"ROLE OF BRYOPHYLLUM PINNATUM IN TREATMENT OF NEPHROLITHIASIS."

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ABSTRACT: Medicinal plants have been valued for millennia as a rich source of therapeutic compounds for the prevention of various ailments all throughout the world. Kidney stones and urinary calculi affect a huge percentage of the population nowadays. Stone sickness has become more prevalent as a result of changes in living conditions, such as industrialization and hunger. The most common stone recorded in India is calcium oxalate kidney stones. Changes in prevalence and incidence, the occurrence of stone kinds and stone position, and stone removal treatment are all discussed. Medicinal herbs have been utilised for centuries because they are safer, more effective, culturally acceptable, and have less adverse effects than manufactured medications. Patients are advised to consume a low-fat diet, as well as fibres from naturally occurring plants and herbal treatments. The current article discusses the steps that should be taken to maximise the potential of medicinal plants for stone dissolving action. Combining herbal remedies with allopathic treatment is an excellent way to eliminate all issues associated with kidney stones. The purpose of this article is to emphasise the use of *bryophyllum pinnatum* as a treatment for urinary stones.

Keywords: Nephrolithiasis, Kidney Stone, *Bryophyllum pinnatum*, Renal Disorder.

1.INTRODUCTION: Stones are more common in men than in women.[1] Kidney stone formation is often referred to as renal calculi or crystal formation.[2] Kidney stones, which are among the most painful urologic conditions, are not a result of modern living. Unfortunately, one of the most prevalent urinary tract conditions is kidney stone formation. Urinary stone disease is a widespread issue that affects a lot of people. Environmental factors and metabolic issues can both contribute to the development of kidney stones, which are solid crystals that form from dissolved minerals in urine. Nearly 70% of all kidney stones reported in economically developed nations are calcium oxalate or phosphate stones.[3] Kidney stone disease (KSD) is a widespread clinical issue in the world. It mainly refers to the development of stones in the kidney (nephrolithiasis), ureter (ureterolithiasis), or urinary bladder(cystolithiasis) as a result of the physicochemical processes of supersaturation, nucleation, aggregation, and retention. The crystal that makes up kidney stones is composed of elements such as calcium oxalate, calcium phosphate, calcium carbonate, magnesium-ammonium phosphate, uric acid, and cysteine. [4]

Kidney stones are quite common and typically affect people between the ages of 30 and 60. [3] Males are affected more than females.[5] It is estimated that renal colic (severe pain caused by a kidney stone) affects about 10-20% of men and 3-5% of women. In India, 12% of the population is

expected to have urinary stones, of which 50% may end up with kidney loss or renal damage.[3] An essential diagnostic tool is imaging of kidney stones.[6]

Factor influencing the development of nephrolithiasis:[2]

20–70 years old is the most susceptible age range for nephrolithiasis incidence. In comparison to women, men are more likely to experience it. [2]

Nephrolithiasis risk is raised by high protein, salt, and calcium intake. [2]

Nephrolithiasis is more likely to develop in families where it already exists. [2]

Nephrolithiasis is exacerbated by intense urination that occurs prior to elimination. [2]

Hypertension makes nephrolithiasis more likely. [2]

An rise in Body Mass Index (BMI) also increases the incidence of kidney stones. [2]

Gastric bypass surgery and inflammatory bowel conditions both affect how the calcium ion is absorbed and encourage the precipitation of calcium and other chemicals that cause kidney stones. [7]

Kidney stone symptoms: [2,8]

- Discomfort below the ribcage, in the side, and in the back. Typically, this discomfort is localized to the side of the renal calculi and does not spread to the opposite side.
- Fluctuating levels of discomfort, with episodes lasting 20 to 60 minutes.
- Waves of discomfort traveling down the lower abdomen and groin from the side and back.
- Pee that is turbid, bloody, or smells bad.
- Discomfort, pain, and swelling after urinating.
- Nausea and Diarrhoea.
- Persistent urination compulsion.
- If there is an infection, a fever and chills.

