

Recent Advances in the Phytochemistry and Therapeutic Potentials of *Bryophyllum pinnatum*

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ABSTRACT

Bryophyllum pinnatum (*B. pinnatum*), a famous medicinal plant has extended a considerable interest due to its multiple pharmacological activities and rich phytochemical composition. The present review critically evaluates recent information on its primary bioactive compounds and the resultant biological effects. Recent reports demonstrated the presence of flavonoids, bufadienolides, triterpenoids, and phenolic acids, all of which exhibit various in vitro and in vivo activities (inflammatory, antimicrobial, antidiabetic, nephroprotective, and antiproliferative etc.). Despite these recent advances, significant gaps in knowledge remain garnering *B. pinnatum* to be therapeutic developed primarily as extract and there remains a lack of clinical evidence that demonstrates its effects and establishes structure-activity relationships. The present review discusses new findings as well as critically evaluates existing information and suggests future directions for the therapeutic development from *B. pinnatum* plants.

Keywords: *Bryophyllum pinnatum*, phytochemistry, pharmacology, flavonoids, bufadienolides, medicinal plant, bioactive compounds

1. Introduction

India is recognized as one of the wealthiest regions for the floristic community in the world and has been a rich source of medicinal plants and its products since antiquity, which man utilised for various purposes based on his needs, particularly food and medicine purpose. Among the plants, approximately 35,000 to 70,000 species have been reported to be used for medicine, not including those used for food and constructions [1]. The leaves of *Bryophyllum pinnatum* possess considerable medicinal properties in the traditional system of medicine. *Bryophyllum pinnatum* leaves are used for medicinal purpose in both ways - internally and externally. The leaves are frequently used for an array of human disorders such as hypertension, diabetes mellitus, bruises, wounds, boils, burns, sloughing ulcers, ophthalmia, corn, diarrhoea, dysentery, abscess, insect bite, arthritis, rheumatism, headache, antifungals, antibacterials, body pains and acute inflammation. The leaves are used for lymphadenitis and ear disease [2]. The principal constituents of this plant include alkaloids, flavonoids, glycosides, steroids, bufadienolides and organic acid [3,4,5].

2. Plant profile

2.1. Plant name: *Bryophyllum pinnatum*

2.2. Synonyms

Bryophyllum calycinum Salisb, *Kalanchoe pinnata* (Lam.) Pers, *Cotyledon pinnata* Lam., *Sedum madagascariense* Clus [6,7].

2.3. Vernacular names

Sanskrit : Parnabeeja, Asthibhaksha
English : Air plant
Hindi : Zakhmhaiyat, Pathharchoor
Kannada : Gandukalinga, Kadu Basale
Malayalam : Elamarunga
Tamil : Malaikalli, Ranakalli
Telugu : Ranapala
Marathi : Gayamari [8, 9].

2.4. Taxonomical classification

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 [10].



2.5. Geographical distribution

Bryophyllum pinnatum is native to Madagascar and has become naturalized in tropical and subtropical areas, inhabiting warm and temperate climates from sea level to 2,600 m (8,500 ft), occupying sites on rock in tropical evergreen and dry deciduous forests, as well as montane forests. It is perennial herb growing widely and used in Folkloric medicine in tropical Africa, Tropical America, India, China, Australia, Asia, Newziland, Philippines. The plant grows all over India in hot and moist areas, especially in Bengal and Uttarakhand. [11]

2.6. Morphology

Bryophyllum pinnatum is an attractive, ornamental, herbaceous, and crassulescent plant often grown in homes and gardens. The plant has a height of 1–1.5 m and an erect, fleshy, and obtusely four-angled stem. The leaves are opposite, decussate, succulent, and glabrous, measuring 10–20 cm in length. The lower leaves are usually simple, while the upper leaves have 3–7 leaflets and long petioles where the petioles would be fringed together around the stem with little ridges. The cremates at the ends of the lateral nerves have vegetative buds that root, enabling the plant to reproduce vegetatively. The flower is drooping, reddish-purple, bell-shaped, ~5 cm long, in large spreading panicles, and the plant also produces membranous follicles that are enclosed in the persistent papery calyx and corolla, containing smooth, ellipsoid seeds for dispersion. This morphology contributes to adaptability and medicinal properties. [12]

