



Review Article

Herbal therapeutics in urolithiasis: A critical review with focus on *Acalypha indica* Linn.Karveer Babanrao Aghade^{1*} ¹Dept. of Pharmacology, MES College of Pharmacy, Sonai, Maharashtra, Mumbai, India

Abstract

Background: Urolithiasis (urinary stone disease) remains a significant global health problem, with high recurrence rates. Current treatments can be invasive, expensive, or associated with side-effects. Herbal medicines have been under investigation as safer, more accessible alternatives. Among them, *Acalypha indica* Linn. (Kalijeera) has shown promising in vitro and in vivo anti-urolithiatic actions.

Aim: To review and synthesize current knowledge on the pathophysiological mechanisms of urolithiasis, existing pharmacological and herbal therapies, with special focus on *Acalypha indica*, its phytochemistry, mechanism of action, efficacy, safety, and gaps in research.

Results: Mechanisms of stone formation include supersaturation, nucleation, growth, aggregation, retention, oxidative stress, and epithelial cell injury. Many herbs (e.g. *Phyllanthus niruri*, *Clitoria ternatea*, *Dolichos biflorus*) and compounds (flavonoids, saponins, alkaloids) have demonstrated anti-urolithiatic properties. *Acalypha indica* in particular exhibits inhibition of calcium oxalate nucleation (in vitro), restoration of membrane-bound ATPases and marker enzymes in urolithic rats, and favorable safety profile at high doses. Phytochemicals such as flavonoids, tannins, and alkaloids are likely involved.

Conclusion: *Acalypha indica* Linn. constitutes a promising herbal drug candidate for urolithiasis. However, there remain key gaps: clinical trials, mechanistic studies, standardization of extracts, doses, and safety in humans. Future work should address these to translate experimental findings into therapeutic use.

Keywords: Urolithiasis, Herbal therapy, *Acalypha indica*, Calcium oxalate, Phytochemicals, Kidney stones

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1. Introduction

Urolithiasis is the formation of calculi in the urinary tract, primarily composed of calcium oxalate. The global prevalence ranges from 5–15%.¹ Pathophysiological mechanisms include supersaturation of urine with stone-forming salts, nucleation, crystal growth, aggregation, oxidative stress, and epithelial injury.^{1–3} Conventional therapies include hydration, citrate supplementation, thiazide diuretics, and surgical removal, but recurrence rates remain high.^{1,4} Herbal medicines are increasingly studied for their cost-effectiveness, safety, and efficacy in stone prevention and dissolution.^{4,5} *Acalypha indica* Linn. (Family Euphorbiaceae) is traditionally used for urinary disorders and has demonstrated significant antiurolithiatic activity.^{2,6}

1. Urolithiasis is defined as the formation of calculi in the urinary tract, most commonly composed of calcium oxalate. The global prevalence ranges approx. 5–15% in many regions, with high recurrence.¹
2. Pathophysiological processes include supersaturation of urine with stone forming salts, nucleation, crystal growth, aggregation, retention, as well as contributions of oxidative stress and cellular injury.²

3. **Conventional treatments:** hydration, inhibitors (e.g. citrate), surgical removal (lithotripsy), and pharmaceuticals (e.g. thiazides). Limitations: side effects, cost, invasiveness, recurrence.
4. Herbal medicines are receiving increased attention. Several recent systematic reviews and preclinical studies show efficacy of plant extracts in reducing stone formation and ameliorating renal damage.^{4,5}
5. *Acalypha indica* Linn. (Family Euphorbiaceae), known locally as Kalijeera, is used in traditional medicine for urinary disorders. Phytochemical studies show presence of flavonoids, saponins, tannins, etc. Some in vitro and in vivo data support anti-urolithiatic effects.
6. **Objective of this review:** To critically evaluate the molecular and mechanistic basis of urolithiasis; to summarize evidence of herbal therapies especially *A. indica*; to highlight gaps and propose future research directions.

