

# Progress and prospects in the management of kidney stones and developments in phyto-therapeutic modalities

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## Abstract

The aim of this article was to review some of the new and commonly used medicinal plants in the treatment of kidney stones, emphasizing medicinal uses, pharmacological activity, and research study of medicinal plants. Renal stones are a common problem worldwide with substantial morbidities and economic costs. The high economic burden associated with kidney stones is linked mainly with healthcare costs. In vitro and in vivo studies on alternative treatment of kidney stones have been searched by using words such as phytotherapy of kidney stones, medicinal plants used in kidney stones, and lithotriptic activity of plants. Articles reviewed showed that medicinal plants have lithotriptic potential. Medicinal plants may be useful in treatment of kidney stones. This study was aimed to explore and elaborate the efficacy and availability of alternative treatment for kidney stones and to provide safe, cost effective, and efficacious management options as well as reduce the burden of disease. Cost effectiveness may enable improvements in treatment efficiency that can benefit patients and the healthcare system. Further randomized clinical trials should be conducted to evaluate the safety and efficacy of medicinal plants.

## Keywords

efficacy, literature review, medicinal plants, kidney stones

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## Introduction

Urolithiasis is a common disorder and affects a considerable number of people worldwide. Globally, 12% of population suffers from kidney stone at a stage of life. During the past decades, incidence of kidney stones increased both in developing as well as developed countries mainly due to sedentary life style, eating habits, and global warming issues. According to a report, US population suffers from kidney stones 1 out of every 11 persons and in Asian countries about 1%–19.1% of the population suffers from urolithiasis such as in India 12% of total population suffers from urolithiasis and half of them have consequent failure of kidney mainly due to high cost of treatment. In

China and United Arab Emirates, prevalence of kidney stones is 6.4% and 6.8 %, respectively. A significant economic burden is associated with kidney stones, with annual estimate exceeding US\$5 billion in the United States. A theme that emerges from recent research is that the complexity of minerals and electrolyte imbalance involving other body systems can

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**Table 1.** Medicinal plants having activity in renal calculi.

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

lead to urinary stone formation. Medicinal plants are used as urolithotriptic agents. During recent decades, medicinal plants have become more effective in stone disease. Medicinal plants reduce pain of kidney stones and prevent lithogenesis. Medicinal plants expel the stones from the kidney. Medicinal plants are commonly used for treatment of kidney stones (calcium oxalate, uric acid, struvite and cysteine).<sup>1</sup> Herbal medicine is an integral part of the development of modern civilization. Various medicinal plants are used in urolithiasis and their effect is documented (Table 1). Medicinal plants having urolithiasis activity include *Cynodon dactylon*, *Holarrhena antidysenterica*, *Berberis vulgaris*, *Rubus idaeus*, *Matricaria chamomilla*, *Abutilon indicum*, *Terminalia arjuna*, *Herniaria hirsute*, *Aerva lanata*, *Solanum surattense*, *Saxifraga*

*ligulata* and *Asparagus racemosus* which are native to Pakistan and found worldwide. All medicinal plants are documented and some of them experimentally documented, but more or less traditionally can be viewed as the alternative source as therapeutics for different forms of kidney stones (calcium oxalate, uric acid, struvite and cysteine). The toxicity is minimum, and when there are side effects of conventional medicine herbal medicine can be a good alternative. There is evidence in treating kidney stones with herbal medicaments. The plant species listed have potential active compounds and may aid researchers in their study of natural products, which may be useful to treat kidney stones (calcium oxalate, uric acid, struvite and cysteine). In present study, we have documented medicinal plant usage in patients with urolithiasis.

Compound isolation is suggested to improve the lithotriptic actions of plants. Further, randomized clinical trials should be conducted to evaluate the safety and efficacy of medicinal plants. Production of suitable formulations of these medicinal plants by pharmaceutical industry could be an interesting and economically beneficial prospect. A significant economic burden is associated with kidney stones, with annual estimates exceeding US\$5 billion in the United States. Therefore, providing safe, cost effective, and efficacious options of treatment with medicinal plants mentioned in this review can reduce the burden of disease. Cost effectiveness may enable improvements in treatment efficiency that can benefit patients and the healthcare system.