Types: The mineral makeup of the stone gives it its name. The most typical stones include calcium oxalate stone, calcium phosphate stone, struvite stone, uric acid stone, cystic stone.[9]

Name of stone	Approximate incidence	Constituents
Calcium oxalate	70 % of all stones	Calcium, oxalate
Calcium phosphate	10 % of all stones	Calcium, phosphate
Uric acid	5-10 % of all stones	Uric acid
Struvite	10 % of all stones	Calcium, ammonia, phosphate
Cystine	Less than 1% of all stones	Cystine

Tab: 1.1[9]

Prevalence: Nephrolithiasis has been more common during the last few decades.[10] In a working-age population, nephrolithiasis disease is widespread and places a significant strain on healthcare resources. Data from the National Health and Nutrition Examination Survey (NHANES) in 1994 estimated that 4.1% of women and 6.3% of men had stone disease.[11] Additionally, studies from around the world indicate that kidney stones have become more common in both sexes over the final quarter of the 20th century. In fact, the expense of treating the ailment in terms of healthcare is

continuing to climb, with nephrolithiasis alone costing the USA $2 billion year, largely because of renal Stones. [12,13]

2. *Bryophyllum pinnatum*: An overview

Bryophyllum pinnatum, commonly known as Pathharcatta.[14] (synonym: Kalanchoe pinnata) [15] The word meaning of *Bryophyllum pinnatum*: Derived from Greek- Bryo means to sprout & phyllon is a leaf. Numerous organic acids, including amino acid, syringic acid, caffeic acid, ascorbic acid, malic acid, and iso-citric acid, are present in *Bryophyllum pinnatum* leaf tissue.[16] The hollow, four-angled perennial plant has a branched stem and grows 1 to 1.5 meters tall, while its opposite, decussate, and succulent leaves are 10-20 cm long. [17] The substance has a sour taste and is astringent.[18]

Taxonomical classification [19]

- Kingdom: Plantae – Plants
- Sub kingdom: Tracheobionta – Vascular plants
- Division: Spermatophyta – seed plants
- Subdivision: Magnoliophyta – Flowering plants
- Class: Magnoliopsida – Dicotyledons
- Subclass: Rosidae
- Order: Rosales
- Family: Crassulaceae – stonecrop
- Genus: Bryophyllum
- Species: *Bryophyllum pinnatum* (lam.) Oken

Botanical Description

Family features**:** The family Crassulaceae [20] refers to the plant of the crassula tribe; the leaves are fleshy and succulent.[19]

There are 25 genera and 450 species in the family.[21]

This family of plants includes herbs and shrubs, with soft, succulent stems and branches. Leaves are simple and alternate, while flowers are hermaphrodite and cymose. Calyx has a 4-5 fid/4-5 partite, petals alternate with sepals, carpels have the same number as petals, and fruits are membrane follicles with few seeds.[19]

Habitat: It originated in southern Africa and Madagascar and has since naturalized all over the tropics.[19]

Morphology: *Bryophyllum pinnatum* is a 0.3-1.2 m tall, succulent herb with four-angled stems, variable and decussate leaves, and oblong-elliptic leaflets. Its flowers hang from slender pedicels and have red stripes, green bases, and pale green tops. The fruit has a persistent papery calyx and corolla, and the seeds are tiny. [19]
Reproduction: By seed & plantlets.[22]

Extraction of Plant Material: The leaves were gathered, shade-dried, and processed into powder. The 500 g of powder was macerated for 24 hours at room temperature in 30% distilled water and 70% ethanol. A filter paper (Whatman size No. 1) was used to filter it, and the filtrate was then evaporated to dryness in a water bath at 37°C. The result was a 30.5 g brownish residue. This was stored in a refrigerator in an airtight bottle until use.[23]

