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Kidney stone risk reduction and size reduction utilizing medical plants

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Abstract

Kidney stones are not only a widespread problem now, but have been for centuries. Many of the plants used historically have now been found to be effective in reducing risk and reducing stone size in modern clinical trials. Both reducing stone size and reducing recurrence of stones after removal are important. Certain medical plants have been shown to slow the formation of calcium oxalate crystals. Several of these medical plants also have antioxidant and antimicrobial effects. The plants with the best clinical trials and supporting preclinical data showing effectiveness in reducing kidney stone formation and recurrence are *Nigella sativa* (black cumin seed), *Dolichos biflorus* (horse gram), *Crataeva nurvala* (varuna bark), and *Tribulus terrestris* (Gokshura). Some of these medical plants have been compared to tamsulosin (Flomax®) and potassium citrate for safety and effectiveness. Reviewed here are 11 medical plants with good clinical data, as well as 24 more plants with preclinical data or historical use.

Keywords: Kidney stones; Calcium oxalate; Medical plants; *Nigella sativa*; *Dolichos biflorus*; Urolithiasis

1. Introduction

Medical plants can reduce super saturation of urine with calcium, thus reducing growth and retention of kidney stones. These plants may increase urine volume so stones can more easily pass. Some may inhibit crystallization of calcium oxalate stones in urine. Improving kidney function can reduce stone recurrence. Some of these plants inhibit enzymes (e.g. glycolate oxidase) that promote stone formation. They may also improve antioxidant levels and exert antimicrobial activity to reduce urinary tract infections [1].

2. Medical plants that inhibit formation and reduce size of kidney stones based on clinical trials

2.1. *Nigella sativa* (black cumin seed)

Nigella sativa was tested on 80 participants with 4 to 10 mm kidney stones in a randomized clinical trial. One gram every 12 hours for 2 weeks of *Nigella sativa* was compared with .4 mg of tamsulosin (Flomax®). Stone sizes decreased from 10 mm to 5 mm with either *Nigella sativa* or tamsulosin. *Nigella sativa* reduced pain and increased stone passage more than tamsulosin [2].

Clinical studies have shown beneficial effects of *Nigella sativa* in the prevention and treatment of renal stones. Sixty patients with renal stones were randomly enrolled in two arms of a randomized, triple-blind, placebo-controlled, clinical trial. The patients were treated with *Nigella sativa* capsules (500 mg) or placebo two times per day for 10 weeks. Patients were assessed in terms of size of renal stones by using sonography before and after the intervention. In the *Nigella sativa* seed group, 44.4% of patients excreted their stones completely, and the size of the stones remained unchanged in 3.7%, and decreased in 51.8% of patients. In contrast, in the placebo group, 15.3% of the patients excreted

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their stones completely, 11.5% had reduction in stone size, 15.3% had increase in stone size, and 57.6% had no change in their stone size. The difference in the mean size of renal stones after the study was significant between the two groups ($p < 0.05$). *Nigella sativa*, as compared with placebo, has been demonstrated to have significant positive effects on the disappearance or reduction of size of kidney stones [3,4].

Less formation of calcium oxalate and kidney stones was found with the use of *Nigella sativa* in two animal models [5]. In animal studies, the use of *Nigella sativa* seed significantly protected test animals against experimentally induced formation of calcium oxalate stones [6]. *Nigella sativa* significantly decreased the number of kidney stone accumulations and calcium oxalate deposition in rats [7].

Nigella sativa shows antioxidant, anti-inflammatory, antiapoptotic, and immune regulating properties. Active phytochemicals include thymoquinone, thymohydroquinone, thymol, and carvacrol. *Nigella sativa* has been used widely for centuries as a food spice. *Nigella sativa* showed limited/no toxicity; however; this information was mostly based on preclinical studies [8].

2.2. *Dolichos biflorus* (Horse gram)

Dolichos biflorus (horse gram or Kulattha) can be used to reduce the recurrence of calcium oxalate stones and it has been shown to have a better result than the use of conventional potassium citrate [9].

An antiurolithiatic effect was greatest for a 3 to 1 mix of *Dolichos biflorus* hydroalcoholic seed extract and *Crataeva nurvala* (varuna) aqueous stem bark extract. Regenerated glomeruli were noted. There was a reduction in urinary oxalate and calcium [10].