### Varieties of renal stones

Calcium oxalate stones

Calcium phosphate stones

Uric acid stones

Cysteine stones

Xanthine stones

### Oxalate stones

These stones are formed due to calcium oxalate and are popularly known as mulberry stones. It is covered with sharp projections, which may bleed early. These are usually single. Due to its irregularity, it produces symptoms early. These stones are usually very hard. In cross-section, it is seen as concentrically placed layers. The crystals can be seen in urine and identified by their envelope like shape.

### Phosphate stones

These may occur as calcium phosphate, ammonium phosphate or triple phosphate (calcium, ammonium, and magnesium). These stones are smooth and dirty white in color. The stone enlarges in alkaline urine. It only gives symptoms when stone is large in size.

### Uric acid

These are hard, smooth, and radiolucent. They are multiple and faceted, and yellow to reddish brown in color. These may be soft and flexible.

### Cysteine stones

These may appear in the patient with cystinuria which may occur in the patient with reduced reabsorption of cysteine from the kidney. These are soft stones. On exposure to air, they change their color into green. This greenish color appears due to the presence of sulfur in them. These cysteine crystals are hexagonal, translucent, and appear in acidic urine.

### Signs and symptoms

Some patients with small-sized stones do not produce any symptoms. Pain is the leading symptom in 75% of cases; pain is fixing, and located in renal angle. In case of ureteric colic, when stones radiate to ureter from the right or left lumbar region and then to the groin, there is also vomiting and sweating due to severe pain. On abdominal examination, there is tenderness in the abdomen muscles and if hydronephrosis has been produced, then the kidney becomes palpable. There is pyuria and hematuria.

### Discussion

#### *Medicinal plants with antilithiatic properties*

*Cynodon dactylon* (*Gramineae*). The whole plant is used. Common name is Couch grass. Its chemical constituents are aromatic ingredient, arundoin, furfuryl alcohol, ionone, phytol, sitosterol, glucoside, stigmasterol acetate, phytone, xanthophylls, carotene, glycosides, saponins, tannins, flavonoids, carotenoids, chlorophyll, quercetin, kaempferol, lutein, myricetin, catechin, rutin, zeaxanthin, and violaxanthin. Its pharmacological activities are astringent, diuretic, laxative, and antidiabetic.<sup>2</sup>

*Abutilon indicum* (*Malvaceae*). Parts used are leaves, root, flower, seed, and bark. Common name is Indian mallow. Its chemical constituents are cineole, geraniol, and tocopherol oil. It is used in diabetes mellitus, liver disorders, and degenerative diseases. Its pharmacological activities are hypoglycemic, antibacterial, analgesic, anti-inflammatory, hepatoprotective, and antioxidant. Prachi et al.<sup>3</sup> reported the use of this plant in kidney stone.

*Terminalia arjuna* (*Combretaceae*). Parts used are leaves. Common name is Arjun. Its chemical

constituents are arjunetin, friedelin, beta sitosterol, arjunic acid, and ellagic acid. It is used in hyperlipidemia and cardiovascular disorders. Its pharmacological activities are hypo-cholesterolemic and cardioprotective. Bark of *Terminalia arjuna* was investigated for its inhibitory effect on calcium oxalate and calcium phosphate crystal formation. Fraction of solvent and crude extract of this plant was used for inhibitory activity. This study was done in vitro. This study indicated that bark of *Terminalia arjuna* has potential to inhibit calcium oxalate and calcium phosphate crystal formation. Most effective fraction of *Terminalia arjuna* was butanol.<sup>4</sup>

*Herniaria hirsuta* (*Caryophyllaceae*). Parts used are aerial parts. Common name is Hairy Rupture Wort. Its chemical constituents are monodesmosidic saponins, tannins, herniarin, alkaloids, essential oil, coumarin, herniarin acid, quercetin, and rutin. It is used in kidney stones. It is antiurolithiatic. Its pharmacological activities are diuretic and lithotriptic. Atmani et al.<sup>5</sup> reported the efficacy of this plant in kidney stone.

*Aerva lanata* (*Amaranthaceae*). The whole plant and leaves are used. Common name is Gorakha ganja. Its chemical constituents are tannic acid, benzoic acid, lupeol, persinol, quercetin, ervoid and aervine. It is used in diabetes mellitus, urinary tract infections, kidney stones, and cancer. Its pharmacological activities are hypoglycemic, diuretic, hepatoprotective and nephroprotective. Soundararajan et al.<sup>6</sup> reported the efficacy of this plant on calcium oxalate urolithiasis in rats.