Traditional uses of *Bryophyllum pinnatum*

The leaves of this plant have been utilized in traditional medicine for anti-cancer [24], anti-microbial, anti-fungal, anti-ulcer, anti-inflammatory, analgesic, anti-hypertensive.[25]

Parts of plants	**Uses as**	**Preparation for**
Leaf	Used as swelling	Application of raw leaf topically overaffected area [26]
Leaf	Used as skin problem scabies	Decoction and juice [26]
Leaf	High BP	Decoction [26]
Leaf	Pain in bones, injury due to numbness of limbs	Rubbing and massaging of leave paste [26]
Leaf	Inflammation in lungs, cough	Syrup, juice with milk [26]
Leaf	Kidney problems, stone, high cholesterol	Ingestion of raw leaves [26]
Leaf	Headache	Crushed leave application [26]
Leaf, flowers	Wound ulcer, diabetes, analgesic, convulsion	Flower and leaf juice [26]
Leaf, root	Dysentery, ulcer, GIT disorders	Decoction of roots and leave juice [26]
Stems, leaf	Antitumor activity	Extract [26]
Leaves	Snake bite	Every hour after a snake bite, 1-3 teaspoons of a decoction of leaves should be taken [26]
Leaves	Sexually transmitted disease	Chopped leaves mixed with Opuntia stricta stem and Euphorbia hypericifolia, heated in 2 L of water and administered O.D as an enema [26]
Seeds	Stye disease	The eye is treated with crushed seed juice (1-2 drops daily for 3 times a day) [26]

Tab:2.1[27]

BIOLOGICAL AND PHARMACOLOGICAL EFFECTS

Bryophyllum pinnatum, commonly known as the Cathedral bells, green mother of millions, miracle leaf, Air Plant, or Mother of Thousands. [19,28]

1.Wound healing activity: In conventional medicine, the plant is applied topically to cure wounds. It is hypothesized that the plant's abundant saponins accelerate wound healing by clumping erythrocytes. Additionally, because of their astringent action, the plant's tannins speed up the healing of wounds. [29,30]

2. Anti-inflammatory activity: The immunological response of the body includes inflammation.[31] The current study was started to look at the anti-inflammatory activities of the plant's leaf aqueous extract in experimental animal models in order to objectively evaluate some of the ethnomedical uses of *Bryophyllum pinnatum* leaves.[32] A new steroidal derivative from leaves, containing flavonoids, has been found to reduce inflammation in carrageenan-induced rat paw edema, outperforming diclofenac in this process.[29]

3. Analgesic activity: Both the hot plate method and the chemical method (acetic acid writhing test) were used on albino mice to determine the studding analgesic activity of BPME.[33]

3. Anti-allergies activity: An in vitro experiment shown that the herb is effective in lowering allergy. It has an anti-allergic action by preventing mast cell degranulation brought on by antigens and also by reducing histamine release.[29]

4. Anti-cancer activity: Human cervical cancer cell growth has been shown to be inhibited by plant chloroform extract and its components in a concentration-dependent manner. The fraction was more effective than the extract and showed substantial anti-human papillomavirus (HPV) activity, which is crucial for the development of cervical cancer. Five bufadienolides have been isolated from leaves and tested for their capacity to block the early Epstein-Barr virus antigen. Bryophyllin A showed the clearest inhibition of all the bufadienolides. The Bryophyllum pinnatum bufadienolides have been highly suggested by study results as prospective chemotherapeutic candidates to cure cancer.[29]

5. Gastroprotective/ Anti-ulcer activity: *Bryophyllum pinnatum* has gastroprotective properties, as evidenced by its remarkable dose-dependent defense against ethanol-induced gastric injury. However, more research is needed to verify its usage in stomach ulcers.[29]

6. Anti-diabetic activity: The herb has long been used for its anti-hyperglycemic properties. After postprandial and streptozotocin-induced diabetes in rats, the aqueous extract of leaves showed impressive hypoglycemic effects. Additionally, a preliminary analysis has supported its usefulness in treating diabetes and cardiac ailments.[29]

