A Review on Kalanchoe pinnata Plant to Treat Urolithiasis

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***Abstract*—Many therapeutic herbs have played a major role in supporting economic growth and accessible healthcare in India. One such herb that has been utilized for its medicinal qualities for thousands of years in India is Kalanchoe pinnata. It is frequently referred to as "Patharchatta." It is a xerophytic shrub with fleshy, thick leaves. Kidney stones and urinary bladder stones are treated with its leaves. The antiurolithiatic action of Kalanchoe pinnata leaves has led to their selection in this study. After the extract was screened using phytochemicals, it was discovered to include saponins, phenolic compounds, and flavonoids. Two crucial assays, the crystal nucleation and aggregation assays, were used to examine the offered study project in vitro. Under in vitro circumstances, the inhibitory potential of the alcoholic extract of Kalanchoe pinnata was examined for the development of calcium oxalate crystals, which are primarily seen in the majority of kidney stones. Utilizing spectrophotometric techniques, the nucleation and aggregation of calcium oxalate crystals were measured independently. According to the results, Kalanchoe pinnata alcoholic extract has a greater ability to prevent crystal formation and aggregation. Kalanchoe pinnata has significant ability to dissolve calcium oxalate, the element most common in forming stones in the urinary tract, and also carries phytochemicals such as flavonoids, quercitrin, glycosides, carotenoids, saponin, kaempferol, and alkaloids that prevent CaOx crystal formation and deposition in renal tubules. The plant extract also reduces the size of calcium oxalate stones and has both treatment and preventive action in urolithiasis. Its pharmacological profile, including immunomodulator, CNS depressant, analgesic, antimicrobial, anti-inflammatory, antiallergic, antileishmanial, antitumor, antiulcer, antibacterial, antifungal, antihistamine, antiviral, febrifuge, gastroprotective, and anticancer activity, is reviewed and discussed. Currently a threatened species requiring conservation, the plant is simultaneously being investigated for its notable contributions to green chemistry.**

***Index Terms*—Kalanchoe pinnata; Pharmacognostical; Phytochemical; Pharmacological; Urolithiasis**

I. INTRODUCTION

Urolithiasis, also known as renal or urinary calculi, is a disorder characterized by the production and retention of stones in the kidney, bladder, or urethra. This can lead to renal colic, urine retention, and flank and abdominal pain. According to estimates, 12% of the global population will experience it, and after five to ten years of treatment, 50% of cases will reoccur. An imbalance between the kidneys' promoters and inhibitors of crystallization is part of the pathophysiology of urolithiasis. The complicated processes of supersaturation, nucleation, aggregation, development, and retention of crystals within the renal tubules are involved in the mechanism of calculi formation. The bulk of stones seen in the urine are calcium oxalate (CaOx) stones. Renal calculi have a complex etiopathogenesis that includes anatomical, environmental, infectious, metabolic, and dietary lifestyle factors [5].

The most recent methods for managing and treating such stone diseases include extracorporeal shock wave

lithotripsy and medical or surgical stone removal. However, they come at a high cost, have a number of negative effects, and do not stop stone formation from happening again. As a result, the utilization of medicinal herbs to treat stone diseases and illnesses is gaining popularity. Urinary stones and kidney disorders can be effectively treated with a variety of medicinal plants and their preparations, according to the Ayurvedic medical system [9].

Perennial herb Bryophyllum pinnatum (Lam.) Oken belongs to the family Crassulaceae. Kalanchoe pinnata and Bryophyllum calycinum are other synonyms. It is found in large quantities in Australia, Madagascar, China, India, and tropical Africa and America. The plant is also referred to as Pāṣāṇabheda in Ayurveda, which means "dissolver of stones." In traditional and ethnomedical practices, Bryophyllum pinnatum leaves are frequently used to treat stone problems and urinary insufficiency [10].