Less kidney stone formation was found with the use of *Dolichos biflorus* [11]. In a study (47 patients took part in this trial), there was a significant reduction in the size of the kidney stones in comparison with potassium citrate after 6 months in the patients who used *Dolichos biflorus* [12].

Dolichos biflorus reduced inflammation by reducing the activity of cyclooxygenase, lipoxygenase, nitric oxide synthase, myeloperoxidase, and the amount of malondialdehyde ($p < 0.05$). The activities of antioxidant enzymes, vitamin C, and antioxidant glutathione levels were increased significantly ($p < 0.05$) after treatment [13].

The functional beverage of *Dolichos biflorus* seeds exhibited antiurolithiatic activity through inhibition of crystallization of calcium oxalate and demonstrated significant antioxidant potential [14]. Aqueous fractions of *Dolichos biflorus* seeds showed a high dissolution of stones; dissolving calcium oxalate [15].

2.3. *Crataeva nurvala* (Varuna bark)

In a prospective, randomized, double-blind, placebo-controlled study, *Crataeva nurvala* had prospects for kidney stone treatment because it dissolved oxalate concretions and anesthetized their passage [16].

Daily intake of *Crataeva nurvala* bark reduced urinary calcium excretion and kidney stone formation. This bark is used to help prevent kidney stones and it is also used with banana stem (*Musa paradisiaca*) for successfully treating kidney stones. In a recent human study, the authors reported that this combination “helped to dissolve renal calculi, facilitated their passage, and reduced pain” [17].

Researchers implanted glass beads in the urinary bladder of rats. They used a normal human dose of *Crataeva nurvala*, with dosage adjusted for albino rats. Incidence of stone formation and stone weight were greatly reduced.

Stones were formed in 56% of the control group, but only 22% in the treated group. Urine output was slightly increased. The net weight of the stones in the treated group was reduced from 80.12 mg to 2.5 mg (Please see Figure 1) [18].

An antiurolithiatic effect was greatest for a 1 to 3 mix of *Crataeva nurvala* aqueous stem bark extract and *Dolichos biflorus* hydroalcoholic seed extract. Regenerated glomeruli were noted. There was a reduction in urinary oxalate and calcium. *Crataeva nurvala* contains alkaloids, glycosides, flavonoids, saponins, and terpenoids [19].

The Ayurvedic formula "Herbmed" that is made up of *Crataeva nurvala* (Varuna bark) and banana stem (*Musa paradisiaca*) was investigated in the management of urinary stones in a randomized, double-blind, placebo control trial, which included 77 patients with calculi more than 5 mm in diameter. Treatment group patients were prescribed one capsule of Herbmed, which was comprised of 250 mg *Crataeva nurvala* and 250 mg *Musa paradisiaca*, in the morning

after breakfast, and one capsule in the evening after dinner. The treatment group of patients with stone size 5–10 mm ($n = 31$) significantly reduced the size of calculi by 33.04% compared with the placebo group ($p = 0.017$). However, results were not significant for calculi with a diameter more than 10 mm. *Crataeva nurvala* decreased the urinary and renal tissue oxalate levels and has an anti-crystallization effect [20].

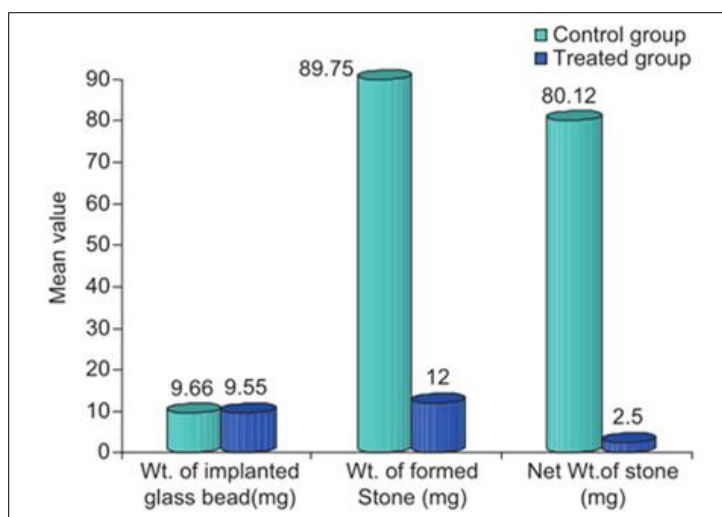


Figure 1 *Crataeva nurvala* greatly reduced kidney stone weight

Crataeva nurvala stem bark and root bark powder reduced risk of kidney stone formation and reduced the size of kidney stones. It alters urinary electrolytes to reduce crystallization in human studies [21].

