Kidney disorders and management through herbs: A Review

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ABSTRACT

Kidneys have a vital role in the normal physiology of humans. Worldwide chronic kidney disease has become a major cause for disability and in worst circumstances leads to death. Major renal disorders occur due to diabetes and its complications termed as diabetic nephropathy (DN). Also nephrolithiasis occurs due to presence of organic debris of carbohydrates, lipids and proteins and supersaturation with calcium oxalate in the renal system. The article comprises of various herbs proven to be used in management of these disorders

Keywords: Diabetes, diabetic nephropathy, kidney stone, herbs, chronic kidney disease (CKD).

INTRODUCTION

The important role of kidneys in normal physiology comprises plasma filtration of metabolic waste products, regulation of plasma volume, hormone secretion and acid-base balance. Any changes in the above indicators lead to a large number of diverse, life threatening renal diseases. Globally, the 12th cause of death in humans is due to chronic kidney disease (CKD) and leads to 17th cause of disability. People with CKD are more prone to cardiovascular disorders (CVD) rather than to reach end-stage renal disease (ESRD) [1]. Around 30% of diabetes mellitus patients (DM) fall ill with diabetic nephropathy (DN) and CKD incidence. According to the Diabetes Atlas 2006 (India), patient’s population with DM is presumed to rise to 69.9 million by 2025 in the absence of preventive measures [2]. “Screening and Early Evaluation of Kidney Disease” (SEEK), a voluntary health screening program which is community-based started in 2006 in India performed analysis of urine and serum creatinine of people. SEEK announced high prevalence of CKD approximately 17.4% applying a glomerular filtration (eGFR) formula. Indian CKD Registry states that diabetes (all types) is the cause of kidney disease in 30% of the patients enlisted in their studies. Just 20% of the ESRD registered patients are on some renal replacement therapies (RRT) [3]. The limitation of ESRD is that it is inpatient thus hospital-based and not an exact figure of population suffering from ESRD. The yearly incidences of ESRD in India is approximately 150–200 per million population (pmp) and Diabetes mellitus is an essential cause of CKD in around 30–40% of these patients [4]. It is evaluated that only 10–20% patients in India with ESRD carry out long-term RRT. In India 3,500 new kidney transplant take place annually, about 3,000 new continuous ambulatory peritoneal dialysis (CAPD) gets initiated and 15,000 new maintenance hemodialysis (MHD) patients [5].

Urine microalbuminuria, especially in patients with DM, is a first indicator in patients at risk of kidney disease well ahead the rise in gross proteinuria or elevated serum creatinine. Deviation in the level of GFR measured from serum creatinine indicates any kidney disease at an early stage [6]. Diabetic nephropathy can be explained with change in levels of microalbuminuria, succeeded by macroproteinuria and also reduction in GFR. Moreover, renal disease in DM can happen without excretion of protein in urine of patients with DM and kidney disorders [7]. Plasma filtration and most of tubular reabsorption occurs in renal cortex, an important functional portion of the kidney present in between the renal capsule and renal medulla, comprising of glomeruli, proximal and distal tubules. Among all studies renal pathologies, diabetic nephropathy (DN) is predominantly most common causes of renal insufficiency culminating in renal failure. DN is a generally a glomerular disorder but recent scientific literature have focused on the marked changes in tubulointerstitial parameters which strongly suggest that approaches concentrating only on either glomeruli or tubules are not sufficient for thorough knowledge of the pathophysiology of complicated renal diseases such as DN [8].
CKD is highly prevalent in south Asian population viz. India, Sri Lanka, Bangladesh and Pakistan, and black people due to higher rates of occurrence of diabetes in Asians and higher rates of increased blood pressure in Caribbean and African people. The socioeconomic status and ethnic origin of several communities in both higher and lower income countries are reason for their greater risk than others [9].

