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Prospects of kidney stone management by phytotherapy: A review

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Abstract

Causes of kidney stone formation, types of kidney stones, some frequently used medicinal plants to cure kidney stones and their pharmacological action are reviewed in this article. Kidney stones are major threat to human life and cause economic burden on human population. Studies on treatment of kidney stones by medicinal plants searching for lithotriptic activity of plants need attention. During this study, it was found that medicinal plants are the most effective source for the treatment of kidney stones. The main objective of this study was to explore the efficacy and availability of medicinal plants as an alternative and to provide economical, side effect free, environment friendly, and easily available treatment to reduce the burden of urolithiasis on patients and healthcare management.

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Introduction

Urolithiasis is the third most common problem that affects a significant population worldwide after urinary tract infections. Throughout the world, 12% people have kidney stone at some stage in life (Mukherjee, 2014). In the course of past decades, occurrence of kidney stones surged all round the world due to inactive life style, eating habits, and environmental matters. In developed countries like in US and in Europe, 10-15% population suffers from this disease. In the Asia, upto 19.1% of population is affected from kidney stone diseases. Due to expensive treatment of urolithiasis in India, 6% population becomes victom of kidney failure (Taylor and Curhan, 2006). In the UAE and China, occurrence of urolithiasis is 6.4% and 6.8 % respectively, whereas the rate of kidney stone formation is less in central and South America and some parts of Africa (Zargooshi, 2001; Moser, 2012).

Pakistan exist in the geographical region known as the "stone belt" stretching from Egypt and Sudan through the Middle East, India, Pakistan, Burma, Thailand, Indonesia and Philippines reporting consistently high incidence of urolithiasis. Poor nutritional status and improper facilities for health are the major reasons for kidney stone in this region (Rizvi and Manzoor, 2002). A concept that appears from modern research is that, medicinal plants are effective urolithotriptic agents. The occurrence of stone disease are not known in Pakistan.

The reason is lack of centralized epidemiological data (Hussain *et al*., 1998). Medicinal plants play effective role in stone disease. Medicinal plants remove stones from kidneys, reduce pain, and prevent lithogenesis. Medicinal plants are effective to treat struvite, calcium oxalate, uric acid, and cysteine stones of kidney. Traditional early medicines and drug discovery were based on natural products (Yaqub *et al*., 2020). Medicinal plants used in urolithiasis are reported in Table 1. Lithotriptic medicinal plants include *Abutilon indicum, Holarrhena antidysenterica, Berberis vulgaris, Rubus idaeus, Raphanus sativus, Matricaria chamomilla, Cynodon dactylon, Terminalia arjuna, Origanum vulgare, Bombax ceiba, Aerva lanata, Solanum surattense, Herniaria hirsute, Saxifraga ligulata* and *Asparagus racemosus* are found in Pakistan and worldwide. The listed plants have powerful bioactive compounds effective for kidney stones treatment.

Medicinal plants are less toxic and good alternative for conventional medicine when they show side effects (Aslam *et al*., 2019). In this study, use of medicinal plants to treat the patients with urolithiasis has been recorded. Compound isolation may boost the lithotriptic activity of plants and making effective drugs from these plants could be an economical benefit. Furthermore, casual clinical tests may be done to evaluate these plants. A substantial expense of more than $5 billion annually in the US is associated with urolithiasis. Hence, medicinal plants can reduce the burden of disease if they are available as safe, affordable, and efficacious treatment (Akram and Idrees, 2019). Availability of medicinal herbs at economical price may improve human health.

Kidney stone

Causes of kidney stone formation

There are many factors which are responsible for the formation of renal calculi. They include metabolic disorder, water quality, climate and urinary tract (Orlando *et al*., 2008). Obesity and kidney stone also has some positive relation. Calcium oxalate stones development increases at the age of 50–60 years (Baker *et al*., 1993). In older patients intestinal absorption of nutrients like calcium, oxalates, phosphates etc. which are responsible for stone formation can be reduced (Saltzman and Russell, 1998; Abrams, 2001). The incidence of urinary stone in male and females is with the ratio of 2:1. Increased level of this risk in males is due to high intake of proteins. This increases the excretion of magnesium and phosphates and reduces citrate concentration in urine. Less risk in females is due to estrogen that lowers urinary calcium and calcium oxalate saturation. Estrogen keeps the urine alkaline that raises the defensive citrate level (Heller *et al*., 2002).

Types of kidney stones

There are over sixty five different molecules reported to be present in kidney stones (Taylor and Curhan, 2006). These molecules get crystallize more than eighty crystalline phases. The most common types are: Calcium oxalate, Calcium phosphate, Uric acid, Cysteine and Xanthine stones.

Cysteine stones: Patients suffering from cysteinuria bear these stones due to low re absorption of cysteine.

These are pulpy and convert into green color in air. The coversion in green color is caused by sulphur in cysteine. Cysteine crystals are found in acidic urine having hexagonal structure.

Table 1. Effectiveness of medicinal plants in kidney stone disease.