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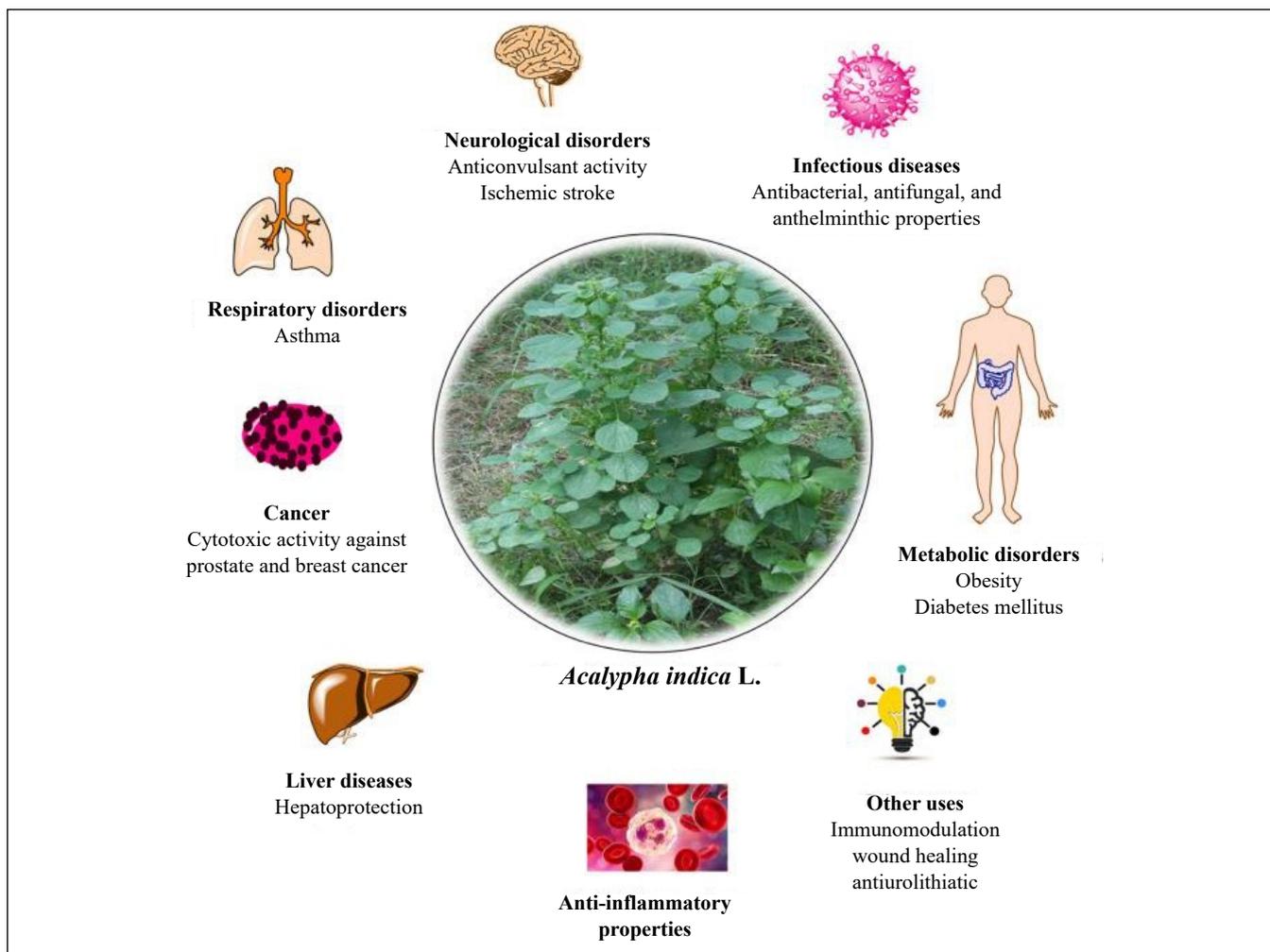


Figure 1: Pharmacological and therapeutic activities reported for *Acalypha indica* Linn (Source: https://www.researchgate.net/figure/Pharmacological-properties-of-Acalypha-indica-L_fig2_374474874)

2. Pathophysiology of Urolithiasis

Stone formation involves stages of supersaturation, nucleation, growth, aggregation, and retention. Oxidative stress and epithelial injury facilitate crystal adhesion.^{1-3,7}

2.1. Supersaturation and nucleation

Urine becomes supersaturated with stone forming salts (e.g. Ca^{2+} , oxalate, phosphate) leading to primary nucleation.^{1,3}

2.2. Crystal growth, aggregation, and retention

Crystals grow, aggregate, sometimes adhere to renal epithelium, get retained. Mechanisms involve inhibitors (e.g. citrate, glycosaminoglycans) and promoters (e.g. oxalate, urinary pH).¹

2.3. Role of oxidative stress and epithelial damage

Reactive oxygen species (ROS) contribute significantly to epithelial injury, inflammation, and favour adhesion of crystals to tubular cells.³

2.4. Molecular mediators

Enzymes like membrane-bound ATPases (Ca^{2+} -ATPase, Mg^{2+} -ATPase, Na^+/K^+ ATPase), marker enzymes. Receptors

and signaling pathways (e.g., osteopontin, crystal-cell interactions) influence stone formation.⁷

3. Conventional Pharmacological Therapies

1. **Pharmaceutical inhibitors:** citrate, thiazide diuretics, allopurinol (for uric acid stones), etc.¹
2. **Interventional methods:** extracorporeal shock wave lithotripsy (ESWL), ureteroscopy, percutaneous nephrolithotomy.¹
3. **Challenges:** recurrence, patient compliance, cost, side effects (e.g. metabolic disorders, renal side effects), limited accessibility in many region.¹

4. Herbal and Phytochemical Therapies

Numerous herbal drugs exhibit anti-urolithiatic potential by inhibiting crystal formation, reducing oxidative stress, and normalizing renal function.^{1,4,5,8}

4.1. Overview

1. A number of reviews and systematic analyses have enumerated medicinal plants with evidence of anti-urolithiatic activity.¹

2. Mechanisms reported include inhibition of nucleation, growth, aggregation of crystals; improvement of renal oxidative status; diuretic action; reduction of supersaturation.¹ **Figure 1**

4.2. *Acalypha indica* Linn.: Evidence

Table 1: Summary of experimental evidence supporting anti-urolithiatic activity of *Acalypha indica* Linn.