3. Phyto-chemical constituents

Bryophyllum pinnatum, a medicinal plant, is rich in various phytochemical constituents that contribute to its therapeutic potential. The bioactive compounds identified in the plant include alkaloids, flavonoids, saponins, tannins, steroids, terpenoids, bufadienolides, fatty acids, proteins, peptides, vitamins, and polysaccharides. The **leaves** are particularly abundant in flavonoids, alkaloids, tannins, triterpenes, phenols, and glycosides, with bufadienolides being a significant component. The **stem** contains alkaloids, phenolic compounds, and triterpenoids, while the **roots** primarily harbor tannins, flavonoids, and glycosides. Additionally, the **flowers** are known to contain steroids and phenolic compounds. These phytochemicals are important to the fundamental pharmacological activities of *Bryophyllum pinnatum*, including the antioxidant, anti-inflammatory, antimicrobial, nephroprotective, hepatoprotective, and anticancer activities, making this plant an important potential medicinal plant. [13,14]

Compound	Class	Biological Activities
Bryophyllin A	Bufadienolide	Cytotoxicity, tocolytic
Quercetin	Flavonoid	Antioxidant, antidiabetic
Kaempferol	Flavonoid	Anti-inflammatory
Rutin	Flavonoid	Cardioprotective
Gallic acid	Phenolic acid	Antioxidant

4. Pharmacological activities

4.1. Anticancer activity

Bryophyllum pinnata leaf extract has demonstrated anticancer and anti-HPV activity in human cervical cancer cells. The plant chloroform extract and its fractions have exhibited stronger cytotoxic and growth inhibitory effects compared to the crude extract. This fraction significantly suppressed AP1-specific DNA binding, leading to the downregulation of oncogenic c-Fos and c-Jun expression and inhibition of HPV18 transcription. Additionally, apoptosis induction was observed, marked by increased Bax expression, suppression of Bcl-2, and activation of caspase-3 and PARP-1 cleavage. Phytochemical analysis indicated the presence of Bryophyllin A, a compound potentially responsible for these effects. These findings suggest that *B. pinnatum* could serve as a natural therapeutic agent for managing HPV infection and cervical cancer, warranting further research to explore its clinical applications [15].

This study investigated the molecular mechanisms of *Bryophyllum pinnatum* leaf-extract-induced apoptosis in colorectal cancer cells (HCT116), utilizing both in vitro and in silico analyses. The leaf extract exhibited the highest cytotoxicity against HCT116 cell line resulting cellular death. In the results, the extract induced G2/M cell-cycle arrest and significantly increased intracellular ROS production, leading to apoptosis. This apoptosis was p53-dependent, with upregulation of p53, BAX, and CASPASE3, and downregulation of BCL2, along with increased nuclear p53 accumulation. qRT-PCR analysis revealed gene-modulatory potential, and GC-MS and HPLC-ESI/MS identified bioactive phytoconstituents. In silico STITCH and molecular docking analyses confirmed strong interactions between these compounds and studied proteins. Quercetin, morin, and β -sitosterol, major constituents, induced significant apoptosis and increased ROS, validating their interactions. These findings demonstrate *B. pinnatum* potential as a natural therapeutic agent for colorectal cancer [16].

4.2. Antimicrobial activity

This study investigated the antimicrobial activities of kaempferol rhamnoside derivatives isolated from *Bryophyllum pinnatum*. The methanol extract exhibited antimicrobial activity with minimum inhibitory concentration (MIC). In the results, partition of the methanol extracts enhanced antimicrobial activity in the EtOAc extract (MIC = 16-128 μ g/ml) but reduced it in the hexane extract (MIC = 256-1024 μ g/ml). Fractionation of the EtOAc extract yielded seven kaempferol rhamnoside, including α -rhamnoisorobin. Notably, α -rhamnoisorobin was the most active compound. These findings demonstrate that *Bryophyllum pinnatum* and its isolated kaempferol rhamnoside possess significant antimicrobial properties, confirming its traditional use in the treatment of infections [17].

Chemical investigation of *Bryophyllum pinnatum* leaves led to the isolation of two novel flavonoids: 5'-methyl-4', 5, 7-trihydroxyl flavone 1 and 4', 3, 5, 7-tetrahydroxy-5-methyl-5'-propenamine anthocyanidins 2. Their structures were analysed using NMR, UV, IR, and MS spectroscopy. In the results, antimicrobial studies demonstrated that both isolated compounds successfully inhibited *Pseudomonas aeruginosa*, *Klebsiella pneumoniae*, *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans*, and *Aspergillus niger*. This antimicrobial activity of the isolated flavonoids could explain the therapeutic efficacy of *Bryophyllum pinnatum* and its traditional use in Nigerian herbal medicine [18].