**DIABETIC NEPHROPATHY**

DN is a major complication mainly associated with type 2 diabetes that leads to ESRD. In India, DN is expected to develop in 6.6 million of the 30 million patients suffering from DM by 2030 [10]. DN is one of the major “microvascular” disorder related to diabetes. The renal lesions which develop in type 1 or 2 diabetes mellitus, are similar [11]. DN is characterized by an increase in various things viz. kidney size, urinary albumin excretion, glomerular volume and kidney function chased by the accumulation of glomerular extracellular matrix, glomerular sclerosis and tubular fibrosis. Proteinuria, hypertension, and progressive renal insufficiency indicate last-stage overt DN [12]. Diabetic kidney disease is reported in about 15%–25% of type I diabetes patients and 30%–40% of patients with type II diabetes. The pathophysiology of DN comprises of hyperfiltration and development of microalbum in urine which is followed by deterioration of kidney functions associated with extracellular and cellular disruption in both places that is glomerular and tubulo-interstitial regions of kidney [13]. It also includes hypertrophy/hyperplasia of glomerulus and the tubules, thickening of tubular basement membranes, thickening of glomerular, and expansion of tubulo-interstitial as well as mesangial compartments [14]. There are changes in hyalinization of arterioles, thickening of branches of intrarenal arteries which causes impairment in autoregulation of glomerular microcirculation, that could ultimately damage the kidney.

**KIDNEY STONE**

Renal colic is the first manifestation of renal stone disease. The formation of solid phases in urinary passages is described as “Nephrolithiasis”, whereas the accumulation and aggregation of salts in renal parenchyma is termed as “nephrocalcinosis”. Nephrocalcinosis is very common and can develop or cannot into nephrolithiasis. Formation of kidney stone is a complex process including chronic events, viz. crystal nucleation, its growth, aggregation, and crystal retention inside the renal tubules [13]. Adequate management of the patient can be done by (i) attenuating the pain; (ii) by favoring retention inside the renal tubules; (iii) by patient can be done by (i) attenuating the pain; (ii) by favoring retention inside the renal tubules; (iii) by preventing obstructive and infectious complications. Further consideration should be prevention of new stone formation and in some cases dissolution of stones only after acute episodes of pain have been managed completely. Therapeutic treatment involves use of opioids, nonsteroidal anti-inflammatory drugs (NSAIDs) and spasmolytics. Efficacy of available drugs is primarily dependent on individual response, though NSAID such as ketorolac, alone or in association with morphine, have given better results to reduce pain. Injections of Voveron/ Diclofenac are administered to patients with acute pain [16]. The chronic mild hyperoxaluria is primary cause of stone formation in humans. All crystals, accumulated salts and stones, which are spontaneously formed in humans, contain organic material viz. carbohydrates, lipids and proteins occluded within as well as on their surfaces for providing architectural integrity, otherwise the stone may crumble and disintegrate in particles. Thus, the interaction between crystals and organic material is very critical and important [15].

According to the chemical composition, kidney stones are classified into various types. As per the literature, calcium oxalate (CaOx) is predominant component of stones accounting for 80% or more of all stones found in kidney. The remaining 20% colics comprise struvite stone, cystine, uric acid, and other types of stones. Crystallization and subsequent lithogenesis happens with many solutes which are found in urine. Urine should be supersaturated with respect to the colic base material for formation into bigger crystals. Thus, lowering supersaturation is effective for preventing stone recurrence. Larger than 5 mm stones fail to pass through urine and need interventional by techniques such as ureteroscopy (URS), percutaneous nephrolithotomy (PNL) or extracorporeal shock wave lithotripsy (ESWL), for their removal from the body. As a result of excessive protein intake with CaOx stones, urinary acid excretion generally elevates. Hyperuricosuria reduces the solubility of calcium oxalate. It encourages formation of stone by heterologous nucleation on the surface of monosodium urate levels. One approach to avoid kidney stone formation is to stop retention of crystals. Reactive oxygen species (ROS) appear to be responsible for injury to renal cells, therefore a reduction in tissue oxidative stress could also be an effective therapeutic measure for recovery [17].

