

# ***Bergenia ligulata*: A Comprehensive Review of Its Phytochemistry, Pharmacology, and Public Health Potential**

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## **Abstract**

*Bergenia ligulata* (Wall.) Engl., commonly known as “Pashanbheda” or “stone breaker,” is a perennial herb of the family *Saxifragaceae*, widely utilized in South Asian traditional medicine for the prevention and treatment of urinary and renal disorders. This review synthesizes current evidence on its ethnomedicinal relevance, phytochemical composition, pharmacological properties, and potential public health applications. Extensive literature from 2005–2025 was examined following PRISMA guidelines through databases including PubMed, Scopus, and ScienceDirect. The phytochemical profile of *B. ligulata* is dominated by bergenin—a C-glycoside of 4-O-methyl gallic acid—alongside arbutin, gallic acid, catechin, protocatechuic acid, and diverse terpenoids and flavonoids, collectively contributing to its bioactivity. Pharmacological studies indicate that *B. ligulata* extracts exhibit multifaceted biological effects, notably anti-urolithiatic, antioxidant, anti-inflammatory, antimicrobial, and hepatoprotective activities. Mechanistically, these effects are mediated through inhibition of calcium oxalate crystallization, modulation of oxidative stress and inflammatory pathways (NF-κB, MAPK), enhancement of diuresis, and preservation of renal tissue integrity. Preclinical evidence strongly supports its traditional use in urolithiasis, though well-designed clinical trials remain scarce. From a public health perspective, *B. ligulata* holds promise as a cost-effective, culturally acceptable phytotherapeutic agent for urinary stone disease prevention in low- and middle-income regions with limited healthcare access. Standardization of extracts, toxicological validation, and

translational clinical studies are essential to advance its integration into evidence-based primary care and herbal pharmacotherapy.

**Keywords:** *Bergenia ligulata*, Pashanbheda, bergenin, phytochemistry, public health, traditional medicine.

## 1. Introduction

Chronic and recurrent disorders of the urinary system—including urolithiasis, urinary tract infections (UTIs), and chronic kidney disease (CKD)—represent a significant global health burden, both in terms of morbidity and healthcare costs. Among these, renal calculi (kidney stones) are especially challenging: recurrence rates can exceed 30–50% within five years, and in low-resource settings the availability of advanced urological interventions is often limited. In such contexts, traditional medicinal plants, long used by local communities, constitute an appealing reservoir of low-cost, culturally acceptable therapeutic options. *Bergenia ligulata* (Wall.) Engl. (family Saxifragaceae), commonly known in traditional South Asian systems (Ayurveda, Unani, Siddha, folk medicine) by vernacular names such as *Pashanbheda* (Sanskrit for “stone breaker”), *Ashmabhid*, *Nagabhid*, and *Zakhme Hayat*, is one of the most prominent plants reputed for its utility in urinary afflictions (Koul et al., 2020). The species is native to temperate Himalayan and sub-Himalayan zones (e.g. Kashmir to Bhutan, Khasi Hills), growing typically at altitudes of ~1,500–3,000 m under moist, rocky substrates (Koul et al., 2020; Wikipedia, n.d.). The rhizome (and sometimes roots) is the part most commonly harvested and used in decoctions, powders, extracts, or infusion forms across traditional practices. Ethnomedical lore attributes to *B. ligulata* a broad spectrum of uses: dissolving or preventing urinary calculi, alleviating painful urination (dysuria), reducing inflammation or swelling of urinary tract tissues, treating UTIs, and even wound healing or other disorders of kidneys, liver, or digestive tract (Roychoudhury et al., 2022). Its nickname “stone-breaker” reflects the central role of its anti-urolithiatic reputation in traditional pharmacopeias (Gurav & Gurav, 2014). From a modern biomedical perspective, considerable attention has been focused on its secondary metabolites, especially bergenin (a C-glycoside of 4-O-methyl gallic acid) and allied phenolic compounds (arbutin, gallic acid, protocatechuic acid, chlorogenic acid, catechin, tannins) as likely mediators of its biological effects (Roychoudhury et al., 2022). Contemporary pharmacological and mechanistic studies—though relatively limited in number—have begun to validate some of these traditional claims. For instance, *in vivo* and *in vitro*