4.3. Antioxidant activity

Essential oils were extracted from air-dried leaves and stems of *Bryophyllum pinnatum* via hydro-distillation, yielding 0.14% from leaves and 0.55% from stems. Analysis by GC and GC-MS identified 15 compounds in the leaf oil and 17 compounds in the stem oil. In the results, the major compounds in the leaf oil were 1-octen-3-ol, supraene, 1-heneicosanol, 2,5-dimethylheptane, and (E)-9-eicosene, while the stem oil's main compounds were (E)-5-eicosene, oleamide, isolongifolol, and β -gurjunene. Both oils contained oleamide, (E)-5-eicosene, hexahydropseudoionone, and phytol. The leaf essential oil and stem oil exhibited moderate antioxidant activity, compared to standards butylated hydroxyl anisole and ascorbic acid. These results report the chemical compounds present in the leaf and stem essential oils of *Bryophyllum pinnatum* and demonstrate their moderate antioxidant properties [19].

The extraction of phenolics from *Bryophyllum pinnatum* was optimized using response-surface methodology (RSM), examining the effects of solvent ratio, plant material/solvent ratio, extraction time, and temperature. In the results, an optimal phenolic yield of 7.952 mg/g gallic acid equivalence (GAE) was achieved with a 1:1 methanol/water ratio, resulting in a ~2-fold yield enhancement and a 37% reduction in extraction solvent. Validation of the RSM model was confirmed by HPLC analysis, showing good agreement between experimental and predicted values. The phenolic extracts were further evaluated for radical scavenging activities using DPPH, FRAP, and ABTS assays. EC₅₀ values obtained were consistent with the phenolic content, and a significant correlation ($p < 0.05$) was observed between total phenolic content and antioxidant activities. These findings demonstrate the effective optimization of phenolic extraction from *B. pinnatum* and confirm its potent radical scavenging potential [20].

4.4. Antihypertensive activity

This study explored the effects of *Bryophyllum pinnatum* live plant fractions on angiotensin-converting-enzyme (ACE) and arginase activities, blood pressure, and biochemical parameters in sodium fluoride (NaF)-induced hypertensive rats. In the results, diastolic blood pressure (DBP), systolic blood pressure (SBP), mean arterial pressure (MAP), heart rate (HR), and arginase activity were reduced, while nitric oxide levels increased, in treated hypertensive rats. The aqueous fraction (AQF), n-hexane fraction (NHF), and ethyl acetate fraction (EAF) increased superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) levels and reduced malondialdehyde (MDA) in these rats. Notably, the n-hexane fraction (NHF) demonstrated the capability to inhibit both ACE and arginase activities and enhance antioxidant biomarkers [21].

This study investigated the effects of aqueous leaf extract of *Bryophyllum pinnatum* on blood pressure in anaesthetized cats and on liver and kidney function in rabbits. In the results, the extract produced a slight decrease in blood pressure in cats and reduced adrenaline-induced blood pressure elevation. In rabbits, serum creatinine significantly decreased, while serum urea significantly increased. Alkaline phosphatase (ALP) activity significantly increased, but aspartate transaminase (AST) and alanine transaminase (ALT) levels showed non-significant increases, with a higher percentage increase in the treated group. Histopathological examination revealed shrunken glomeruli, tubular necrosis, hyaline droplets in the kidneys, and liver cell necrosis, lymphocytic infiltration, and peri cuffing of the bile duct in the liver of treated rabbits. Furthermore, the treated group exhibited lower body weight gain compared to the control group. While the study confirms the traditional use of *B. pinnatum*

for lowering blood pressure, it concludes that the extract's limited blood pressure-lowering effect and potential organ toxicity limit its use as a primary antihypertensive agent [22].

4.5. Antidiabetic activity

Antidiabetic principle was isolated from the methanolic leaf extract of *Bryophyllum pinnatum* using bioactivity-guided fractionation. The ethyl acetate fraction (A and B) of the extract lowered blood glucose in alloxan-induced diabetic rats and enhanced inhibitory activity against α -amylase and α -glucosidase respectively. NMR analysis identified fraction A as quercetin and fraction B as kaempferol. Molecular docking studies revealed that these compounds interact with amino acid residues crucial for substrate binding and hydrolysis. Furthermore, kaempferol and quercetin reversed altered lipid profiles and oxidative stress biomarkers. These findings indicate that kaempferol and quercetin are the primary antidiabetic principles responsible for the activity of *B. pinnatum* [23].