The leaves of the Kalanchoe pinnata plant naturally contain various anti-oxidant properties. The leaf powder of this plant was traditionally used for curing burning during urination, blocked urination, and leprosy. Compounds present in the plant can act as anticancer agents. Many tribes in Muzaffarnagar, Uttar Pradesh, use fresh leaf juice, combined with the powder of two to three black peppercorns (Piper nigrum Linn.), as a traditional remedy. The alcoholic extract of the leaves of Kalanchoe pinnata showed antioxidant activity [15], and in vitro studies have demonstrated inhibitory action of Kalanchoe pinnata leaves on the crystallization of calcium oxalate [1]. The purpose of this study is therefore to review how an alcoholic extract of Kalanchoe pinnata leaves affects the development of urinary calculi (urolithiasis).

This plant has diverse pharmacological activities, including toxicity to cattle, cytotoxicity, antihistaminic, immunosuppressive, antimutagenic, anticancer, antihypertensive, hepatoprotective, wound healing, uterine contractility, antidiabetic, antinociceptive, anti-inflammatory, analgesic, insecticidal, fungitoxic, phytotoxic, antileishmanial, neuropharmacological, nephroprotective, antiulcer, antimicrobial, tracheal antispasmodic, anti-allergic, antioxidant, antidepressant, anti-urolithiatic, gastroprotective, and anthelmintic activity. The studies reported are variable, and many have not been repeated and confirmed [8].

II. LITERATURE REVIEW

2.1 Taxonomic Profile

Kingdom: Plantae; Sub-kingdom: Viridaeplantae; Division: Tracheophyta; Sub-division: Spermatophytina; Class: Magnoliopsida; Superorder: Saxifraganae; Order: Saxifragales; Family: Crassulaceae; Genus: Kalanchoe; Species: Kalanchoe pinnata (Lam.) Pers. Synonyms include Cotyledon pinnata and Crassula pinnata. Common names include Jakh Me Hayat/Panfuti (Hindi), Astibhaksha/Parnabeeja (Sanskrit), Air Plant/Miracle-Leaf (English), Koppata (Bengali), Ghaymaari (Gujarati), Simahmudu (Telugu), Ranakalli (Tamil), and Ilayinmeltai/Ilamulachi (Malayalam) [2, 12, 13].

Figure 1. Kalanchoe pinnata

2.2 Morphological Description

The plant is a glabrous herb 0.3–1.2 m high with obtusely four-angled stems; younger stems are reddish with white speckles, while older stems are lighter in colour. Leaves are variable and decussate: the lower typically simple or occasionally compound (8–12 × 6–8 cm), the upper typically 3–5- or occasionally 7-foliolate, with petioles connected by a ridge around the stem; leaflets may be serrated, crenate, or elliptic. Leaves frequently develop plantlets with roots, stems, and leaves at the ends of the lateral nerves, which fall off and sprout new plants. Flowers are reddish-purple with slender pedicels suspended in large, spreading panicles; the calyx is striated with triangular teeth, pale green above and red-green at the base, and the corolla is reddish-purple, constricted in the middle, and inflated and octagonal at the base. Fruits are enclosed in the persistent papery calyx and corolla, and seeds are small, smooth, and ellipsoid [3, 22].

Distribution: The plant occurs in thickets and dry second-growth forests and is widely distributed in

open settlement areas, introduced from Malaya or tropical Asia in prehistory; it blooms from December to March. It is grown wild and in gardens across the hills of Bengal, the Deccan, and North-Western India, and is native to Madagascar. The leaves are rich in ascorbic acid, riboflavin, thiamine, niacin, magnesium, calcium, potassium, phosphorus, sodium, and trace minerals such as iron and zinc [1, 2, 22].

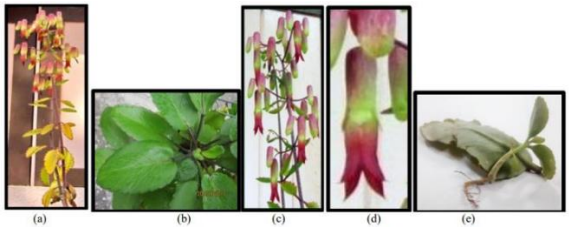

Figure 2. Plant morphology

2.3 Microscopical Characters

A transverse section of the leaf through the midrib displays collenchymatous tissue, meristele, upper and lower epidermis, and a vascular bundle; the lamina shows a layer of epidermis, hypodermis, palisade cells, and meristele (Figure 3). The leaf surface preparation shows a circular outline with anisocytic stomata (Figure 4). Longitudinal sections of the leaf petiole show prismatic calcium oxalate crystals embedded in parenchymatous cells, along with annular and spiral vessels (Figure 5). Powder microscopy reveals a portion of the vascular bundle, the epidermis, and annular and spiral xylem vessels (Figure 6) [8].