experiments show that extracts and bioactive fractions of *B. ligulata* can inhibit calcium oxalate crystal nucleation, aggregation, and deposition; promote diuresis and saluretic effects; reduce oxidative stress in renal tissues; modulate mitochondrial function; and restore biochemical markers in animal models of hyperoxaluria (Bashir & Gilani, 2009; Sharma et al., 2017). More recent work shows that isolated bergenin itself can mitigate mitochondrial dysfunction, reactive oxygen species (ROS) generation, and tubular damage in hyperoxaluria models (Aggarwal et al., 2014). Nevertheless, the existing data remain fragmentary, with limited dose-response studies, scarce clinical trials, and incomplete toxicological profiling. To date, no single review has adequately bridged the gap between ethnobotanical tradition, phytochemistry, pharmacology, translational potential, and public health integration for *B. ligulata*. Given the continuing prevalence of urinary system disorders and the appeal of phytomedicines in low- and middle-income regions, a rigorous, integrative review is timely. Therefore, this review aims to: (i) Elucidate the botanical, taxonomic, and ethnopharmacological foundations of *B. ligulata*; (ii) Synthesize the pharmacological and mechanistic evidence (in vitro, in vivo, ex vivo) focusing on urinary/renal effects as well as ancillary bioactivities (anti-inflammatory, antimicrobial, antioxidant, etc.); (iii) Discuss the public health and policy implications of using *B. ligulata* in complementary preventive or therapeutic strategies in resource-limited settings. By aligning traditional wisdom with modern scientific scrutiny, this review seeks to contribute a balanced, actionable foundation for further research, development, and potential deployment of *B. ligulata* in public health strategies.

## 2. Methodology

I conducted a comprehensive narrative review on *Bergenia ligulata* using a systematic approach following PRISMA principles. Literature published between 2005 and 2025 was searched from major databases including PubMed, Scopus, ScienceDirect, and Google Scholar, using keywords such as “*Bergenia ligulata*,” “ethnomedicine” “Pashanbheda,” “phytochemistry,” “pharmacology,” “toxicity,” and “public health significance.” Only peer-reviewed English articles related to the phytochemical composition, pharmacological activities, toxicity, or ethnomedicinal importance of *B. ligulata* were included. Duplicates, non-scientific reports, and studies with unclear taxonomy were excluded. From each selected paper, I extracted information on the plant part used, bioactive compounds, experimental model, dosage or concentration, and observed

biological activity. All collected data were organized and analyzed thematically to summarize findings under phytochemistry, pharmacology, and health relevance.

## 2. Botanical and Ethnomedicinal Profile

*Bergenia ligulata* belongs to the family Saxifragaceae. It is a perennial herb with thick rhizomes, large fleshy leaves, flower stalks bearing clusters of pinkish to reddish flowers and broad distribution in the Himalayas: from Kashmir eastwards through Nepal, Sikkim, Bhutan, and in the hill states of Northeastern India. It is also reported from Pakistan and certain adjoining areas. Altitudinal range varies, but generally it grows in rocky, shady slopes, often in the temperate or subalpine zones (Gurav & Gurav, 2014). The rhizome is the primary medicinal part, though leaves are sometimes used in folk decoctions or external applications. Traditional medicinal systems have long attributed to *B. ligulata* properties consistent with its name “stone breaker.” In Ayurveda and Unani texts, it appears under formulations used for dissolving kidney and bladder stones, treating painful urination, fever, jaundice, wounds, and inflammation (Koul et al., 2020). In Himalayan tribal communities, use of powdered rhizome, decoctions, or combinations with other herbs is common. For example, among Bhotia tribes, dried rhizome powder is consumed to treat kidney stones; among Monpa and Naga tribes, leaf preparations are used for wounds or cool compresses (V. Kumar & Tyagi, 2013). These ethnomedicinal practices are regionally variable in preparation method, dosage, and combination herbs, but widespread enough to indicate strong cultural familiarity (Roychoudhury et al., 2022). A recent micropropagation protocol using leaf explants (in vitro) has been reported that could help propagate endangered populations for sustainable harvesting (Rani et al., 2023).

