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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 chronicle events, viz. crystal nucleation, its growth, aggregation, and crystal retention inside the renal tubules [15]. Adequate management of the patient can be done by (i) attenuating the pain; (ii) by favoring progression and spontaneous expulsion of stones from body and (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, urine uric 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, pharmacognosists 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

Cisplatin induced nephrotoxicity				
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 hippocsatanum	Horse chestnut	Sapindaceae	Seeds	[22]
Aloe barbadensis	Aloe vera	Asphodelaceae	Leaf	[23]
Bauhinia variegata	Kachnar	Caesalpiniaceae	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 nurvala	Varuna	Capparaceae	Stem bark	[28]
Cucurbita pepo	Pumpkin	Cucurbitaceae	Fruits	[25]
Cyclea peltata	Rajpatha	Menispermaceae	Leaves	[29]

Dichrostachys cinera	Chinese lantern	Mimosaceae	Roots	[30]
Ficus religiosa	Peepal	Moraceae	Latex	[31]
Kigelia africana	Sausage	Bignoniaceae	Matured fruits	[32]
Lepidium sativum	Pepper Wort	Cruciferae	Seeds	[33]
Pedalium murex	Bada gokhru	Pedaliaceae	Fruits	[34]
Picrorhiza kurroa	Kutki	Scrophulariaceae	Rhizome	[35]
Silybum marianum	Milk thistle	Asteraceae	Seeds	[36]
Veronia cinerea	Sahadevi	Compositae	Aerial parts	[37]
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]
Strychnos potatorum	Clearing nut	Loganiaceae	Seeds	[40]
Diabetic nephropathy				
Allium sativum	Garlic	Alliaceae	Cloves	[41]
Andrographis paniculata	Kalmegh	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 thonningii	Blume	Morarceae	Stem bark	[51, 52]
Foeniculum vulgare	Fennel	Apiaceae	Fruits	[53]
Fragaria × ananassa	Strawberry	Rosaceae	Leaves	[54]
Ganoderma lucidum	Mushroom	Polyporaceae	Fruits	[55]
Ginkgo biloba	Maiden Hair	Gikgoaceae	Leaves	[56]
Glycyrrhiza uralensis	Chinese liquorice	Fabaceae	Roots	[57]
Gongronema latifolium	Amaranth globe	Asclepiadaceae	Leaves	[58]
Gymnema montanum	Bidaria Tingens Deche	Asclepidaceae	Leaves	[59]
Helianthus annuus	Sunflower	Asteraceae	Leaves	[60]
Helichrysum ceres	Beentje	Asteraceae	Leaves	[61]
Hypoxis hemerocallidea	African potato	Hypoxidaceae	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	Avacado	Lauraceae	Leaves	[71]
Pterocarpus santalinus	Red sandal wood	Fabaceae	Heartwood	[72]
Rheum officinale	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]

Vitis vinifera	Grape vine	Vitaceae	Fruit wine	[81]
Zingiber officinale	Ginger	Zingiberaceae	Rhizome	[41]
Nephrolithiasis				
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	Takusha	Alismataceae	Rhizome	[86]
Bergenia ciliate	Megaseas	Saxifragaceae	Leaves	[87]
Boerhaavia diffusa	Punarnava	Nyctaginaceae	Roots	[88]
Bryophyllum pinnatum	Pattharchata	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 peltata	Rajpatha	Menispermaceae	Roots	[93]
Cynodon dactylon	Bermuda grass	Poaceae	Fresh plant	[94]
Daucas carota	Carrot	Apiaceae	Root	[88]
Desmodium styracifolium	Coin-leaf desmodium	Leguminosae	Triterpene	[95]
Helianthus annuus	Sunflower	Asteraceae	Leaves	[60]
Herniaria hirsuta	Hairy rupturewort	Caryophyllaceae	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 tinctorium	Dyer's madder	Rubiaceae	Roots	[113]
Sesbania grandiflora	Agastya	Fabaceae	Leaves	[114]
Spergularia purpurea	Purple sandspurry	Caryophyllaceae	Whole plant	[115]
Tribulus terrestris	Chhota gokhru	Zygophyllaceae	Fruits, roots	[116]
Trigonella foenum graecum	Methi	Fabaceae	Seeds	[117]
Zea mays	Maize	Poaceae	Styles	[118]

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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