Active constituents of *Crataeva nurvala* are: glucosinolates, glucoside of flavan-3-ol, (-) epiafzelechin-5-O-p-D-glucos, and diosgenin (this one may be missing in dried bark). Urinary excretion of calcium was increased. Positive side effects include increased urination and reduced pain in benign prostatic hypertrophy and reduced urinary tract infections. Twenty-six patients were able to pass the stones within four months of treatment using strong tea made with the bark (decoction) [22].

2.4. *Tribulus terrestris* (Gokshura)

Tribulus terrestris fruit or root exhibited a significant mean reduction in number and size of kidney stones in 90 days in a randomized, open-label clinical trial ($n=60$). Reduction in pain, burning, and hematuria was significant [23]. *Tribulus terrestris* is a nephroprotective agent, and is commonly used in India and China to treat urinary tract disease. In animal studies it reduced the formation of kidney stones and may have helped to reverse early stage urolithiasis. In vitro research supports the animal data and further suggests that *Tribulus terrestris* also protects against calcium oxalate induced renal injury [24]. *Tribulus terrestris* showed significant dose-dependent protection against urolithiasis induced by glass bead implantation in albino rats [25].

The extract of *Tribulus terrestris* not only has a potential to inhibit nucleation and growth of the calcium oxalate crystals, but also has a cytoprotective role. Glycolate oxidase is one of the principal enzymes involved in the pathway of oxalate synthesis. Glycolate oxidase converts glycolate to glyoxylate by oxidation, and finally to oxalate. Glycolate oxidase is inhibited by quercetin and kaempferol, found in *Tribulus terrestris*. *Tribulus terrestris* has diuretic, antiurolithic, immunomodulatory, hypolipidemic, cardioprotective, hepatoprotective, anti-inflammatory, analgesic, antispasmodic, and antibacterial activities. This plant was found to inhibit stone formation in various models of urolithiasis [26].

2.5. *Cicer arietinum* seeds (Chickpea)

In patients using *Cicer arietinum* seeds, complete stone dissolution occurred in 9 (23.7%) patients and a reduction in stone size was observed in 17 (44.7%) patients, while no response to treatment was observed in the placebo group. The mean stone size was reduced from 7.15 ± 1.34 mm to 4.28 ± 3.09 mm in the *Cicer arietinum* group ($p < 0.001$) and was increased from 7.08 ± 1.09 mm to 7.15 ± 1.09 mm in the placebo group. The changes of the stone size were significantly higher in the *Cicer arietinum* seed group ($p < 0.001$). The increases of the urinary volume and urinary magnesium level were significantly higher in the treatment group ($P=0.04$ and $P=0.02$, respectively) [27].

2.6. *Lapis judaicus* (Jews' stones)

Lapis judaicus, 2 grams per day for 10 weeks in 60 patients, was used in a double-blind, randomized clinical study. As the kidney stones were in the lower pole of the kidney, they could not pass spontaneously. There were no reports of serious pain indicating stone passing in patients in this trial. Stone size was cut in half (8.45-4.23 mm) and urinary magnesium concentrations were almost doubled. *Lapis judaicus* can decrease urinary supersaturation by affecting the urinary composition (especially decreasing calcium excretion). A potent calcium oxalate crystallization inhibitor, it may increase the formation of a more soluble salt form of calcium oxalate and its consequent dissolution in urine. In vivo studies have shown that it has an inhibitory effect on the crystallization of calcium oxalate and is also antimicrobial [28].

2.7. *Ammi visnaga* (Khella)

Ammi visnaga was used for its potent diuretic activity and to prevent renal epithelial damage [29]. *Ammi visnaga* inhibited the crystallization process by inhibiting the growth of crystals and their aggregation [30]. *Ammi visnaga* seed extract was able to relieve pain and is an effective treatment for urolithiasis. It reduced stones in the kidney and urethra [31]. Less kidney stone formation was found using *Ammi visnaga* [32].