### Classification

|            |                        |
|------------|------------------------|
| Kingdom    | Plantae                |
| Subkingdom | Tracheophyta           |
| Division   | Magnoliophyta          |
| Class      | Magnoliopsida          |
| Order      | Saxifragales           |
| Family     | Saxifragaceae          |
| Genus      | <i>Bergenia Moench</i> |

|         |                                  |
|---------|----------------------------------|
| Species | <i>Bergenia ligulata</i> (Wall.) |
|---------|----------------------------------|

### 3. Phytochemistry

Modern phytochemical profiling reveals that *B. ligulata* is rich in phenolic compounds, glycosides, flavonoids, terpenoids, and lipids. The compound bergenin (a C-glycoside of 4-O-methy-gallic acid) is the signature bioactive molecule and is used as a chemical marker in many studies. Other compounds consistently identified include arbutin, gallic acid, chlorogenic acid, protocatechuic acid, catechin, syringic acid, ferulic acid, "+-afzelechin", paashaanolactone, various terpenes (e.g. caryophyllene, 1,8-cineole), sterols ( $\beta$ -sitosterol, stigmasterol), tannic acid, quercetin, reynoutrin, etc (Roychoudhury et al., 2022). Ultra-high performance liquid chromatography coupled with hybrid linear ion trap triple quadrupole mass spectrometry (UHPLC-QqQLIT-MS/MS) in some studies has quantified eight of the major bioactives (bergenin, arbutin, gallic acid, protocatechuic acid, chlorogenic acid, catechin, syringic acid, and ferulic acid). Among *Bergenia* species, *B. ligulata* tends to have highest total content of these eight compounds (Koul et al., 2020). The variation in compound content is influenced by geographic origin, altitude, part of plant (rhizome vs leaf vs root), stage of harvest, and extraction method (solvent type, temperature). For example, in the antibacterial profiling study by Rajbhandari et al. (2013), along with bergenin, other minor compounds such as 11-O-p-hydroxybenzoylbergenin, 6-O-galloylarbutin, and epiafzelechin were isolated, marking first reports of those in *B. ligulata* from Nepal (Rajbhandari et al., 2013). Analytical methods used include HPLC, LC-MS, FTIR, GC-MS, UV-Vis spectrophotometry, NMR, sometimes XRD (for structure elucidation), and bioactivity-guided fractionation. For example, structure-activity work comparing bergenin, p-hydroxybenzoylbergenin, and 11-O-galloylbergenin shows that 11-O-galloylbergenin tends to have stronger antioxidant and urease inhibitory activity ( $IC_{50}$  values in DPPH scavenging / reducing power assays) than other compounds (Sadat et al., 2015). A recent GC-MS analysis of methanolic and aqueous rhizome extracts identified ~45 phytochemical constituents in methanol extract and ~35 in aqueous extract. Common major constituents included dihydro-3-methylene-5-methyl-2-furanone, oleic acid, n-hexadecenoic acid, etc.; both extracts showed cytotoxic effects on certain cancer cell lines with acceptable biocompatibility to HEK-293 (human embryonic kidney) cells (Nadeem et al., 2025). These data show *B. ligulata* is phytochemically diverse, with multiple molecules potentially

contributing to its pharmacological effects; the presence of numerous antioxidant and phenolic compounds supports many observed activities.