Thus, interdisciplinary research between pharmacologist, pharmacognostists and clinical investigators is essential to develop new plant-derived high potency, high-quality natural products to prevent or completely treat DN and renal colics. Dialysis and transplantation are the methods of management of ESRD. In developing countries, ethno-medicinal plants have traditionally been used for the treatment of diabetes as well as related complications. In fact, recent pre-clinical and clinical studies have confirmed beneficial effects of many plants on some or the other processes connected with reduced kidney functions in experimental animals [18, 19]. Some of the active phytochemicals are responsible for their potential activities. The therapeutic effect and pharmacological properties of few ethno-botanical herbs which have been used traditionally in the management of DN and urolithiasis have been established [Table 1].

**Table 1: Plants used in treatment of kidney disorders**

| Plant Name            | Common Name      | Family           | Plant part/ extract | Reference |
|-----------------------|------------------|------------------|---------------------|-----------|
| Aerva Javanica        | Dessert cotton   | Amaranthaceae    | Fresh roots         | [20]      |
| Aerva lanata          | Mountain knotgrass | Amaranthaceae    | Aerial plants       | [21]      |
| Aesculus hippocastanum| Horse chestnut   | Sapindaceae      | Seeds               | [22]      |
| Aloe barbadensis      | Aloe vera        | Asphodelaceae    | Leaf                | [23]      |
| Bauhinia variegata    | Kachnar          | Caesalpinaceae   | Stems               | [24]      |
| Carica papaya         | Papaya           | Caricaceae       | Seeds               | [25]      |
| Cassia auriculata     | Matara tea/ Tarwar | Fabaceae        | Roots               | [26]      |
| Ceratonia siliqua     | Carob            | Fabaceae         | Pods and leaves     | [27]      |
| Crataeva maravala     | Varuna           | Capparaceae      | Stem bark           | [28]      |
| Cucurbita pepo        | Pumpkin          | Cucurbitaceae    | Fruits              | [29]      |
| Cyclea peltata        | Rajpatha         | Menisperaceae    | Leaves              | [29]      |
| Plant Name                      | Common Name             | Family       | Part Used       | References |
|--------------------------------|-------------------------|--------------|-----------------|------------|
| Dichrostachys cinera           | Chinese lantern         | Mimosaceae   | Roots           | [30]       |
| Ficus religiosa                | Peepal                  | Moraceae     | Latex           | [31]       |
| Kigelia africana               | Sausage                 | Bignoniaceae | Maturated fruits | [32]       |
| Lepidium sativum               | Pepper Wort             | Cruciferae   | Seeds           | [33]       |
| Pedaliaceae                    | Bada gokhru             | Pedaliaceae  | Fruits          | [34]       |
| Picrorhiza kurroa              | Kutila                  | Scrophulariaceae | Rhizome    | [35]       |
| Silybum marianum               | Milk thistle            | Asteraceae   | Seeds           | [36]       |
| Veronia cinerea                | Sahadevi                | Compositae   | Aerial parts    | [37]       |
| Aegle marmelos                 | Wood apple              | Rutaceae     | Leaves          | [38]       |
| Aerva lanata                   | Mountain knotgrass      | Amaranthaceae| Whole plant     | [21]       |
| Orthosiphon stamineus          | Kidney tea              | Lamiaceae    | Whole plant     | [39]       |
| Strychnos potatorum            | Clearing nut            | Loganiaceae  | Seeds           | [40]       |
| Gentamicin induced nephrotoxicity |                        |              |                 |            |
| Aloe barbadensis               | Aloe vera               | Asphodelaceae| Leaves          | [23]       |
| Aegle marmelos                 | Wood apple              | Rutaceae     | Leaves          | [38]       |
| Aerva lanata                   | Mountain knotgrass      | Amaranthaceae| Whole plant     | [21]       |
| Orthosiphon stamineus          | Kidney tea              | Lamiaceae    | Whole plant     | [39]       |
