25: 576–588.
140. Jayanthy A, Deepak M, Remashree AB. Pharmacognostic characterization and comparison of fruits of *Tribulus terrestris* L. and *Pedalium murex* L. Int J Herb Med 2013, 1: 29–34.
141. Shelke TT, Kothai R, Adkar PP, et al. Nephroprotective activity of ethanolic extract of dried fruits of *Pedalium murex* Linn. Cell Tissue Res 2009, 9: 1687–1690.
142. Cheon J, Man W, Ho C, et al. *Salviae radix extract* prevents cisplatin-induced acute renal failure. Nephron 2001, 88: 241–246.
143. Bhuvaneswari P, Krishnakumari S. Nephroprotective effects of ethanolic extract of *Sesamum indicum* seeds (Linn.) in streptozotocin induced diabetic male albino rats. Int J Green Pharma 2012, 6: 330–335.
144. Anilakumar KR, Pal A, Khanum F, et al. Nutritional, medicinal and industrial uses of Sesame (*Sesamum indicum* L.) seeds-an overview. Agr Consp Sci 2010, 75: 159–168.
145. Ghaisas MM, Navghare VV, Takawale AR, et al. Antidiabetic and nephroprotective effect of *Tectona grandis* Linn. in alloxan induced diabetes. Ars Pharm 2010, 51: 195–206.
146. Kpemissi M, Eklu-Gadegbeku K, Veerapur VP et al. Antioxidant and nephroprotection activities of *Combretum micranthum*: a phytochemical, in-vitro and ex-vivo studies. Heliyon 2019, 5: e01365.
147. Ibrahim A, Al-Hizab FA, Abushouk AI et al. Nephroprotective effects of benzyl isothiocyanate and resveratrol against cisplatin-induced oxidative

stress and inflammation. Front Pharmacol 2018, 9: 1268.
148. Sundararajan R, Bharampuram A, Koduru R. A review on phytoconstituents for nephroprotective activity. Pharmacophore 2014, 5: 160–182.
149. Naghizadeh B, Mansouri SMT, Mashhadian, NV. Crocin attenuates cisplatin-induced renal oxidative stress in rats. Food Chem Toxicol 2010, 48: 2650–2655.
150. Venkatesan N, Punithavathi D, Arumugam V. Curcumin prevents adriamycin nephrotoxicity in rats. Br J Pharmacol 2000, 129: 231–234.
151. Nabavi SM, Habtemariam S, Nabavi SF et al. Protective effect of gallic acid isolated from *Peltiphyllum peltatum* against sodium fluoride-induced oxidative stress in rat's kidney. Mol Cell Biochem 2013, 372:233–239.
152. Rajappa R, Magesh SB, Sarvajayakesavulu S, et al. Nephroprotective effect of Naringenin against multiple low dose streptozotocin (MLDSTZ) induced renal damage in mice. Biomed Pharmacol J 2017, 10: 583–593.
153. Abdel-Raheem IT, Abdel-Ghany AA, Mohamed GA. Protective effect of quercetin against gentamicin-induced nephrotoxicity in rats. Biol Pharm Bull 2009, 32: 61–67.
154. Ma Z, Cao X, Guo X, et al. Establishment and validation of an in vitro screening method for traditional Chinese medicine-induced nephrotoxicity. Evid Based Complement Alternat Med 2018, 2018: 1–15.
155. Kumari V, Narayanan PK. An exploratory study to evaluate the nephro-protective effect of *Scopariadulcis.* Linn. ethanol extracts in gentamycin induced toxicity in HEK 293 cells. Int J Pharm Sci Rev Res 2017, 45: 11–13.