Tea prepared from the fruits of *Ammi visnaga* has been traditionally used by patients with renal stones in Egypt and elsewhere. The aqueous extract of this fruit accelerated the dissolution of cystine stones in the kidneys. The fruit and its two major constituents, namely khellin and visnagin, showed beneficial effects in the management of kidney stone disease caused by hyperoxaluria [33].

2.8. Pomegranate

Pomegranate extract, 1 g daily for 90 days, lowered supersaturation of calcium oxalate in urine and lowered calcium 39 percent in urine [34]. Pomegranate juice in a clinical trial decreased serum paraoxonase activity and supersaturation of calcium oxalate [35].

2.9. *Oenothera biennis* (Evening primrose seed oil)

In a human study, daily ingestion of Evening primrose seed oil (1000 mg per day) significantly increased citraturia (urinary citrate levels), while reducing urinary oxalate, calcium, and the Tiselius risk index, which is a measurement of risk for forming kidney stones [36].

2.10. Wu-Ling-San

A formula, Wu-Ling-San, with *Rhizoma alismatis*, *Poria cocos* Wolf, *Polyporus umbellatus* Fries, *Rhizoma Atractylodis*, *Macrocephalae*, and *Ramulus Cinnamomi Cassiae* effectively inhibited the process of calcium oxalate nucleation, crystallization, and aggregation, increasing urine volume in a prospective, randomized, controlled clinical trial [37].

2.11. Cystone®

Tests in synthetic urine show that this medical plant formula has the potential to serve as an inhibitor of calcium oxalate stone formation. Cystone® significantly reduced the average particle size of precipitated crystals relative to un-dosed synthetic urine (30.9% less). It also decreased the rate of crystal growth significantly [38].

In 40 clinical trials of Cystone®, in 636 patients, data indicate that there was a significant decrease in presence of renal calculi and the calculi size decreased from 6.21 mm to 0.57 mm ($p < 0.0067$). Side effects were rare and mild. Presence of renal calculi in 636 subjects was reduced to only 78 subjects after treatment. Best results were in kidney and ureter, versus bladder. It increased urine volume and significantly decreased oxalate, uric acid, and calcium in the urine [39]. Cystone has shown its utility as a promising anti-urolithiatic medicine in clinical trials [40].

3. Medical plants that inhibit and reduce kidney stones from pre-clinical data

3.1. *Asparagus racemosus* (Shatavari root)

Asparagus racemosus had an inhibitory potential on lithiasis and inhibited crystallization [41]. *Asparagus racemosus* was found to inhibit formation of calcium oxalate stones in test animals [42]. *Asparagus racemosus* had an inhibitory potential on lithiasis [43].

3.2. *Phyllanthus niruri* (Chanca piedra/Stonebreaker)

Phyllanthus niruri is native to the tropics and has a long history of use for helping to prevent and pass kidney stones. In several animal studies; daily intake of this herb helped to prevent the formation of kidney stones [44]. The continued administration of a small volume of aqueous *Phyllanthus niruri* extract induced a significant reduction in calculus growth; which may be related to urethral relaxation [45]. *Phyllanthus niruri* has shown its utility as a promising anti-urolithiatic medicine in clinical trials [46].

3.3. *Orthosiphon grandiflorus*

Orthosiphon grandiflorus is antilithiatic in humans [47]. However, in an in vitro system, there was an absence of any anti-lithogenic effects of *Orthosiphon stamineus* [48]. Tests in synthetic urine show that *Orthosiphon grandiflorus* has the potential to serve as an inhibitor of calcium oxalate stone formation. It significantly reduced the average particle size of precipitated crystals 20% relative to un-dosed synthetic urine. The extract decreased the rate of growth of calcium oxalate stone formation significantly [49].

3.4. *Trigonella foenum-graecum* (Fenugreek)

Fenugreek lowers urinary concentrations of stone forming constituents [50]. Fenugreek seeds are commonly used in northern Africa to prevent and treat kidney stones. In an animal study it was found that Fenugreek seed significantly reduced calcification in the kidney and helped prevent kidney stones [51].