#### **4. Pharmacological Activities and Mechanisms**

##### **4.1 Anti-urolithiatic / Anti-stone Activity**

The anti-urolithiatic (anti-lithiasis) potential of *Bergenia ligulata* represents its most extensively investigated pharmacological domain, reflecting its long-standing ethnomedicinal use in the management of renal calculi and urinary disorders. Experimental and mechanistic studies strongly support the traditional claim that *B. ligulata* possesses lithotriptic properties, capable of preventing stone formation and facilitating the dissolution of urinary calculi. A researcher first demonstrated that ethanolic and aqueous extracts of *B. ligulata* rhizomes inhibited calcium oxalate (CaOx) crystallization in vitro and significantly reduced stone formation in ethylene glycol–induced urolithiatic rats, primarily through suppression of nucleation, aggregation, and crystal growth (Bashir & Gilani, 2009). The observed effects were attributed to increased urinary citrate and magnesium levels, diuretic action reducing supersaturation, and antioxidant activity mitigating oxidative stress in renal tissues. *B. ligulata* attenuated oxidative damage in renal tissue exposed to CaOx crystals, thereby disrupting the oxidative stress–mediated adhesion of crystals to the epithelium (Saha et al., 2014). Recent mechanistic insights reveal that ethanolic extracts of *B. ligulata* can attenuate oxalate-induced injury in renal epithelial (NRK-52E) cells by reducing apoptosis and modulating key inflammatory pathways, including NF- $\kappa$ B, MAPK, and osteopontin (OPN). Moreover, the extract altered CaOx crystal morphology, converting the more calcium oxalate monohydrate (COM) form to the less injurious calcium oxalate dihydrate (COD) form, while reducing oxidative stress biomarkers (Singh et al., 2021). In vivo, ethylene glycol–induced rat models have shown that dichloromethane fractions of aqueous *B. ligulata* extract significantly lowered urinary oxalate, calcium, uric acid, and urea levels, preserving renal histoarchitecture and improving antioxidant enzyme status (Sharma et al., 2017). The isolated compound bergenin—one of the major bioactive constituents of *B. ligulata*—demonstrated potent anti-urolithiatic efficacy at 10 mg/kg in hyperoxaluric rats, reversing weight loss, enhancing creatinine clearance, restoring antioxidant enzyme levels (superoxide dismutase, catalase), and reducing lipid peroxidation and renal tubular damage (Aggarwal et al., 2014). Comparable findings were reported in earlier studies using methanolic extracts of *B. ligulata* rhizomes, which inhibited  $\text{CaC}_2\text{O}_4$  crystal

formation and aggregation, and exhibited significant free-radical scavenging activity against DPPH and lipid peroxidation in vitro. In male Wistar rats administered 0.75% ethylene glycol, methanolic extracts (5–10 mg/kg) prevented renal  $\text{CaC}_2\text{O}_4$  crystal deposition, polyuria, weight loss, and oxidative stress, while enhancing urinary magnesium excretion—suggesting a combined mechanism involving diuretic, hypermagnesuric, and antioxidant actions ((Ballabh et al., 2008); (Bashir & Gilani, 2009)). Both *B. ligulata* extracts and isolated bergenin exhibited marked dissolution of urinary calculi in kidney and urinary constituents (Satish & Umashankar, 2006). In comparative in vitro analyses, *B. ligulata* inhibited calcium oxalate monohydrate crystal growth more effectively than *Tribulus terrestris*, implying a key role of biomacromolecules in COM inhibition (Gurav & Gurav, 2014). Furthermore, dichloromethane fractions of *B. ligulata* extract demonstrated significant anti-aggregatory effects against kidney stones at 7 mg/kg for 21 days, confirming bergenin as the principal antilithiatic molecule through spectroscopic analysis (Aggarwal et al., 2014; Sharma et al., 2017). Although animal and in vitro studies consistently validate the antilithiatic efficacy of *B. ligulata*, clinical evidence remains limited. A registered open-label, non-randomized clinical trial proposed to assess “Calcury” tablets containing *B. ligulata* in renal calculi patients; however, results are not yet widely published (Haritha et al., 2021). Robust randomized controlled human trials are therefore necessary to confirm efficacy, optimize dosing, and evaluate safety. Notably, many experimental designs employ high, non-physiological doses, and often overlook factors such as urinary pH, diet, and stone composition (calcium oxalate, uric acid, or struvite). Nevertheless, preclinical findings collectively establish *B. ligulata*—particularly its rhizomal extract and bergenin—as a promising natural anti-urolithiatic agent that operates through multifactorial mechanisms including antioxidant defense, modulation of inflammatory mediators, inhibition of CaOx crystal nucleation and aggregation, diuretic action, and protection of renal cellular integrity.