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| Aerva lanata                   | Mountain knotgrass      | Amaranthaceae| Whole plant     | [21]       |
| Orthosiphon stamineus          | Kidney tea              | Lamiaceae    | Whole plant     | [39]       |
| Diabetic nephropathy           |                        |              |                 |            |
| Allium sativum                 | Garlic                  | Alliaceae    | Cloves          | [41]       |
| Andrographis paniculata        | Kalamegh                | Acanthaceae  | Roots           | [42]       |
| Astragalus membranaceus        | Milk vetch              | Fabaceae     | Roots           | [43]       |
| Berberis integerrima           | Barberry                | Berberidaceae| Roots           | [44]       |
| Brassica oleracea              | Red Cabbage             | Brassicaceae | Leaves          | [45]       |
| Camellia sinensis              | Green tea               | Theaceae     | Leaves          | [46]       |
| Cinnamomum zeylanicum          | Dalchini                | Lauraceae    | Oil             | [47]       |
| Curcuma longa                  | Turmeric                | Zingiberaceae| Curcumin        | [48]       |
| Ekebergia capensis             | Cape ash                | Meliaceae    | Leaves          | [49]       |
| Eugenia jambolana              | Black berry             | Myrtaceae    | Seeds           | [50]       |
| Ficus thomningii               | Blume                   | Moraceae     | Stem bark       | [51, 52]   |
| Foeniculum vulgare             | Fennel                  | Apiaceae     | Fruits          | [55]       |
| Fragaria × ananassa            | Strawberry              | Rosaceae     | Leaves          | [54]       |
| Ganoderma lucidum              | Mushroom                | Polyporaceae | Fruits          | [55]       |
| Ginkgo biloba                  | Maiden Hair             | Gikgosaceae  | Leaves          | [56]       |
| Glycyrrhiza uralensis          | Chinese liquorice       | Fabaceae     | Roots           | [57]       |
| Gongronema latifolium          | Amaranth globe          | Asclepiadaceae| Leaves        | [58]       |
| Gymnema montanum               | Bidaria Tingens Deche   | Asclepiadaceae| Leaves       | [19]       |
| Helianthus annuus              | Sunflower               | Asteraceae   | Leaves          | [60]       |
| Helichrysum ceres              | Beentje                 | Asteraceae   | Leaves          | [61]       |
| Hypoxis hemerocallidea         | African potato          | Hyoxidaceae  | Corm            | [62, 63]   |
| Indigofera tinctoria           | True indigo             | Fabaceae     | Leaves          | [64]       |
| Linum usitatissimum            | Flax seeds              | Linaceae     | Seeds           | [65]       |
| Momordica charantia            | Bitter gourd            | Cucurbitaceae| Seeds          | [50]       |
| Moringa oleifera               | Drumstick/Horseradish   | Moringaceae  | Leaves          | [66]       |
| Olea europaea                  | European olive          | Oleaceae     | Leaves          | [67, 68]   |
| Opuntia megacantha             | Prickly pear            | Cactaceae    | Leaves          | [69]       |
| Panax quinquefolius            | American ginseng        | Araliaceae   | Roots           | [70]       |
| Persea americana               | Avocado                 | Lauraceae    | Leaves          | [71]       |
| Pterocarpus santalinus         | Red sandal wood         | Fabaceae     | Heartwood       | [72]       |
| Rheum officinalis              | Rhubarb                 | Polygonaceae | Resin          | [73]       |
| Salvia miltiorrhiza            | Chinese sage            | Lamiaceae    | Roots           | [74]       |
| Sclerocarya birrea             | Marula                  | Anachardiaceae| Stem bark    | [75]       |
| Sesamum indicum                | Sesame                  | Pedaliaceae  | Seeds           | [76]       |
| Silybum marianum               | Milk thistle            | Asteraceae   | Seeds           | [77, 78]   |
| Tectona grandis                | Teak                    | Lamiaceae    | Bark            | [79]       |
| Terminalia chebula             | Black myrobalan         | Combretaceae | Fruits         | [80]       |
CONCLUSION