7. Nephroprotective effects: Scientific investigation has verified the kidney-protective characteristics of *Bryophyllum pinnatum*. A dose-dependent impact was discovered by the investigation. The reserch explored whether the plant’s antioxidants and radical scavengers could

mitigate kidney damage induced by gentamicin in Wistar rats. Leaf juice is reportedly more effective than anticholinergic medications at treating hyperactive bladder.[27]

8. Urolithic activity: This extract considerably lowers urinary oxalate levels, indicating that it might be helpful in the treatment of urolithiasis. For many years, this plant has been used to treat kidney stones. *Bryophyllum pinnatum* breaks down calcium oxalate dehydrate crystals into monohydrates to dissolve kidney stones. Kidney stone formation and oxidative stress were reduced by leaf extracts.[27]

Phytochemical Composition of *Bryophyllum pinnatum*:

Bryophyllum pinnatum is known to contain a variety of phytochemicals, which are naturally occurring compound found in plants. Some of the key phytochemicals present in *Bryophyllum pinnatum* including: lipids, triterpenes, glycosides, flavonoids, cardienolides, organic acids [34] mallic acid [16], steroids, and glycosides. Bufadienolides, a class of very potent compounds, are found in the leaves. Bufadienolides like bryotoxin A, B, and C, which have antibacterial, antitumor, cancer-preventive, and insecticidal properties and are structurally and functionally very similar to two other cardiac glycosides, digoxin and digitoxin.[35]

litreture review: Leaf extracts from *Bryophyllum pinnatum* showed a protective effect against renal calculi that were caused by ethylene glycol. Extracts may have an antilithiatic impact by dissolving prepared stones, preventing the production of CaOx crystals, or by having antioxidant action. The ethnomedical usage of *Bryophyllum pinnatum* leaves to treat kidney stones is supported by this study.[14]

Mechanisms of Kidney Stone Formation

Physical, chemical, and supersaturation alterations in urine play a role in the biological process of Kidney stone development. A solution is referred to as being supersaturated when it includes more dissolved material than the solvent would typically be able to dissolve. In urine, solutes precipitate due to supersaturation, which causes nucleation and the formation of crystal concretions. The process that leads to stone development in the kidneys includes crystal nucleation, growth, aggregation, and retention.[36] The mechanics underlying plaque growth and formation are poorly understood.[37]

Crystal Nucleation: The kidneys produce kidney stones by creating a nucleus, or nidus, from supersaturated urine. This process occurs when charged molecules like calcium and oxalate interact, creating insoluble crystals. Nucleation can occur free-particle or fixed-particle. [36]

Crystal Growth: Crystal growth is a process where new crystal components lower the total free energy in a crystal nucleus, requiring particle production and stone formation. Crystal surface binding substances, like human serum albumin and prothrombin, inhibit CaOx crystal growth. However, the significance of crystal development for CaOx, the most common stone component, is questioned. The probability of a single particle reaching pathophysiologically relevant size is extremely low, even at an uninhibited rate of 2 mm per minute. [38]

Crystal Aggregation: Aggregation is the process through which a tiny, hard mass of a crystal in solution clings together to form a bigger stone. Crystal aggregation is likely implicated in crystal retention inside the kidneys, as is acknowledged by all models of CaOx urolithiasis. The most important stage in the production of stones is thought to be crystal aggregation.[36]

Crystal-Cell Interaction: Crystal-cell interactions in renal tubular cells are crucial for urinary stone illness and kidney stone formation. Crystal retention occurs when crystals connect to renal epithelial cells. Inhibited by urine macromolecules, a unique set of signals controls cell reactions to binding crystals.[38]

