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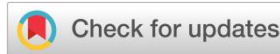
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Review Article

Exploring the Therapeutic Potential: Phytochemistry and Pharmacology of *Bryophyllum pinnatum*

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Abstract

Bryophyllum pinnatum, a renowned medicinal plant with a rich history in various traditional medical practices, has been utilized for treating a range of ailments such as fever, smallpox, otitis, cough, asthma, headache, convulsion, and general debility. The plant's diverse secondary metabolites, including steroids, flavonoids, terpenoids, fatty acids, bufadienolides, proteins, peptides, vitamins, and polysaccharides, have been identified. Over the past thirty years, extensive research has unveiled the plant's pharmacological effects both in vivo and in vitro, demonstrating its antimicrobial, anti-ulcer, antihypertensive, antileishmanial, anti-cancer, antidiabetic, and immunomodulatory properties.

This comprehensive review aims to provide a consolidated overview of *Bryophyllum pinnatum*, encompassing its traditional uses, phytochemistry, and pharmacological studies. By presenting a wealth of information, this paper seeks to inspire further exploration into the potential beneficial applications of the plant. Additionally, it sheds light on the clinical uses and prospects of *Bryophyllum pinnatum*, offering valuable insights for future research endeavors.

Keywords: *Bryophyllum pinnatum*, Chemical Constituent, Biological activities, antioxidant effect, Therapeutic potential

Introduction:

Bryophyllum pinnatum is a succulent plant in the Crassulaceae family that goes by several names, including the air plant, cathedral bells, life plant, and miracle leaf. This perennial herb, which originated in Madagascar, has spread to many tropical and subtropical areas of the world. There, it is frequently grown for both decorative and therapeutic purposes. *Bryophyllum pinnatum* is characterized by fleshy, succulent leaves that are arranged in an alternate pattern along its stems.¹ The leaves are green and often have a serrated or lobed margin. One distinctive feature of the plant is the presence of small plantlets that develop along the margins of the leaves, which can fall to the ground and take root, giving rise to new plants. The plant has a sturdy stem and can grow up to 1 to 2 meters in height. While native to Madagascar, *Bryophyllum pinnatum* has become naturalized in various tropical and subtropical regions, including parts of Asia, Australia, and the Americas. It is well adapted to a variety of habitats, including rocky terrain, open woodlands, and disturbed areas.² The plant's ability to reproduce through both seeds and vegetative propagation contributes to its widespread distribution. *Bryophyllum pinnatum* has cultural significance in traditional medicine practices in some regions. Various parts of the plant, including leaves and stems, are believed to possess

medicinal properties. In traditional medicine, it has been used to treat that while the plant has been traditionally used in folk medicine, scientific evidence supporting its medicinal efficacy is limited, and caution should be exercised. *Bryophyllum pinnatum*, commonly known as the "miracle leaf" or "life plant," has been the subject of interest in traditional medicine for its potential medicinal properties, including its purported activity in addressing kidney stones.³ Kidney stones, or renal calculi, are solid deposits that form in the kidneys from minerals and salts in the urine. These stones can cause severe pain and discomfort when they obstruct the urinary tract.⁴ While conventional medical treatments exist, some traditional practices involve the use of *Bryophyllum pinnatum* as a natural remedy for kidney stones.⁵

Morphology:

Bryophyllum pinnatum is a succulent herb, standing at a height of 0.3-1.2 meters. The stems are obtusely four-angled, with older ones displaying a pale coloration while younger ones exhibit a reddish hue with white undertones.¹⁰ The leaves, typically simple or compound, feature an upper arrangement of 3-5/7 foliolate leaves with long petioles.¹¹

At the terminal ends of the stems, the bell-shaped, drooping flowers, which may reach a length of 7 centimeters, cluster into branching clusters to create terminal inflorescences. Every bloom is carried by a 10–25 mm stalk, or pedicel, which is attached to the tubular calyx partly.¹² There are patches of pink or reddish-colored hue across the calyx. The 3-6 centimeter-long petals, which range in color from yellowish-green to dark red, are also partially united into a tube called a corolla tube. The corolla tube splits into four petal lobes close to the apex. Winter and spring are the seasons when flowers blossom most commonly.¹³

Table 1: Classification and Morphological characteristics of *Bryophyllum pinnatum*

Kingdom	Plantae
Subkingdom	Tracheobionta
Super division	Spermatophyta
Division (<i>Phylum</i>)	Angiosperms (Flowering Plants)
Class	Eudicots
Subclass	Rosidae
Order	Saxifragales
Family	Crassulaceae
Genus	Bryophyllum
Species	<i>Bryophyllum pinnatum</i>