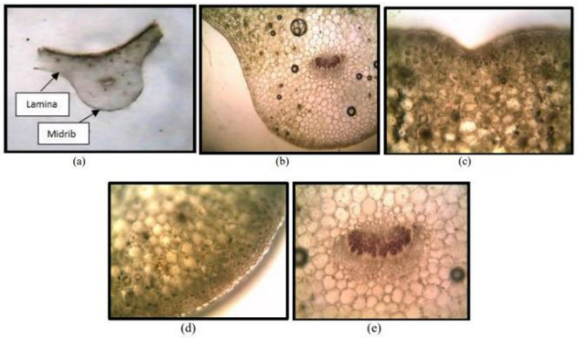

Figure 3. T.S. of K. pinnata leaf passing through the midrib: (a) whole section in dissecting microscope (4X), (b) midrib, (c) upper region

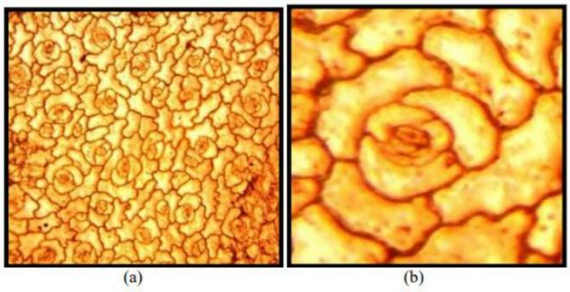

Figure 4. Anisocytic stomata in leaf surface preparation: (a) view in 10X, (b) magnified image

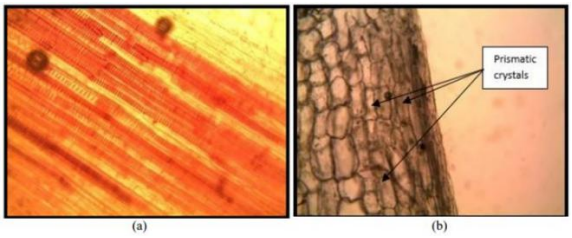

Figure 5. L.S. of leaf petiole: (a) annular and spiral vessels, (b) parenchymatous cells

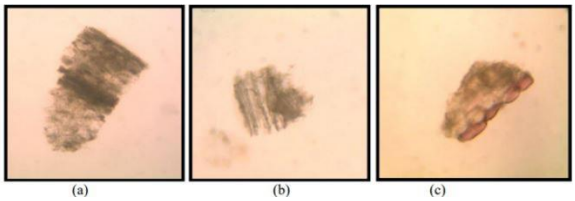

Figure 6. Powder study: (a) epidermis, (b) xylem vessel, (c) vascular bundle

2.4 Collection of Plant Material

The Kalanchoe pinnata leaves used in the reviewed studies were gathered from the Gandhi Market region in the Tiruchirappalli district of Tamil Nadu. The collected leaves were cleaned with running water and shade-dried for 10–15 days, after which they were ground into powder using a mortar and pestle [41].

2.5 Preparation of Extract

Reported extraction procedures include: (i) aqueous extraction using water as solvent via a hot percolation procedure, with the filtrate collected for further study [41]; (ii) extraction of approximately 1.0 kg of coarsely ground, shade-dried plant material using 80% v/v aqueous ethanol over a 72-hour maceration period at room temperature, followed by filtration and drying in a rotary evaporator at 40–50 °C under low pressure, with residues stored in a vacuum desiccator [1]; (iii) maceration of about 500 g of fresh leaves for three

days with constant stirring in ethanol–water (30:70) to obtain alcoholic (AlcE) and hydro-alcoholic (HAlcE) extracts, filtered and dried in a rotary evaporator [31]; and (iv) manual cutting of fresh leaves, boiling in 100 mL distilled water, cooling, and filtration through Whatman filter paper to obtain an aqueous extract stock solution [39].