Endocytosis of CaOx Crystals: Stone formation involves various cellular and extracellular processes. Modulators targeting crystal retention processes could prevent stone growth. Obstructing crystal binding substances like osteopontin, hyaluronic acid, and sialic acid can also help. Oxidative stress and reactive oxygen species cause stone calcification, damaging renal epithelial cells and causing kidney damage. [36]

3. Formation and Pathophysiology of Kidney Stones

Types of Kidney Stones

75% of stones are made mostly of calcium oxalate, but up to 50% of these also contain calcium phosphate, 10-20% of stones are made of magnesium ammonium phosphate, also known as struvite or triple phosphate; 5% of stones are made of urate; and 1-2% of stones are made of cysteine.[39] Super saturation of urine with calcium and oxalate is the major cause of pathological mineralization in kidneys leading to nephrolithiasis.[40]

https://www.caresathome.com/blog/kidney-stone

1.Calcium oxalate stones: In the latter half of the 18th century, Karl W. Scheele (1742–1786) discovered oxalate and uric acid stones. Both the monohydrate and the dihydrate forms of calcium oxalate stones (CaOx) are possible. This distinction is crucial because dihydrate stones are linked to hypercalciuric circumstances and monohydrate stones to hyperoxaluric conditions. Idiopathic CaOx

stone formers are the great majority of people with CaOx stones since they do not have a systemic illness.[39]

2. Calcium phosphate stones: Calcium phosphate stones (CaP) are typically found in levels ranging from 1 to 10% and make up the bulk of kidney stones. Stones are referred to as CaP stones when CaP makes up more than 50% of them. Apatite, which makes up the majority of bones and teeth, or brushite, which is calcium monohydrogen phosphate, are both forms of CaP that can be found in urinary stones. It is well known that brushite stones have a very high recurrence rate and grow quickly.[41] One of the most frequent causes of phosphate stones is UTI.[42]

3. Uric acid stones: Urianary components and stone composition could be determined in the late 18th century, which is when uric acid stones first appeared. As a result, Scheele discovered that uric acid was a prevalent component of stones. When the pH of the urine is excessively low, uric acid stones might form. The other primary factor that leads to uric acid stones is hyperuricosuria, albeit this factor is less significant than urine pH. Healthy people have an average daily total urine urate concentration of 500 mg (3 mmol/day). Only 180 mg/L (1 mmol/L) of the total urate species may dissolve at a pH of 5.35. Low ammonia excretion, as well as other circumstances that cause an excessive acid load or alkali loss, including persistent diarrhea, can all contribute to low urine pH.
Patients with gout, diabetes mellitus, metabolic syndrome, and a high protein diet are more likely to have low urine pH and uric acid stones. Not all of the pathophysiology has been uncovered. Renal ammonia excretion may be decreased by insulin resistance. As body weight increases, urine pH decreases, which is related to insulin resistance. Obesity, diabetes mellitus, hypertension, and metabolic syndrome have all been linked in studies to kidney stone disease. One such study showed that the metabolic syndrome is characterized by acidic urine, and that the degree of insulin resistance was related to this. Gouty diathesis (54%), hypocitraturia (54%) and hyperuricosuria (43%) were the most prevalent metabolic abnormalities among obese patients, according to another study of about 1000 renal stone formers. These abnormalities all showed up at concentrations that were significantly higher than those of the non-obese stone formers. Two-thirds of these patients had uric acid calculi, according to stone analysis. Compared to 5% of all stone-forming individuals, 30–40% of stone formation in diabetic people contains uric acid.[39]

4. Struvite stones: Magnesium ammonium phosphate (MgNH4PO4 6H20) makes up the crystallized mineral known as struvite, which was first discovered in the 18th century.
The terms "infection stones" and "triple phosphate" have both been used to describe struvite urinary stones.
Early chemical tests of the stones revealed the presence of calcium, magnesium, ammonium, and phosphate (i.e., three cations and one anion), leading to the coining of the phrase "triple phosphate." It was also usual to identify carbonate ions, which were thought to be related to calcium as calcium carbonate (CaCO3).