Chemical constituent

Bryophyllum pinnatum, rich in diverse chemical constituents, showcases a complex profile with a range of bioactive compounds.⁶ The plant is identified for having a variety of macro and microelements as well as alkaloids, flavonoids, tannins, phenolic compounds, and saponin glycosides. Among the macro elements are magnesium, calcium, potassium, sodium, and phosphorous, while microelements include iron and zinc.⁷ Additionally, the plant is a source of essential vitamins, encompassing ascorbic acid, riboflavin, thiamin, and niacin. Further chemical analysis reveals the presence of specific acids, including syringic acid, caffeic acid, 4-hydroxy-3-methoxy cinnamic acid, 4-hydroxy benzoic acid, parahydroxy cinnamic acid, para coumaric acid, ferulic acid, protocatechuic acid, and phosphoenolpyruvate.⁸ The leaves of *Bryophyllum pinnatum* are particularly rich in compounds such as protocatechuic acid, astragalin, luteolin, rutin, kaempferol, quercetin, and kaempferol-o-glycosides. Among its ingredients, three flavonoids differentiate out as they have been discovered and separated, proving their important function in providing antileishmanial action. The plant also includes Bryophyllin A, B, C, and Bryophyllon, which are examples of bufadienolides.⁹

Many different chemical components have been identified in *Bryophyllum pinnatum*, and these elements have been linked to the plant's medicinal properties.

Alkaloids: The plant's alkaloids have a variety of pharmacological actions. Certain alkaloids have the ability to diuretic, which can help in the excretion of certain kidney stones. However, *Bryophyllum pinnatum*'s particular alkaloids and their effect on kidney stones.¹⁴

Flavonoids: Flavonoids are substances found in *Bryophyllum pinnatum* that have been identified for their ability to act as antioxidants. The ability of flavonoids to lower oxidative stress—which may contribute to the development of kidney stones—has been investigated.¹⁵

Triterpenoids: These are another class of plant-found chemicals. Triterpenoids have been investigated for their diuretic and anti-inflammatory properties, which may have an impact on kidney stone treatment.¹⁶

Betalains: Some varieties of *Bryophyllum pinnatum* contain betalains, which are pigments with potential antioxidant properties.¹⁷

Bufadienolides: Thirteen bufadienolides have been reported in *Bryophyllum pinnatum*, and among them, three are glycosides.¹⁸ Glycosides are compounds that contain a sugar molecule. These bufadienolides exhibit various bioactivities, notably cytotoxic and insecticidal properties. Cytotoxicity refers to the ability to kill or inhibit the growth of certain cells, while insecticidal properties suggest toxicity to insects.¹⁹ Several bufadienolides, including Bersaldegenin-1-acetate, Bersaldegenin-1,3, 5-orthoacetate, Bryotoxin C, and glycosides Bryophyllins A, have been found in all species of *Kalanchoe pinnata*.²⁰ This indicates a widespread distribution of these compounds in this plant species. Bryophyllum C and B have been reported only in *Kalanchoe pinnata*, suggesting that these bufadienolides are specific to this particular species.²¹ Methyl daigremonate has been identified only in *Bryophyllum daigremontianum*, emphasizing that certain bufadienolides are unique to specific *Kalanchoe* species.²¹

Flavonoids, phenols and phenylpropanoids:

In *Kalanchoe pinnata*, a variety of flavonoids have been identified, showcasing a rich chemical composition that includes derivatives of kaempferol and quercetin, as well as flavone glycosides such as acacetin, diosmetin glycosides, and luteolin.²² Additionally, unique compounds like epigallocatechin-3-osyringate and ethenylamino-substituted anthocyanidin, with a biogenetically distinct structure, have been reported. The flavonoids identified in *Kalanchoe pinnata* encompass numerous derivatives, primarily kaempferol glycosides and quercetin.²³ The presence of flavone glycosides, including acacetin, diosmetin glycosides, and luteolin, adds to the diversity of flavonoids in the plant. Notably, epigallocatechin-3-osyringate and ethenylamino-substituted anthocyanidin, with their distinct biogenetic structures, contribute to the unique chemical profile of *Kalanchoe pinnata*.²⁴ Aerial parts of the plant contain various other compounds, including ferulic acid, protocatechuic acid, phosphoenolpyruvate, protocatechuic acid, syringic acid, 4-hydroxy-3-methoxy-cinnamic acid, 4-oh-benzoic acid, p-oh-cinnamic acid, and paracoumaric.²⁵ The restricted occurrence of these flavonoids in *Kalanchoe pinnata*, coupled with their abundance in comparison to other species, suggests that flavonoids could serve as chemical markers for the plant.²⁶ This chemical richness may contribute to the therapeutic potential of *Kalanchoe pinnata*. Leaves of *Kalanchoe pinnata* have been found to contain astragalin, luteolin, kaempferol, and rutin, further highlighting the diversity of flavonoids in different plant parts.²⁷