#### **4.2 Antioxidant / Free Radical Scavenging Activity**

Oxidative stress is a key contributor to renal injury, inflammation, and urolithiasis, as it promotes crystal adhesion, lipid peroxidation, and cellular apoptosis within renal tissues. The antioxidant potential of *Bergenia ligulata* has therefore been widely examined in both in vitro and in vivo models to elucidate its role in mitigating oxidative damage. Extracts and isolated fractions of *B. ligulata* have demonstrated substantial free radical scavenging activity in multiple standard assays,

including 2,2-diphenyl-1-picrylhydrazyl (DPPH), ferric reducing antioxidant power (FRAP), 2,2'-azino-bis (3-ethylbenzothiazoline-6-sulfonic acid) (ABTS), nitric oxide scavenging, and reducing power assays. Gohain et al. (2020) reported that the methanolic and n-butanol fractions of *B. ligulata* exhibited notably low IC<sub>50</sub> values in DPPH scavenging assays, with the n-butanol fraction showing the highest potency (~4.5 µg/mL) compared to approximately 30 µg/mL for the aqueous extract (Agnihotri et al., 2015). Earlier studies also indicated moderate antioxidant capacity, with methanolic extracts displaying IC<sub>50</sub> values around 50 µg/mL (Gurav & Gurav, 2014). These findings collectively suggest a dose-dependent radical scavenging efficiency that correlates positively with the extract's total phenolic and bergenin content. Mechanistically, the antioxidant efficacy of *B. ligulata* is primarily attributed to its diverse array of polyphenolic compounds, including bergenin, catechin, gallic acid, and tannins, which act as electron or hydrogen atom donors to neutralize reactive oxygen species (ROS) and free radicals. Additionally, these constituents can chelate transition metal ions such as Fe<sup>2+</sup> and Cu<sup>2+</sup>, thereby preventing metal-catalyzed free radical generation. Structure–activity relationship analyses have revealed that derivatives such as 11-*O*-galloylbergenin possess enhanced DPPH radical scavenging activity (lower EC<sub>50</sub> values) relative to other analogues (Sadat et al., 2015). The relevance of this antioxidant activity extends beyond in vitro assays: in vivo studies suggest that these effects underpin the nephroprotective and antiurolithiatic properties of *B. ligulata*, as protection against oxidative insult reduces crystal adherence and tubular cell apoptosis in hyperoxaluric conditions. Moreover, the antioxidant action of *B. ligulata* is closely intertwined with its anti-inflammatory potential. Ethanolic extracts have been shown to downregulate the expression of pro-inflammatory mediators such as NF-κB and MAPKs, suppress cytokine release, and attenuate edema and serum markers of inflammation in animal models. This dual antioxidant–anti-inflammatory mechanism provides a plausible explanation for its protective effects in renal and hepatic pathologies. Beyond nephroprotection, *B. ligulata* extracts have also displayed cytoprotective and anticancer activities; GC–MS-based studies revealed that methanolic and aqueous rhizome extracts induce apoptotic morphological changes, including nuclear fragmentation, in various cancer cell lines, while maintaining biocompatibility toward normal human embryonic kidney (HEK-293) cells (Nadeem et al., 2025).

#### **4.3 Anti-inflammatory and Analgesic Effects**



Inflammation of renal and urinary tissues is a major pathological contributor to the symptomatology of urolithiasis and related urinary disorders, often manifesting as pain, edema, and epithelial injury. In this context, the anti-inflammatory potential of *Bergenia ligulata* has been investigated in various animal models, revealing moderate to significant activity in reducing inflammatory responses. Experimental studies cited in earlier pharmacological reviews have shown that *B. ligulata* extracts exert anti-inflammatory effects comparable to standard cyclooxygenase (COX) inhibitors. In particular, treatment with rhizome extracts was associated with suppression of edema formation and downregulation of COX-2 expression in rodent models, suggesting interference with the prostaglandin synthesis pathway (Gurav & Gurav, 2014). Although detailed molecular investigations are limited, available evidence indicates that *B. ligulata* may modulate key inflammatory mediators such as NF- $\kappa$ B and MAPKs, thereby reducing cytokine release and inflammatory signaling cascades. These effects may be closely linked to its potent antioxidant activity, which mitigates reactive oxygen species (ROS) production and prevents oxidative activation of proinflammatory transcription factors. Consequently, the observed nephroprotective and antiurolithiatic benefits of *B. ligulata* may, in part, arise from its anti-inflammatory influence on renal epithelial tissues subjected to crystal-induced oxidative stress. In contrast, reports of direct analgesic effects are limited and inconclusive. According to studies summarized by (Gurav & Gurav, 2014), oral administration of hydroalcoholic *B. ligulata* extract (250 mg/kg) did not elicit a statistically significant analgesic response in hot plate and tail clip models in mice, implying that the plant does not act directly on nociceptive pathways. Therefore, any perceived reduction in pain during urolithiasis or urinary inflammation is more likely secondary to its anti-inflammatory and mild diuretic actions, which collectively alleviate pressure, edema, and irritation in the urinary tract rather than modulating pain receptors directly.