2.6 Chemical Constituents

The plant contains iron, zinc, vitamins (ascorbic acid, riboflavin, thiamine, and niacin), alkaloids, flavonoids, phenolic substances, tannins, and macroelements (magnesium, calcium, potassium, phosphorus, sodium) [39]. Protocatechuic acid, phosphoenolpyruvate, para-coumaric acid, ferulic acid, 4-hydroxybenzoic acid, 4-hydroxy-3-methoxy-cinnamic acid, p-hydroxycinnamic acid, syringic acid, and caffeic acid have been isolated from the aerial parts. Astragalin, 3,8-dimethoxy-4,5,7-trihydroxyflavone, friedelin, epigallocatechin-3-O-syringate, luteolin, rutin, kaempferol, quercetin, and several quercetin/kaempferol glycosides occur in the leaves [40]. Three unusual flavonoids with antileishmanial activity have been isolated [41]; bryophyllol, bryophollone, bryophollenone, bryophynol, and related triterpenoid and sterol derivatives have also been reported [42]. Insecticidal bufadienolides (bryophyllin A and C) [43] and five bufadienolides with antitumor action [44] have been identified, along with a minor glycoside [45], cardienolide/steroidal constituents [40], amino acids and sugars [46], and various metabolic enzymes and proteins [47, 48]. Malic, p-hydroxybenzoic, syringic, and caffeic acids in K. pinnata extract each showed 2.70–4.65 wt% inhibition, cumulatively accounting for the 15% inhibition observed in synthetic urine, indicating that organic acid content is a crucial component of antiurolithic activity [6].

Table 1. Chemical constituents of Kalanchoe pinnata

Secondary metabolites	Chemical name
Flavonoids	Quercetin, kaempferol, apigenin, acacetin, diosmetin glycosides, and luteolin
Phenolic acids	Caffeic acid, syringic acid, ferulic acid, malic acid, oxalic acid, and p-hydroxybenzoic acid
Triterpenes	α- and β-amyrins, friedelin, glutinol, and taraxerol
Steroids	Bryophyllin derivatives, β-sitosterol, stigmasterol
Other compounds	Epigallocatechin gallate, avicularin, taxifolin, luteolin-7-glucoside, scutellarin, myricetin, hispidulin 7-glucuronide, genistin, and baicalin

Table 2. Compounds and their properties

Compound	Properties
Flavonoids	Hinder formation of CaOx stones; diuretic, anti-inflammatory, anti-bacterial, and other protective effects
Quercitrin	Effective in preventing stone-forming disease and decreasing CaOx crystal deposition in renal tubules
Phenolics	More effective in dissolving calcium phosphate stones than oxalate stones
Kaempferol	Inhibits crystallization, nucleation, and aggregation of crystals
Glycoside	Prevents kidney damage and decreases urinary disorders
Steroids	Reduces the time of stone passage from urine

[4]

Table 3. Minerals of Kalanchoe pinnata (Farwa Nadeem et al., IJCBS 16(2019):5–10 [39])

Parameter	Value
Calcium	96.5 µg/g
Potassium	76.40 µg/g
Phosphorus	26.42 mg/100 g
Ascorbic acid	44.03 mg/100 g
Riboflavin	0.20–0.42 mg/100 g
Thiamine	0.11–0.18 mg/100 g
Niacin	0.02–0.09 mg/100 g
Total ash	5.1%