*Crataeva nurvala* (*Capparaceae*). Parts used are roots. Common name is Veruna. Its chemical constituents are triperpenoids, flavonoids, glucocapparine, betulinic acid, cadabicine, glucosilinate, ceryl alcohol, lupeol, and flavonoids. It is used in dysuria, amoebic dysentery, renal diseases, and swollen gums. Its pharmacological activities are lubricant, diuretic, and lithotriptic. Urolithic property of *Crataeva nurvala* has been reported.<sup>7</sup>

*Asparagus racemosus* (*Liliaceae*). Parts used are leaves. Common name is Nungarei-angouba. Its chemical constituents are tannic acid, volatile oil, mucilage, saponin, flavonoids, asparagine, sitosterol, saponin, and asparagenin. It is useful in expelling

stones from the urinary tract. Its pharmacological activities are antispasmodic, aphrodisiac, demulcent, antibacterial, diuretic, anti-diarrheal, anti-tumor, expectorant, antiepileptic, galactagogue, stomachic, anti-inflammatory, appetizer, and tonic. *A. racemosus* was investigated for its inhibitory effect on stone formation. Lithiasis was induced by administering 0.75 % ethylene glycolated water to adult male albino rats orally for 28 days. Ethylene glycol altered the urine chemistry by elevating the levels of phosphate, oxalate, and calcium that are responsible for kidney stones. Raised levels of phosphate, calcium, and oxalate were decreased by use of ethanolic extract of *Asparagus racemosus*. Creatinine level was also reduced by this extract and magnesium level was increased that is inhibitor of stone formation. Histological finding shows that *Asparagus racemosus* improves signs of deterioration induced by ethylene glycol. These observations show that *Asparagus racemosus* inhibits ethylene-glycol-induced stone formation.<sup>8</sup>

*Origanum vulgare* (*Lamiaceae*). Parts used are stems and leaves. Common name is wild marjoram. Its chemical constituents are triacontanol, beta sitosterol, oleanolic acid, and ursolic acid. It is used in spleen inflammation. Its pharmacological activity is anti-inflammatory. Anti-urolithiatic activity of *Origanum vulgare* has been reported.<sup>9</sup>

*Raphanus sativus* (*Brassicaceae*). Parts used are roots. It contains glycosides, anthocyanin, kaempferol, phenethyl isothiocyanate, benzyl isothiocyanate, allyl isothiocyanate, glucosinolates, and 4-(methylthio)-3-butenyl isothiocyanate. Its pharmacological activities are antiurolithiatic, antimutagenic, antimicrobial, anticancer, antiproliferative hepatoprotective, and antioxidant. Castro-Torres et al.<sup>10</sup> reported its efficacy in kidney stones.

*Bombax ceiba* L. (*Bombacaceae*). Parts used are seeds. It contains tannin, quercetin, kaempferol, shamimin, mangiferin, naphthalene derivatives, phenolic compounds, proteins, lupeol, phytosterols, beta sitosterol, glycosides, and alkaloids. It is used in dysuria, strangury, chronic inflammation, and calculous affections. Its pharmacological activities are antioxidant, hypoglycemic, analgesic, anti-inflammatory, hypotensive, cardiac stimulant, cytotoxic, diuretic, and antioxidant. Gadge and Jalalpure<sup>11</sup> reported efficacy in urolithiasis.



*Nigella sativa* (*Ranunculaceae*). Parts used are seeds. It contains alpha hederin, nigellidine, nigellicine, nigellimine-N-oxide, carvacrol, thymol, dithymoquinone, thymohydroquinone, and thymoquinone. It is used in cancer, diabetes mellitus, inflammation, and nephrolithiasis. It is antibacterial, analgesic, appetite stimulant, anti-diarrheal, digestive, diuretic, liver tonic, antihypertensive, antioxidant, gastroprotective, renal protective, hepatoprotective, bronchodilator, spasmolytic, anti-inflammatory, antimicrobial, immunomodulator, anticancer, and antidiabetic. Harsoliya et al.<sup>12</sup> reported that *Nigella sativa* is useful in urolithiasis.

This article gives comprehensive review on medicinal plants used to treat urolithiasis. These data could be used to highlight medicinal plants that could be studied more rigorously, and their clinical trials should be conducted. After clinical trials, these plants can be basis to recommended current clinical use.

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