Type of study	Method / model	Key findings
In vitro nucleation assay	Leaf/root extracts (methanolic, ethanolic) of <i>A. indica</i> using calcium-oxalate nucleation inhibition assay	Highest inhibition ~71% for methanolic root extract; ethanolic leaf extract also significant. (jyoungpharm.org)
In vivo enzyme / membrane-bound ATPases	Ethylene glycol induced urolithiasis in rats; extract dose ~200 mg/kg	Restoration of Ca ²⁺ -ATPase, Mg ²⁺ -ATPase, Na ⁺ /K ⁺ ATPase activities; normalization of marker enzymes in kidney and liver. (PubMed)
Phytochemical profiling	Leaves, roots – detection of alkaloids, flavonoids, tannins, saponins etc.	These compounds are potential contributors to antioxidant, anti-crystallization properties. (jedronline.org)

Table 1 summarizes in vitro and in vivo studies confirming *A. indica*'s inhibition of calcium oxalate nucleation, normalization of ATPase enzyme activity, and antioxidant effects.^{2,6}

4.3. Other herbal drugs with evidence

Phyllanthus niruri, *Clitoria ternatea*, *Dolichos biflorus*, *Annona squamosa*, etc. have shown efficacy in animal models and some in vitro systems. (Phyto Journal) Mechanistic studies for many herbs remain limited; clinical trial data is sparse. (PubMed)

5. Mechanisms of Action of *Acalypha indica* & Similar Herbs

The herb acts via inhibition of nucleation, antioxidant protection, ATPase enzyme modulation, and possible diuretic effects. Phytochemicals such as flavonoids and tannins contribute to these effects.^{2,3,6}

- Crystal nucleation inhibition:** The extracts prevent early nucleation of calcium oxalate crystals in vitro.²
- Antioxidant activity:** By restoring membrane-bound ATPases and reducing marker enzyme leakage

(AST, ALT, etc.), the oxidative damage in kidneys is ameliorated.^{2,3}

- Enzyme modulation:** ATPases are essential for ion homeostasis; *A. indica* improves their activity, helping restore balance of calcium, magnesium, sodium/potassium in renal cells.²
- Diuretic/lithotriptic-like effects:** Some herbs increase diuresis or alter urinary constituents so as to reduce supersaturation. (Not yet well-studied for *A. indica* beyond nucleation assays.)
- Anti-inflammatory/ cytoprotective effects:** Via reduction of ROS, cell damage, inflammation, helping reduce adhesion of crystals to epithelium.

6. Safety and Standardization

Acute toxicity studies report no adverse effects up to 2000 mg/kg in rats.² Extract standardization and human trials are needed for clinical validation.^{2,8,7,9}

A. indica acute toxicity studies up to 2000 mg/kg in rats showed no major adverse effects in preliminary short-term observation. (Phytochemical variability: the content of active compounds (flavonoids, tannins etc.) depends on part used (leaf vs root), extraction solvent, locality. Needs standardization. Human safety data is minimal; clinical trials are lacking. Possible herbal-drug interactions and long-term toxicity should be explored.^{2,9}

7. Gaps in Current Research

- Scarcity of clinical trials involving *A. indica* or many herbal interventions.
- Limited mechanistic studies for *A. indica*, need studies on oxidative stress markers, crystal-cell interactions, apoptosis, mitochondrial pathways.
- Standardization of extracts (which solvent, part, dose, frequency).
- Long-term safety and toxicity studies.
- Bioavailability of active compounds; formulation development.
- Comparative studies vs standard drugs.

8. Future Directions and Recommendations

- Design and conduct well-powered randomized clinical trials for herbal candidates particularly *A. indica*.
- Standardize extraction and characterization of phytochemicals (HPLC, LC-MS etc.).
- Investigate molecular mechanisms: e.g. ROS pathways, ATPases, epithelial adhesion, urinary inhibitors.
- Explore synergistic effects of combining *A. indica* with other herbal extracts or with conventional therapy.
- Develop pharmaceutical formulations (capsules, tablets, etc.) ensuring stability, bioavailability.
- Toxicological studies for chronic administration.

9. Conclusion

Acalypha indica Linn. shows promising antiurolithiatic potential through multiple mechanisms. However, clinical and mechanistic studies are essential for translational application.^{1–16}

Herbal therapies represent a promising avenue for prevention and treatment of urolithiasis. *Acalypha indica* Linn. emerges as a particularly interesting candidate, showing in vitro and in vivo efficacy, good safety profile, and plausible mechanism (enzyme modulation, antioxidant, nucleation inhibition). However, to translate experimental findings into clinical practice, more systematic research is needed—especially clinical trials, standardization, mechanistic exploration, and long-term safety. Integration of herbal drugs such as *A. indica* into therapeutic protocols may provide more accessible, safer, and cost-effective treatment options especially in regions with limited resources.

10. Source of Funding

None.

11. Conflict of Interest

The authors declare no conflict of interest.

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