Activity on Kidney Stones: Certain traditional use of *Bryophyllum pinnatum* indicate a diuretic effect. The minerals and other components that contribute to kidney stone development may be cleared out with increased urine output.²⁸ Since inflammation can be a significant role in kidney stones, the plant's anti-inflammatory qualities may help reduce kidney stones. The

plant's antioxidants can help in lowering oxidative stress, which has been linked to the development of kidney stones.²⁹ According to some research, *Bryophyllum pinnatum* may have the ability to relax smooth muscle, which may help kidney stones flow through the ureter.³⁰

Habitat: *Kalanchoe pinnata* is naturally found in hot and humid tropical regions around the world. Specifically, it is native to Madagascar, an island nation off the southeastern coast of Africa. The plant thrives in warm climates and is often cultivated or found growing in various tropical and subtropical areas.³¹

Parts Used: In traditional medicine systems, almost all parts of the *Kalanchoe pinnata* herb have been utilized for the treatment of various ailments in folkloric practices. However, extensive research has primarily focused on the leaves of the plant.³²

The Ayurvedic properties:

Rasa: Kashaya (Astringent), Amla (Sour)

Guna: Laghu (Light)

Virya: Sheeta (Cool)

Vipaka: Madhura (Sweet)

Doshaghna: Vatakaphahara (Balancing Vata and Kapha Doshas)

Karma (Actions): Ashmarighna (Stone-breaking, often referring to its potential in treating kidney stones), Vranaropaka (Wound healing), Mootrala (Diuretic), Shonita sthapanana (Hemostatic, stopping bleeding), Rakta stambaka (Stopping bleeding), Grahi (Astringent, useful in diarrhea and promoting absorption)

Rogaghna (Effectiveness in Diseases): Ashmari (Kidney stones), Atisara (Diarrhea), Raktasrava (Bleeding disorders), Visuchika (A type of intestinal disorder, often associated with dysentery)

These Ayurvedic properties suggest that *Kalanchoe pinnata* has a cooling nature (Sheeta Virya) and astringent taste (Kashaya Rasa), making it potentially beneficial in conditions associated with excess heat and bleeding.³³ The herb is also noted for its wound-healing and diuretic properties. The balance of Vata and Kapha doshas indicates its potential to address disorders related to these energies in the body.³⁴

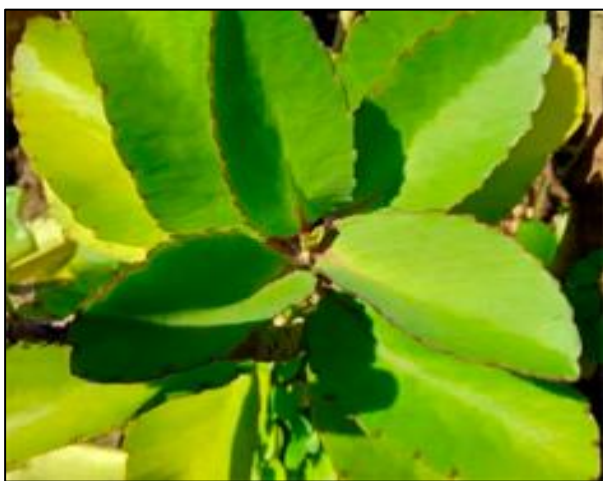


Figure 1: *Bryophyllum pinnatum*

Pharmacological activities of *Bryophyllum pinnatum*

Diuretic and anti-urolithiatic activity:

According to recent studies, the diuretic and anti-urolithiatic activities of *Kalanchoe pinnata* were investigated.³⁵ In these studies, a hydroalcoholic extract of the leaves was administered to male Wistar rats, both orally and intraperitoneally. The assessment of diuretic and anti-urolithiatic effects involved observing the urine output, measured by comparing the urine volume collected from individual animals placed in metabolic cages.³⁶ The findings of the study indicated that the extract exhibited significant diuretic and anti-urolithiatic activities.³⁷ Notably, when the extract was administered intraperitoneally, it demonstrated a more potent diuretic effect compared to oral administration. This suggests that the mode of administration plays a role in the intensity of the diuretic response.³⁸ These results contribute to the understanding of the therapeutic potential of *Kalanchoe pinnata* in the management of conditions related to diuresis and urolithiasis.³⁹