3.5. *Camellia sinensis* (tea)

Camellia sinensis, in a clinical trial, decreased urinary oxalate excretion and calcium oxalate deposit formation [52].

3.6. *Hibiscus sabdariffa*

Hibiscus sabdariffa is used in Thai traditional medicine. *Hibiscus sabdariffa* is used for the prevention and treatment of urinary stones. A clinical trial, which tested a cup of tea made from 1.5 g of dry *H. sabdariffa*, which was taken two times daily by 18 patients for 15 days, revealed a significant increase in uric acid excretion and clearance from kidneys by urine [53].

3.7. *Biophytum sensitivum*

The methanolic extract of the whole plant of *Biophytum sensitivum* showed significant anti-urolithiatic activity as indicated by improvement in stone weight [54].

3.8. *Origanum vulgare* (Oregano)

Origanum vulgare is widely used as spice and medicine. It works as a lithotripter, diuretic, and antispasmodic. The crude aqueous extract of the aerial part of *Origanum vulgare* exhibited in vitro inhibitory activity in the nucleation and aggregation of calcium oxalate crystals. *Origanum vulgare* extract also decreased the number of crystals produced in calcium oxalate test solutions [55].

3.9. *Ipomoea eriocarpa*

The leaf extract of *Ipomoea eriocarpa* is useful to prevent the recurrence of urolithiasis in the early stages of stone development. Possible mechanisms include increased diuresis and lowering of urinary concentrations of stone-forming components [56].

3.10. *Berberis vulgaris* (Barberry root bark)

Berberis vulgaris was found to inhibit calcium oxalate crystallization and reduce kidney damage caused by oxidative stress. The water extract was the most effective preparation [57].

3.11. *Melia azedarach*

The aqueous and ethanol leaf extracts of *Melia azedarach* possess potent antiurolithiatic activity against ethylene glycol-induced calcium oxalate urolithiasis in rats. The antiurolithiatic effects may be mediated through a combination of calcium oxalate crystal inhibition, diuretic, antioxidant, and renal epithelial cell protective [58].

3.12. *Desmodium styracifolium*

Tests in synthetic urine show a potential for *Desmodium styracifolium* to serve as an inhibitor of calcium oxalate stone formation. *Desmodium styracifolium* significantly reduced the average particle size of precipitated crystals relative to un-dosed synthetic urine (21.6% less). It decreased the rate of growth of kidney stones significantly [59].

3.13. Other medical plants used to reduce kidney stones

Urtica dioica (nettles), *Petroselinum crispum* (parsley), *Zea mays* (corn silk), and *Nasturtium officinale* were used for their diuretic effect. *Althea officinalis* (marshmallow root) was used for its anti-inflammatory and soothing effect in urolithiasis management [60]. The aqueous decoction of *Celosia argental* (Viratarvadigana) is used for the dissolution and excretion of stones. *Didymocarpus pedicellata*, commonly known as Patharphodi or Shila pushp, is useful for kidney and bladder stones [61]. The aqueous and alcoholic extracts of the root wood of *Moringa oleifera* significantly reduced elevated urinary oxalate [62]. Serum urea and creatinine levels were significantly lower with Ashwagandha. Rutin and curcumin are polyphenolic compounds that reduce the number of calcium oxalate deposits in the kidney. Ginger reduced super saturation of calcium oxalate and thus decreased stone deposition in renal tubules [63].

4. Conclusion

Many of the medical plants used historically for kidney stones have now been found to be effective in reducing risk and reducing kidney stone size in modern clinical trials. Reducing recurrence of stones after removal is important. Certain medical plants have been shown to slow the formation of calcium oxalate crystals and significantly reduce stone size. Several of these medical plants have nephroprotective, antioxidant, and antimicrobial effects. The plants with the best clinical trials and supporting preclinical data showing effectiveness in reducing kidney stone formation and recurrence are *Nigella sativa* (black cumin seed), *Dolichos biflorus* (horse gram), *Crataeva nurvala* (varuna bark), and *Tribulus terrestris* (Gokshura). Some of these medical plants may be more effective and safer than tamsulosin and potassium citrate. Our goal is to provide busy clinicians with accurate information about the use of medical plants to reduce risk and recurrence of kidney stones.

Compliance with ethical standards

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Disclosure of conflict of interest

No conflict of interest.

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