#### **4.4 Antimicrobial and Antimicrobial Enhancement Activity**

Urinary tract infections (UTIs) frequently occur as comorbidities in patients with urolithiasis, the antimicrobial potential of *Bergenia ligulata* is of considerable pharmacological relevance. Several studies have reported that crude extracts and isolated compounds from *B. ligulata* possess antibacterial and antifungal properties, with activity demonstrated against a range of Gram-positive, Gram-negative, and fungal pathogens. Ethanol and aqueous leaf extracts of *B. ligulata* against *Escherichia coli*, *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Candida albicans*,

and *Penicillium* spp. using the agar well diffusion method. Zones of inhibition ranged from approximately 6.9 to 12.8 mm, with *E. coli* showing the highest susceptibility (12.81 mm for ethanolic extract and 11.53 mm for aqueous extract at 250 mg/mL). The minimum inhibitory concentration (MIC) values were reported as ~6.25 mg/mL for *P. aeruginosa* (ethanolic extract) and for combined aqueous–ethanolic extracts against *C. albicans*. These findings indicate that *B. ligulata* possesses broad-spectrum antimicrobial activity, with notable efficacy against enteric and opportunistic pathogens relevant to urinary and systemic infections (P. Kumar et al., 2022). Further chemical and mechanistic investigations have identified several bioactive constituents responsible for these antimicrobial effects. Isolated compounds such as bergenin, 11-*O*-p-hydroxybenzoylbergenin, 6-*O*-galloylarbutin, and epiafzelechin from the methanolic extract of *B. ligulata*, demonstrating activity predominantly against Gram-positive bacteria like *S. aureus* (Rajbhandari et al., 2013). A subsequent bioassay-guided fractionation study on drug-resistant bacterial and fungal pathogens revealed that the ethyl acetate sub-fraction, rich in bergenin (~38.2% by weight), exhibited MIC values of 31.25 µg/mL against *E. coli*, 250 µg/mL against *S. aureus*, and approximately 62.5 µg/mL against *C. albicans*. Molecular docking and ADME (absorption, distribution, metabolism, excretion) analyses further predicted favorable pharmacokinetic and drug-likeness profiles for bergenin, supporting its role as both an antimicrobial agent and a potential bioenhancer (Rolta et al., 2022). Additionally, beyond bacterial and fungal infections, *B. ligulata* has shown significant antiparasitic potential. In a *Leishmania donovani* infection model in BALB/c mice, bergenin-rich root extracts produced a ~95.56% reduction in parasite load at higher doses. This was accompanied by a shift in immune response toward a Th1-dominant profile (increased IL-12 and IFN-γ, with suppression of IL-10 and IL-4) and enhanced delayed-type hypersensitivity (DTH) responses, all without inducing hepatic or renal toxicity (Kaur & Kaur, 2018). Collectively, these findings suggest that *B. ligulata* exhibits broad-spectrum antimicrobial efficacy and holds promise as a natural bioenhancer capable of augmenting conventional antimicrobial therapies. Nevertheless, the current evidence is largely limited to in vitro and preclinical models; standardized MIC determinations, mechanistic validations, and well-designed clinical trials are essential to confirm its therapeutic value and establish its role in managing infection-associated urolithiasis and other microbial pathologies.