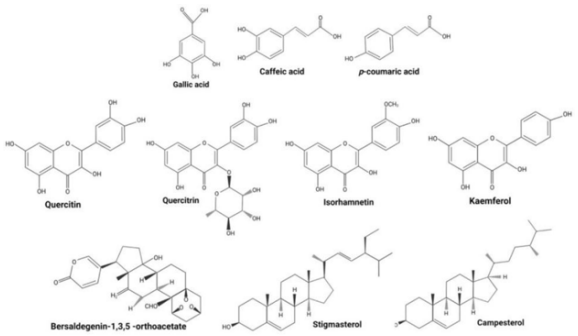

Figure 7. Structure of phytochemicals

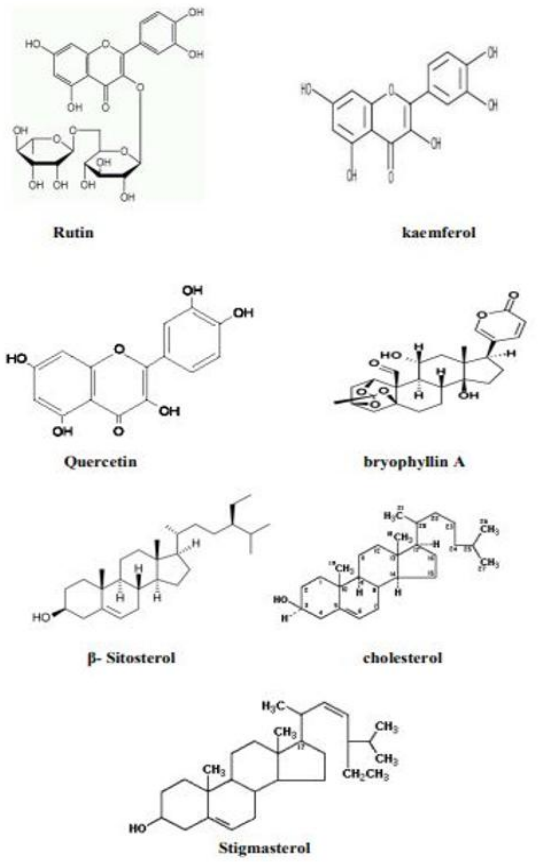

Figure 8. Structure of phytochemicals [6, 7]

2.7 Epidemiology

In India, kidney stones afflict over 2 million people annually, with higher prevalence in Maharashtra, Gujarat, Delhi, Rajasthan, Punjab, Haryana, and several Northeastern regions. More than 50% of people with nephrolithiasis in India are at risk of losing kidney function or suffering renal damage. Bladder stones accounted for nearly 30% of all urinary stones in India in 1965, falling to 5% by 1985; over the same period, the prevalence of calcium oxalate stones in the upper urinary tract rose from 26% to 82%, while struvite stones fell from 20% to 5%. Between 3% and 5% of people will experience nephrolithiasis in their lifetime, and depending on stone type, up to 50% will have a recurrence within ten years. Stone disease prevalence is reported to be roughly twice as high in White populations as in Asian populations [13].

2.8 Types of Nephrolithiasis

Calcium oxalate stones and calcium phosphate stones are the most prevalent types, typically small, thick, and sharp-edged; they may arise from Randall's plaques and are influenced by hypercalcemia, medication, diet, urine pH, and hyperoxaluria. Uric acid stones form when a diet high in animal protein raises urinary uric acid concentration. Struvite stones result from decomposition of magnesium ammonium phosphate, often following recurrent urinary tract infections, and are more common in women. Cystine stones are rare and hereditary. Calcium phosphate stone incidence has increased over the past two decades, and calcium phosphate stones form in high-pH environments while calcium oxalate stones form in low-pH environments. Inadequate hydration, obesity, and digestive diseases such as inflammatory bowel disease are additional risk factors, as calcium binds to fat while oxalate remains free to travel to the kidney.

2.9 Mechanism of Stone Formation

Stone formation proceeds through urinary supersaturation, nucleation of crystals, crystal growth, aggregation of crystals into larger particles, and interaction between crystals and renal tubular epithelial cells that absorb the adherent crystals. Aggregation, encouraged by crystal-binding macromolecules such as uromodulin, is considered the most critical phase of stone formation [32].

2.10 Pharmacological Activity

The pharmacological activities reported for Kalanchoe pinnata / Bryophyllum pinnatum are summarised below.

Antilithiatic activity: Fresh leaf juice dissolved existing stones regardless of position, type, or prior treatment, with diuretic effects and increased citrate/decreased oxalate excretion (Gahlaut et al., 2012). Aqueous extract reduced renal injury, epithelial deterioration, and tubular dilatation in ethylene-glycol-induced renal calculi in rats (Shukla et al., 2014), and extract tablets reduced calcium oxalate crystal accumulation (Gilhotra et al., 2013) [14, 15, 16].

Anticancer activity: Bufadienolides, particularly bryophyllin A, showed inhibitory effects on Epstein-Barr virus early antigen activation in Raji cells [17].