The antidiabetic potential of the ethanol leaf extract of *Bryophyllum pinnatum* was investigated in alloxan-induced hyperglycaemic Wistar albino rats, along with its effects on haematological profiles. Phytochemical analysis revealed the presence of flavonoids and alkaloids as abundant constituents. Diabetes was induced using alloxan monohydrate. Treatment of the extract resulted in a significant ($p<0.05$) reduction in blood glucose levels compared to the positive control group. Furthermore, the extract led to a significant increase ($p<0.05$) in red blood cell count, haemoglobin count, and packed cell volume in the treatment groups. Additionally, there was a significant decrease ($p<0.05$) in malondialdehyde, low-density lipoprotein, triacylglycerol, and total cholesterol concentrations in these groups. These findings demonstrate that the ethanol extract of *B. pinnatum* exhibits anti-hyperglycaemic activity and positive modulation of haematological and lipid parameters in alloxan-induced diabetic rats [24].

4.6. Anti-inflammatory activity and analgesic activities

The anti-inflammatory and analgesic activities of this new steroid were evaluated using carrageenan-induced paw edema in rats and acetic acid-induced writhing in mice. In the results, the steroidal compound demonstrated significant anti-inflammatory activity, achieving 87.29% and 84.45% inhibition of paw edema, comparable to diclofenac. Furthermore, it showed 75.72% protection against acetic acid-induced writhing in mice, indicating significant analgesic effects. These findings suggest that the anti-inflammatory and analgesic activities of the aqueous extract of *B. pinnatum* are primarily attributed to this novel steroidal compound [25].

The topical anti-inflammatory effects of the ethanol extract of *Bryophyllum pinnatum* leaves (EEBP) were evaluated in acute and chronic mice ear edema models induced by various irritants. Chemical characterization of EEBP by HPLC-UV DAD identified the presence of flavonoids, including rutin, quercetin, luteolin, and luteolin 7-O- β -d-glucoside. In the results, topical application of EEBP significantly ($P<0.001$) inhibited ear edema induced by Croton oil (57% inhibition), arachidonic acid (67%), phenol (80%), capsaicin (72%), and EPP (75%) in acute models. In the chronic model using multiple Croton oil applications, EEBP reduced ear thickness by 55% after 9 days. Histopathological analyses confirmed these findings, showing reduced edema, epidermal hyperplasia, inflammatory cell infiltration, and vasodilation. These results suggest that EEBP is an effective topical anti-inflammatory agent in both acute and chronic inflammatory processes, potentially through inhibition of the arachidonic acid pathway, supporting the traditional use of *Bryophyllum pinnatum* for skin disorders [26].

4.7. Hepatoprotective activity

This study investigated the effects of a boiled *Bryophyllum pinnatum* leaf extract on alcohol-induced liver damage in Albino Wistar rats. Rats were administered alcohol to induce liver damage, followed by treatment with the boiled leaf extract. In the results, the alcohol-treated group exhibited increased ALT levels compared to the normal control, indicating mild hepatic damage. However, the group treated with the *Bryophyllum pinnatum* extract showed a decrease in ALT, AST, and ALP levels when compared to the alcohol-treated group. This suggests that the *Bryophyllum pinnatum* leaves contain compounds capable of reducing alcohol-induced liver damage. The study concluded that the extract demonstrated minimal anti-hepatotoxic activity, potentially preventing alcohol-induced liver damage, and recommended further pharmacological studies to establish its efficacy as a definitive anti-hepatotoxic agent [27].

4.8. Antiulcer activity

A methanolic fraction of *Bryophyllum pinnatum* leaf extract was investigated for its anti-ulcer activity across 9 experimental animal models. In the results, pre-medication tests in rats showed significant protective action against gastric lesions induced by aspirin, indomethacin, serotonin, reserpine, stress, and ethanol. Significant protection was also observed against aspirin-induced ulcers in pylorus-ligated rats and histamine-induced duodenal lesions in guinea pigs. Furthermore, the extract significantly enhanced the healing process of acetic acid-induced chronic gastric lesions in rats. These findings demonstrate that the methanolic fraction of *Bryophyllum pinnatum* leaf extract possesses significant anti-ulcer activity [28].