Anti-depressant activity:

Kalanchoe pinnata has been studied in animal models to assess its effects on the central nervous system.³² The observed sedative and CNS depressant actions suggest an influence on the neurological and behavioral aspects of the animals.⁴⁰ The leaf extract of *Kalanchoe pinnata* has been found to have the ability to increase the levels of the neurotransmitter GABA in the brain.⁴¹

Anti-fungal activity:

The research aimed to explore the antifungal properties of traditional Nigerian herbs, with a specific emphasis on their efficacy against strains of *Candida* species responsible for vaginal candidiasis.⁴² Various strains of *Candida* species, including *Candida albicans*, *C. glabrata*, *C. tropicalis*, and *C. pseudotropicalis*, were used in the evaluation of the antifungal activity of *Kalanchoe pinnata*.⁴³ The ethanolic extract of *Kalanchoe pinnata* was used in the study to assess its inhibitory effects on the different *Candida* species.⁴⁴ The findings revealed that none of the strains of *C. pseudotropicalis* were inhibited by the ethanolic extract of *Kalanchoe pinnata*.¹⁰ In contrast to the limited inhibitory effects on *C. pseudotropicalis*, the ethanolic extract demonstrated positive antifungal effects on other species of *Candida*, such as *C. albicans*, *C. glabrata*, and *C. tropicalis*.⁴⁵

Hepatoprotective activity:

The hepatoprotective activity of *Bryophyllum pinnatum* was assessed through in vivo and in vitro histopathological studies in rats, administered orally.¹⁴ The comparison between the aqueous extract or juice of the leaves and the ethanol extract revealed that the aqueous extract demonstrated greater efficacy. In either in vivo and in vitro evaluations, the aqueous extract or juice exhibited superior hepatoprotective effects when compared to the ethanol extract of *Bryophyllum pinnatum*.⁴⁶ This suggests that the administration of the plant's aqueous extract was more effective in preserving liver health, as evidenced by histopathological examinations in rat models.⁴⁷ Interestingly, while the ethanol extract of *Bryophyllum pinnatum* also demonstrated hepatoprotective activity, the findings highlight the relatively heightened effectiveness of the aqueous extract or juice.⁴⁸

Antileishmanial activity

Bryophyllum pinnatum's antileishmanial action has been demonstrated by the separation and identification of certain flavonoids, one of which is quercitrin.⁴⁹ The plant's methanolic extract effectively isolated this flavonoid, highlighting the critical role flavonoids play in the plant's ability to prevent leishmaniasis.⁵⁰ Among the flavonoids that have been found, quercitrin, quercetin, and ofzelin have been found to be significant contributions to the antileishmanial activity that *Bryophyllum pinnatum* exhibits. Their presence suggests a synergistic effect that might improve the plant's therapeutic benefit against the parasitic illness leishmaniasis, which is brought on by the *Leishmania* parasite.⁵¹ Quercitrin, in particular, stands out as a significant compound, showcasing its potential as a key component in the plant's antileishmanial properties.⁵² The isolation and recognition of these flavonoids not only contribute to our understanding of the plant's pharmacological activities but also the way for further exploration of these compounds in the development of novel antileishmanial treatments.⁵³

Anti-oxidant activity:

The leaves of *Kalanchoe pinnata* demonstrate maximum scavenging effects, indicating a potent ability to neutralize free radicals. The ethanolic extract of *Kalanchoe pinnata* exhibits higher total phenolic and flavonoid content compared to other extracts.⁵⁴ The high antioxidant activity of *Kalanchoe pinnata* is attributed to the presence of a significant number of flavonoids and phenols in the extract. Phenolic constituents in the extract have the ability to interact with transition metals by filling their aqua coordination sites.⁵⁵ This interaction can result in the generation of metal coordinates and insoluble complexes, contributing to antioxidant effects. Phenolic compounds, such as flavonoids, are known for their chelation properties, forming stable complexes with metal ions.⁵⁶ This chelation can prevent the metals from participating in oxidative processes. Flavonoids are known for their strong antioxidant properties, and their presence in high amounts contributes to the overall antioxidant activity of the plant extract.⁵⁷ Phenolic compounds, including flavonoids, are effective at scavenging free radicals, preventing oxidative stress, and offering protection against various diseases.⁵⁸