Wound-healing activity: Ethanolic extract reduced oedema and wound area, attributed to phenolic antioxidants and steroidal glycosides (Nayak et al., 2010) [18].

Antileishmanial activity: Aqueous extract reduced lesion size and parasite load in mice infected with

Leishmania amazonensis, attributed to flavonoid glycoside content (Muzitano et al., 2009) [19, 23].
Antimicrobial and antioxidant activity: Methanolic and ethyl acetate extracts, and isolated kaempferol rhamnosides, showed free-radical scavenging and antimicrobial activity (Tatsimo et al., 2012) [20].
Antiviral activity: Chloroform extract suppressed viral protein expression relevant to HPV-associated cervical cancer cell lines (Mahata et al., 2012) [21].
Anthelmintic activity: Methanolic and aqueous root extracts showed activity against roundworms and earthworms, with methanolic extract most effective, attributed to tannin content (Majaz et al., 2011) [22].
Insecticidal activity: Two bufadienolides showed strong insecticidal activity against silkworm larvae, attributed to a 1,3,5-orthoacetate moiety (Supratman et al., 2000) [24].
Anti-allergic activity: Aqueous extract suppressed mast cell degranulation, relevant to allergic respiratory disease (Cruz et al., 2012) [25].
Antipyretic activity: Hydroalcoholic extract lowered body temperature in yeast-induced pyrexia in rats, attributed to flavonoid content (Biswas and Mondal, 2015) [26].
Immunomodulatory activity: Aqueous extract reduced delayed hypersensitivity reactions in mice with ovalbumin-induced allergy, indicating immunosuppressive action (Rossi-Bergmann et al., 1994) [27].
Gastroprotective activity: Methanol-soluble fraction prevented chemically induced gastric and duodenal ulcers and improved healing rate in rats and guinea pigs (Pal and Chaudhuri, 1991) [28].
Antiproliferative activity: Methanolic, methanolic-aqueous, and aqueous extracts showed modest antiproliferative activity against HT-1080 fibrosarcoma cells (Ueda et al.) [29].
Anticonvulsant activity: Leaf extract (50–200 mg/kg) showed dose-dependent effects on muscle tone and anticonvulsant tests in rodents, with maximum activity at 200 mg/kg [33].
Antifungal activity: Ethanolic extract inhibited several Candida species except C. pseudotropicalis (Ogunshe et al.) [34].
Anti-nociceptive and anti-inflammatory activity: Aqueous leaf extract (25–800 mg/kg i.p.) showed strong antinociceptive effects and reduced egg-albumin-induced paw inflammation in rodents [35].
Antiulcer activity: Ethanolic extract was effective against acute ulcers, while aqueous extract did not prevent indomethacin-induced gastric lesions [36].
Nephroprotective activity: Aqueous leaf extract showed nephroprotective activity against gentamicin-induced nephrotoxicity in rats, alongside in vitro antioxidant activity (Harlalka et al.) [37].
Neurosedative and muscle relaxant activity: Saline leaf extract prolonged pentobarbital-induced hypnosis, reduced exploratory behaviour, produced dose-dependent muscular coordination effects, and delayed picrotoxin-induced convulsion onset [38].

III. CONCLUSION

This review provides solid evidence for the antiurolithic properties of K. pinnata leaf extract in CaOx bulk crystallization. The plant extract shows a significant inhibitory effect and reduces CaOx precipitation, even at supersaturated concentrations, and is even more effective at the lower concentrations typical of native urine. Dissolution studies on human kidney stones showed an approximately 18% mass reduction after washing five times with dilute plant extract, and the extract solution dissolved the outer surface of kidney stones, suggesting potential for detachment of stones from kidney epithelial cells. This reduction in stone size increases the likelihood of spontaneous passage with urine. The weight of evidence indicates that the antiurolithic properties of K. pinnata leaf extract arise from the organic acids present in the plant extract. Given its accessibility and favourable pharmacological profile, K. pinnata merits further controlled in vivo and clinical investigation as a low-cost adjunct or alternative in the prevention and management of urolithiasis, alongside conservation efforts given its status as a threatened species.

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