Botanical name	Origin of plant	Family	Parts used	Functions	Model animal
Hibiscus sabdariffa Linn.	India and Malaysia	Malvaceae	Petals	Antioxidant, antilithiatic	Rats
Phyllanthus niruri	Southern India and China	Phyllanthaceae	Whole plant	Anti-HIV, antilithiatic	*In vitro*
Nigella sativa L.	Middle East and Asia	Ranunculaceae	Seeds	Anticancer, antilithiatic	Rats
Cynodon dactylon	Australia and Africa	Poaceae	Aerial parts	Antidiabetic, antilithiatic	Rats
Hyptis suaveolens	South America, West Indies and Mexico	Lamiaceae	Leaves	Antidiabetic, antilithiatic	*In vitro*
Sesbania grandiflora	Philippines, Tropical Asia, Indonesia and Malaysia	Fabaceae	Leaves	Cardioprotective, antilithiatic	Rats
Aerva lanata	Africa	Amaranthaceae	Whole plant	Antidiabetic, antilithiatic	Rats
Orthosiphon grandiflorus	Africa	Lamiaceae	Whole plant	Hepatoprotective, antilithiatic	Clinical trials
Tribulus terrestris	Australia, Africa, Southern Asia and Europe	Zygophyllaceae	Fruit	Diuretic, antilithiatic	Rats
Pyracantha crenulata Roem.	Southeast Asia and Southeast Europe	Rosaceae	Berries, flowering tops	Anti-inflammatory, antilithiatic	Rats
Costus spiralis Roscoe	Tropical South America	Costaceae	Leaves	Antimicrobial, antilithiatic	Rats
Raphanus sativus	Asia	Brassicaceae	Roots	Antifungal, antilithiatic	Rats
Nigella sativa	Middle East and Asia	Ranunculaceae	Seeds	Anticancer, antilithiatic	Rats
Randia echinocarpa	Mexico	Rubiaceae	Fruits	Antioxidant, antilithiatic	Rats
Achyranthes aspera Linn.	India and China	Amaranthaceae	Roots	Antinociceptive, antilithiatic	Rats
Herniaria hirsuta L.	California	Caryophyllaceae	Aerial parts	Hypolipidemic, antilithiatic	Rats
Aerva lanata	Africa and Uganda	Amaranthaceae	Leaves	Antidiabetic, antilithiatic	Rats
Asparagus racemosus	India and Srilanka	Asparagaceae	Roots	Galactagogue, antilithiatic	Rats
Helianthus annuus Linn.	India and America	Asteraceae	Leaves	Antibacterial, antilithiatic	Rats
Acalypha indica L.	India and Tropical Africa	Euphorbiaceae	Leaves	Analgesic, antilithiatic	Rats
Rotula aquatica	India	Boraginaceae	Roots	Antimitotic, antilithiatic	Rats
Bergenia ligulata	Himalaya	Saxifragaceae	Rhizome	Antioxidant, antilithiatic	Rats

Calcium oxalate stones: Calcium oxalate stones are also known as mulberry stones. Among renal stones, 70% stones are calcium oxalate.

These are formed due to dietary intake of milk along with oxalic acid containing foods, like spinach (Ahmad *et al.*, 2016). It is shaped irregular like sharp overhangs, which bleed. These are very hard and seen as concentrically placed layers. Their envelope like shape help them to be identified in urine.

Phosphate stones: They occur as calcium, ammonium, magnesium or tripple phosphate. Their occurrence is 10% among all stones. These crystals are plane and off white colored. The stone augment in basic urine and express symptom if stone size is enlarged.

Uric acid stones

Uric acid stones are formed due to very high levels of uric acid in the urine or too acidic urine permanently. High acidity in urine is linked to the inherited problems of uric acid or protein processing in the diet. These stones are smooth, radiolucent and hard. These are complex, yellow to reddish brown and pulpy flexible too.

Symptoms of kidney stone

Patients having tiny stones do not express any symptom. Unbearable discomfort is the major

symptom in 75% patients. In case of ureteric colic, there is vomiting and sweating due to serious pain. In abdominal checking, muscles of abdomen tendered and upon hydronephrosis kidney becomes palpable and result in pyuria and hematuria (Du *et al.*, 2020).

Antilithiatic characteristics of medicinal plants

Raphanus sativus (Radish)

Roots are edible part of Raphnus sativus used in therapeutics. It caries kaempferol, anthocyanin, allyl isothiocayanate, glucosinolates, 4-(methylthio)-3-butenyl isothiocyanate, phenethyl isothiocyanate,, glycosides, and benzyl isothiocyanate.

Its medicinal effects are antiurolithiasic, anticancer, antiproliferative, antimicrobial, antimutagenic, antioxidant, and hepatoprotective (Castro *et al.*, 2012).

Aerva lanata (Gorakha ganja)

The potency of gorakha ganja has reported on oxalate stone in rats (Soundararajan *et al.,* 2006). The whole plant and leaves are used. Its chemical components are benzoic acid, quercetin, lupeol, tannic acid, ervoside, persinol, and aervine.