## 5. Public Health Relevance and Case Studies

## 5.1 Epidemiology and the Burden of Urinary Stone Disease

Urolithiasis remains a significant global health issue, affecting approximately 5–10% of the population worldwide and contributing substantially to morbidity and healthcare costs (Koul et al., 2020). The prevalence varies geographically, with particularly high rates reported across Asia. In West Asia, Southeast Asia, and South Asia, prevalence estimates range from 5% to 19.1%, with recurrence rates of 21–53% over 3–5 years (Liu et al., 2018). Within South Asia, rural and low-income populations bear a disproportionate burden due to limited access to diagnostic imaging, urological care, and preventive health services. Environmental and lifestyle factors play pivotal roles: high ambient temperature and low humidity accelerate dehydration, while dietary practices — such as high oxalate and low calcium intake — increase stone risk. Insufficient water consumption, limited dietary diversity, and low awareness of preventive behaviors further compound the problem. The resulting health burden extends beyond urolithiasis itself, as recurrent stones and infections may predispose individuals to chronic kidney disease (CKD), an increasingly recognized noncommunicable disease affecting nearly 700 million people globally. These patterns highlight an urgent need for affordable, culturally acceptable preventive strategies, particularly in low- and middle-income countries (LMICs). *B. ligulata* extracts or formulations (after validation) could serve in primary care settings (herbal clinics, traditional medicine practitioners) for prevention of stone recurrence, management of early disease, or possibly as adjuncts.

## 5.2 Ethnomedical Use and Case Examples of Traditional Interventions

Although large-scale clinical trials of *Bergenia ligulata* in human populations are lacking, ethnomedical reports and local case series underscore its longstanding role in traditional healthcare systems. In the Himalayan foothills and northeastern states of India, traditional healers commonly administer rhizome powder or aqueous decoctions of *B. ligulata* to individuals presenting with symptoms of renal colic or urinary discomfort. Ethnobotanical surveys document consistent use across multiple tribal communities, where the dried rhizome is consumed either alone or in combination with other lithotriptic herbs (Roychoudhury et al., 2022). While largely anecdotal, the recurrence of similar practices across geographically distinct populations suggests a perceived preventive or early-intervention benefit. Comparable use patterns have been reported in primary health clinics in rural Uttarakhand and North Bengal, where herbal outpatient services often integrate *B. ligulata* decoctions for managing urinary disorders. Though quantitative clinical

outcomes (e.g., stone size reduction or recurrence rate) remain sparsely documented, patient-reported improvements in pain relief, urinary flow, and frequency have been noted when the herb is administered alongside conventional hydration and dietary guidance.

In preclinical contexts, the protective effects observed in hyperoxaluric rat models — including reduced crystal deposition and preservation of renal tissue structure following bergenin administration — provide biological plausibility for these traditional claims. Translation of these findings into standardized, clinically tested formulations could eventually support their deployment as community-level preventive measures in high-risk regions.

## 6. Research Gaps and Future Directions

1. Clinical trials: Phase I safety studies and randomized controlled trials for urolithiasis prevention/adjunctive therapy (Sharma et al., 2017).
2. Standardization: Pharmacopoeial monograph development (minimum bergenin content, validated HPLC methods) (Chitte et al., 2024).
3. Toxicology: Comprehensive subchronic/chronic and reproductive toxicity testing under GLP (Koul et al., 2020).
4. Mechanistic work: Molecular pharmacology on bergenin targets, PK/PD studies and potential drug interactions (Patel et al., 2012).
5. Formulation science: Development of stable, bioavailable formulations (e.g., standardized ethanolic extracts, phytopharmaceutical preparations) (Liu et al., 2023).
6. Health systems research: Implementation studies in primary care settings to assess acceptability, cost-effectiveness, and real-world safety (Hewagama & Hewawasam, 2022).

## 9. Conclusion

*Bergenia ligulata* exemplifies the convergence of traditional medicine and modern pharmacology. Substantial preclinical evidence supports its antiurolithiatic, antioxidant, anti-inflammatory, antimicrobial, and hepatoprotective properties, largely linked to bergenin and related phenolics. These findings validate its ethnomedicinal use, particularly in urinary and renal disorders. Despite

this promise, translation into clinical and public health practice remains limited by the lack of standardized extracts, toxicological assessments, and controlled human studies. Establishing these prerequisites is essential to confirm safety, efficacy, and reproducibility. In resource-limited settings with a high burden of urolithiasis, *B. ligulata* could serve as a cost-effective adjunct to preventive and integrative health strategies. Future research should focus on developing standardized formulations, conducting rigorous clinical trials, and ensuring ethical and sustainable utilization. With coordinated efforts among researchers, clinicians, and policymakers, *B. ligulata* holds potential to evolve from a traditional remedy to an evidence-based tool in public health and primary care.

### Conflict of Interest

There are no conflicts of interest declared by the author.

### Ethical Approval

Because this research did not include humans or animals, no ethical approval is required.

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