5. Cystine stones: In 1810, Wollaston discovered the first cystine stone.[43] Cystine, ornithine, arginine, and lysine are among the dibasic amino acids that are affected by cystinuria's renal and intestinal transport abnormalities. The most likely to precipitate of these is cysteine because it is the least soluble. Cystinuria has a complex inherited pattern. While heterozygotes' urine excretion of

cystine and dibasic amino acids can vary significantly and cause nephrolithiasis, some patients exhibit conventional autosomal recessive inheritance. Additionally, an autosomal dominant pattern with partial penetrance can be used to transmit the illness.

Wollaston named the first cystine stone cystic oxide when he identified it in 1810. Since urinary cystine is frequently not routinely measured at the first kidney stone presentation, the diagnosis of cystine stones depends on a high index of suspicion. Young age of presentation, moderately radiopaque stones, family history, and intraoperative sulphate odor from stone fragmentation are all reasons for suspicion. To make the diagnosis, a 24-hour urine test or stone analysis is required.[39]

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Composition of Kidney Stones

Urinary stones can have crystals, noncrystalline phases, or organic material (the matrix) as part of their chemical makeup. Macromolecules such glycosaminoglycans (GAGs), lipids, carbohydrates, and proteins make up the organic matrix of urinary stones. By encouraging or inhibiting the mechanisms that lead to kidney stone production, these chemicals have a major impact. Proteins (64%), nonamino carbohydrates (9.6%), hexosamine as glucosamine (5%), water (10%), and inorganic ash (10.4%) make up the majority of the stone matrix. The kidney stone assembly process uses the matrix as a template. Phospholipids (8.6% of the total lipid) make up the matrix of all stones, which makes up around 10.3% of the stone. Calcium oxalate and calcium phosphate stones can be formed more easily thanks to the organic matrix component cell membrane phospholipids. The main element of the matrix in all types of stones is albumin. A quarter of calcium phosphate (CaP) patients develop stones containing brushite, a hard phosphate mineral with an increasing incidence rate. Calcium phosphate (CaP) may be found in the urinary system as brushite (calcium monohydrogen phosphate dihydrate, CaHPO42H2O), carbonate apatite, or hydroxyapatite. Shock wave and ultrasonic lithotripsy treatment are ineffective on brushite.[36]

DIAGNOSIS:

Blood tests: Look for high blood levels of uric acid or calcium. The results of a blood test can help doctors monitor kidney health and may lead them to search for further medical problems.[46]

Urine testing: A 24-hour urine collection test can determine whether your kidneys are excreting too many minerals that can lead to stones or not enough compounds that can prevent stones. The doctor might advise collecting at least two urine samples over the course of two days for this test. [46]

Imaging tests: High-speed computed tomography (CT) and ultrasonography are imaging tests used to identify kidney stones in the urinary system, replacing simple abdominal X-rays that overlook microscopic stones. Ultrasonography involves injecting dye into an arm vein. [46]

Kidney Stone Treatment:

The urologist decides how to treat a particular clinical issue after learning the examination's findings. A wide range of therapeutic options are currently available to urologists, including:
Medicines aimed at independent removal of stones; [8]
Medicinal treatment aimed at dissolving stones; [8]
Open surgical interventions;[8]
Remote pulse-wave lithotripsy;[8]
Endoscopic contact lithotripsy; [8]
Percutaneous Nephrolithotripsy; [8]
Endoscopic surgical interventions.[8]
Bryophyllum pinnatum is known to contain a variety of phytochemicals, which are naturally occurring compound found in plants. Some of the key phytochemicals present in *Bryophyllum pinnatum* including.[8]

Conclusion:

Bryophyllum pinnatum is a well-known herb, used worldwide. Studies have confirmed the ethanobotanical use of *Bryophyllum pinnatum* and supported the therapeutic utility of the plant in various disorders mainly in diseases of the urinary system without adverse side effects.

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