It is effective in cancer, urinary tract infections, diabetes mellitus, kidney stones. Its medicinal tasks are hypoglycemic, diuretic, liver and kidney protection.

Nigella sativa (Black cumin or Kalonji)

Seeds of nigella also called kalonji are used as medicine. Bioactive compounds of kalonji are: nigellidine, carvacrol, thymol, nigellicine, nigellimine-N-oxide, alpha hederin, dithymoquinone, thymohydroquinone, and thymoquinone. Kalonji seeds have miraculous effects and used in all diseases like cancer, diabetes, nephrolithiasis. Further, it shows antibacterial, antioxidant, analgesic, renal protective, bronchodilator, immunomodulator, anti-diarrheal, digestive, appetite stimulant, diuretic, liver tonic, antihypertensive, gastroprotective, hepatoprotective, spasmolytic, anti-inflammatory, antimicrobial, antidiabetic and anti urolithiasis effect (Harsoliya *et al.,* 2012).

Abutilon indicum (Indian mallow)

Leaves, bark, flower, root and seed of Abutilon indicum of family malvaceae are used in phytotherapy. Its bioactive compounds are cineole, tocopherol oil and geraniol. It has been found effective in the treatment of degenerative diseases, diabetes mellitus, liver disorders. It has antioxidant, hypoglycemic, antibacterial, hepatoprotective, anti-inflammatory, and analgesic properties. This plant is reported effective in kidney stone also (Prachi *et al.,* 2009).

Terminalia arjuna (Arjun)

Leaves of arjun used in phytotherapy constitute bioactive compounds: friedelin, beta sitosterol, arjunic acid, arjunetin, and ellagic acid. Its medicinal actions are hypo-cholesterolemic and cardioprotective. Most effective fraction of *Terminalia arjuna* was butanol (Chaudhary *et al.*, 2010).

Herniaria hirsuta (Hairy Rupture Wort)

Aerial parts are used as therapeutic agent. Its bioactive compounds are: alkaloids, quercetin, monodesmosidic saponins, herniarin, essential oil, coumarin, tannins, herniarin acid, and rutin. Along with other pharmacological uses, it is also used to treat kidney stones. It is antiurolithiatic, diuretic and lithotriptic (Atmani *et al.,* 2003).

Crataeva nurvala (Veruna)

Roots of veruna are used. Its chemical constituents are glucosilinate, ceryl alcohol, triterpenoids, flavonoids, cadabicine, lupeol, glucocapparine, betulinic acid. It is used in renal diseases, swollen gums, dysuria, and dysentery. Its medicinal tasks are urolithic, lithotriptic, lubricant, diuretic (Agarwal *et al.,* 2010).

Asparagus racemosus (Nunggarei-angouba)

Asparagus leaves are used therapeutically. Bioactive components of asparagus include asparagine, volatile oil, flavonoids, sitosterol, mucilage, saponin,

sapogenin, tannic acid, and asparagenin. It helps in removing stones from urinary tract. Its medicinal effects are antispasmodic, antibacterial, diuretic, aphrodisiac, demulcent, anti-diarrheal, anti-tumor, galactagogue, stomachic, expectorant, antiepileptic, and anti-inflammatory (Christina *et al.*, 2005).

Origanum vulgare (Wild marjoram)

Biochemical constituents of *Origanum vulgare* are triacontanol, oleanolic acid, ursolic acid and beta sitosterol. Stems and leaves are used in therapy. Medicinally, it is anti-inflammatory and urolithotriptic (Khan *et al.,* 2011).

Cynodon dactylon (Couch grass)

Whole plant of *Cynodon dactylon* is used in phytotherapy. Bioactive ingredients of *C. dactylon* cotain aromatic compounds, zeaxanthin, phytone, arundoin, ionone, phytol, glucoside, furfuryl alcohol, stigmasterol acetate, tannins, saponins, xanthophylls, chlorophyll, carotene, glycosides, sitosterol, flavonoids, carotenoids, kaempferol, lutein, myricetin, , quercetin, rutin, catechin, violaxanthin. Pharmacologicaly it is used as an astringent, laxative, antidiabetic and diuretic (Jarald *et al*., 2008).

Bombax ceiba L. (*Red cotton tree*)

Seeds of *bombax ceiba* are functional part. Its bioactive compounds are: tannin, shamimin, mangiferin, quercetin, kaempferol, naphthalene derivatives, proteins, phytosterols, phenolic compounds, beta sitosterol, lupeol, glycosides, and alkaloids. It treats effectively calculous infections, dysuria, chronic inflammation, and strangury. Its medicinal actions are: antioxidant, analgesic, hypoglycemic, cytotoxic, anti-inflammatory, hypotensive, diuretic, cardiac restorative and urolithotriptic (Gadge and Jalalpure, 2012).

Conclusion

Kidney stone formation is the worldwide major issue. A comprehensive study was made in this review article on medicinal plants utilization in urolithiasis treatment. Leaf, bark, flowers, roots and seeds of the plants discussed in this review are used for medicinal purpose to treat urolithiasis. These data may be helpful for future study of medicinal plants and their clinical trials for urolithiasis as well as some other diseases.

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