The review summarizes all the plants which have been scientifically proven for the treatment of DN and urolithiasis and thus a systematic research attempt is need of the hour to explore botanicals as alternative and/or complementary medicines which could be formulated in potent dosage forms so as to be easily available to people all around the world.

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| Plant Name                  | Common Name                   | Family       | Part Used        | Reference(s) |
|-----------------------------|-------------------------------|--------------|------------------|--------------|
| Vitis vinifera              | Grape vine                    | Vitaceae     | Fruit wine       | [81]         |
| Zingiber officinale         | Ginger                        | Zingiberaceae| Rhizome          | [41]         |
| *Aerva lanata*              | Chaya/ Mountain knotgrass     | Amaranthaceae| Leaves           | [82, 83]     |
| *Ammannia baccifera*        | Monarch redstem               | Lythraceae   | Aerial parts     | [84]         |
| *Asparagus racemosus*       | Shatavari                     | Asparagaceae | Whole plant      | [85]         |
| *Alisma orientale*          | Takasha                       | Alismataceae | Rhizome          | [86]         |
| *Bergenia ciliata*          | Megaseas                      | Saxifragaceae| Leaves           | [87]         |
| *Boerhaavia difusa*         | Punarnava                      | Nyctaginaceae| Roots            | [88]         |
| *Bryophyllum pinnatum*      | Patharchata                   | Crassulaceae | Leaves           | [88]         |
| *Citrus limon*              | Lemon                         | Rutaceae     | Lemon juice      | [89, 90]     |
| *Costus spiralis*           | Cana-do-brejo                 | Zingiberaceae| Whole plant      | [91]         |
| *Crataeva nurvala*          | Varuna                        | Capparaceae  | Bark             | [92]         |
| *Cyclea pelata*             | Rajpatha                      | Menispermaceae| Roots            | [93]         |
| *Cynodon dactylon*          | Bermuda grass                 | Poaceae      | Fresh plant      | [94]         |
| *Daucas carota*             | Carrot                        | Apiaceae     | Root             | [98]         |
| *Desmodium styracfolium*    | Coin-leaf desmodium           | Leguminosae  | Triterpene       | [95]         |
| *Helianthus annuus*         | Sunflower                     | Asteraceae   | Leaves           | [96]         |
| *Herniaria hirsuta*         | Hairy rupturewort             | Caryophyllace| Fresh herb       | [96]         |
| *Hibiscus sabdariffa*       | Roselle                       | Malvaceae    | Leaves           | [97]         |
| *Ipomoea eriocarpa*         | Tiny morning glory            | Convolvulaceae| Leaves          | [98]         |
| *Jasminum auriculatum*      | Jasmine                       | Oleaceae     | Flowers          | [99]         |
| *Mimosa pudica*             | Laajvanti                     | Mimosaceae   | Leaves           | [100]        |
| *Moringa oleifera*          | Drumstick/ Horseradish        | Moringaceae  | Root             | [101]        |
| *Musa sapientum*            | Banana                        | Musaceae     | Stem             | [102]        |
| *Nigella sativa*            | Black caraway/ kalonji        | Ranunculaceae| Seeds            | [103]        |
| *Orthosiphon stamineus*     | Java tea                      | Lamiaceae    | Leaves           | [104]        |
| *Phyllanthus niruri*        | Gale of the wind              | Phyllanthaceae| Whole plant     | [105]        |
| *Punica granatum*           | Anaar                         | Lythraceae   | Fruit juice      | [106]        |
| *Quercus stenophylla*       | Oak                           | Fagaceae     | Leaves           | [107]        |
| *Randia echinocarpa*        | Chacua                        | Rubiaceae    | Fruit            | [108]        |
| *Raphanus sativus var. nigra*| Radish                       | Cruciferae   | Tubercle         | [109]        |
| *Rosa canina*               | Dog rose                      | Rosaceae     | Fruit            | [110]        |
| *Rotula aquatic*            | Pashanbhed                    | Boraginaceae | Extract          | [111]        |
| *Rubia cordifolia*          | Indian madder                 | Rubiaceae    | Roots            | [112]        |
| *Rubia tinctoria*           | Dyer’s madder                 | Rubiaceae    | Roots            | [113]        |
| *Sesbania grandiflora*      | Agastya                       | Fabaceae     | Leaves           | [114]        |
| *Spergularia purpurea*      | Purple sandspurry             | Caryophyllace| Whole plant     | [115]        |
| *Tribulus terrestris*       | Chhotra gokhru                | Zygophyllace| Fruits, roots    | [116]        |
| *Trigonella foenum graecum* | Methi                         | Fabaceae     | Seeds            | [117]        |
| *Zea mays*                  | Maize                         | Poaceae      | Styles           | [118]        |
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