Anti-pyretic activity

Test animals, specifically rats, were subjected to hyperthermic conditions. Pyrexia, or fever, was induced in the rats using brewer's yeast.⁵⁹ The laboratory specimens (rats) were administered a hydroalcoholic extract of *Kalanchoe pinnata*. The administration of the hydroalcoholic extract of *Kalanchoe pinnata* resulted in a reduction in body temperature in the hyperthermic rats. The observed reduction in body temperature indicated the antipyretic efficacy of *Kalanchoe pinnata*.²⁴ The antipyretic activity of *Kalanchoe pinnata* is attributed to the flavonoids content in the plant extract.⁶⁰ The ability of *Kalanchoe pinnata* to reduce fever in the experimental model suggests its potential application as an antipyretic agent.¹⁴ Flavonoids, which are known for their diverse biological activities, including anti-inflammatory properties, may contribute to the antipyretic effects observed in the study.⁶¹

Anti-tussive activity

Aqueous extract of *Bryophyllum pinnatum* demonstrated notable antitussive and antihistaminic effects in guinea pigs, particularly in the context of ovalbumin sensitivities.⁶² Guinea pigs subjected to doses of 200 and 400 mg/kg/day of the aqueous extract over a

21-day period exhibited enhanced resistance to the effects of histamine exposure, achieved through an aerosol containing 0.2% histamine in a glass chamber.⁶³ In the treated group, the time elapsed before the onset of preconvulsive dyspnea substantially increased, indicating a significant antitussive effect. Notably, the administration of 400 mg/kg/day led to a pronounced reduction in phenol red secretion, while both dosage levels resulted in a reduction in coughing fits. Additionally, the aqueous extract exhibited the ability to decrease mucus viscosity in the sensitized group, comparable to the effects observed with the administration of salbutamol at 5 mg/kg/day.⁶⁴ Moreover, several physiological parameters underwent significant changes in response to the extract, including white blood cell counts, tracheal morphometry, and lymphocyte counts.⁶⁵ These findings collectively underscore the potential of *Bryophyllum pinnatum*'s aqueous extract in mitigating histamine-induced respiratory distress, suggesting its utility as a promising natural remedy with antitussive and antihistaminic properties.⁶⁶

Medicinal application:

The juice extracted from the leaves of *Bryophyllum pinnatum* serves various medicinal purposes, including its use as a remedy for kidney stones.⁴⁹ The root extract is employed as a laxative and diuretic, beneficial for liver health, tuberculosis, and addressing mental disorders. The plant's healing properties extend to wound care, as evidenced by evaluations involving excision and incision.⁶⁷ *Bryophyllum pinnatum* has a versatile history of application, aiding in the treatment of diverse conditions such as body pain and skin issues.⁶⁸ Notably, it is recognized for its efficacy in facilitating the detachment of infants' umbilical cords.⁶⁹ The plant boasts anti-inflammatory, antimicrobial, antitumor, antiulcer, insecticidal, antidiabetic, and antioxidant properties. Boiling *Bryophyllum pinnatum* leaves yields a water extract used to treat fever, headache, and discomfort in the stomach.⁷⁰ This herb has proven to be quite beneficial, especially when it comes to treating stomach issues and kidney stones. Because of its many therapeutic benefits, it is a useful tool in conventional medicine.⁷¹

Conclusion:

Bryophyllum pinnatum is renowned for its healing attributes, has been extensively utilized in traditional medicine to tackle diverse health concerns. This thorough investigation explores the plant's ethnomedicinal uses, phytoconstituents, and established pharmacological effects. The analysis not only examines its clinical applications but also takes into account toxicological considerations. The review emphasize the plant's extensive medicinal applicability across various regions globally, showcasing its effectiveness in addressing conditions like fever, ulcers, antimicrobial and antifungal activities, oxidative diseases diabetes, depression, insomnia, etc .

Despite existing clinical evidence supporting the plant's effectiveness in pregnancy management, the standardization and clinical assessment for numerous conditions, as indicated by experimental studies, remain pending. This underscores the necessity for additional research to meticulously evaluate the clinical efficacy of *Bryophyllum pinnatum* extracts and standardize products based on their active constituents. Bridging this gap will contribute to a more comprehensive comprehension of the plant's medicinal potential and facilitate its integration into clinical practice, benefiting individuals worldwide.

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