This study evaluated the gastroprotective effects of *Bryophyllum pinnatum* whole plant aqueous extract and mucilage (MUC) against ethanol-induced gastric ulcers in rats. Rats were pretreated with aqueous extract (500 and 750 mg/kg), MUC (500 mg/kg), or rabeprazole (20 mg/kg) for 7 days. In the results, the aqueous extract at 750 mg/kg and MUC at 500 mg/kg significantly decreased the incidence of ulcers, reduced gastric volume, free and total acidity, and ulcerative index compared to the control group. Total carbohydrate content was increased. The 750 mg/kg aqueous extract showed a reduction in these parameters comparable to rabeprazole. *B. pinnatum* extract, MUC and rabeprazole showed protection index. These findings indicate that *B. pinnatum* whole plant extract and MUC possess potent gastroprotective effects [29].

4.9. Other pharmacological activities

4.9.1. Immunomodulation effects

This study investigated the immunomodulatory effects of *Bryophyllum pinnatum* treatment on pregnant pristane-induced lupus mice. Pregnant mice were divided into four groups and *Bryophyllum pinnatum* administered orally from gestational day 9. In the results, *Bryophyllum pinnatum* treatment reduced the percentages of Th1 ($p=0.006$), Th2 ($p=0.005$), Th17 ($p=0.000$), and mature B cells ($p=0.007$) in a dose-dependent manner. B1 and B2 groups exhibited significantly lower systolic blood pressure compared to the control ($p=0.026$ and $p=0.022$, respectively). The B1 group showed significantly lower anti-dsDNA levels

($p=0.014$), but no significant differences were found in urine albumin levels. Notably, *Bryophyllum pinnatum* significantly increased fetus body weight in a dose-dependent manner ($p=0.000$). These findings suggest that *Bryophyllum pinnatum* treatment improves pregnancy outcomes and modulates immune responses in pregnant pristane-induced lupus mice, indicating its potential as an immunosuppressive agent [30].

4.9.1. Neuropharmacological activity

The neuropharmacological effects of aqueous leaf extracts of *Bryophyllum pinnatum* (AEBP) were investigated in mice. The extract, at dosages of 50, 100, and 200 mg/kg, produced a dose-dependent decrease in exploratory activity. In the results, AEBP exhibited a marked sedative effect, demonstrated by a significant reduction in gross behaviour and potentiation of pentobarbitone-induced sleeping time. The extract delayed the onset of strychnine- and picrotoxin-induced convulsions, with a significantly higher protective effect against picrotoxin-induced seizures. It also decreased the rate of picrotoxin-induced mortality in mice. These combined effects indicate that the aqueous leaf extract of *Bryophyllum pinnatum* possesses depressant action on the central nervous system [31].

4.9.2. Antileishmanial activity

This study investigated the antileishmanial activity of unusual flavonoids isolated from *Bryophyllum pinnatum*. An aqueous leaf extract yielded kapinnatoside, a kaempferol di-glycoside, along with two previously reported flavonoids, quercetin 3-O- α -l-arabinopyranosyl (1 $\rightarrow$ 2) α -l-rhamnopyranoside and 4',5-dihydroxy-3',8-dimethoxyflavone 7-O- β -d-glucopyranoside. In the results, the structures of these flavonoids were determined using NMR and HR-MALDI mass spectrometry. The quercetin glycoside may serve as a chemical marker for *Bryophyllum pinnatum* due to its restricted occurrence and abundance. The three flavonoids were tested against *Leishmania amazonensis* amastigotes, comparing their activity to quercitrin, quercetin, and afzelin. The results suggest that a quercetin aglycone-type structure and a rhamnosyl unit linked at C-3 are important for antileishmanial activity [32].

4.9.3. Nephrotoxicity activity

This study evaluated the nephroprotective effect of *Bryophyllum pinnatum*-mediated silver nanoparticles (AgNPs) in ethylene glycol-induced urolithiasis in rats. In the results, animal studies on Wistar rats showed a significant increase in serum total protein, albumin, and globulin, and a significant decrease in AST, ALT, creatinine, BUN, calcium, and phosphorus in the groups treated with *B. pinnatum*-mediated AgNPs compared to the urolithiasis-induced groups. No crystalluria was observed in rats given the AgNPs. Histopathological analysis revealed mild degenerative changes and restoration of kidney parenchyma in the AgNP-treated groups. These findings demonstrate the beneficial preventive and therapeutic nephroprotective effect of *B. pinnatum*-mediated AgNPs against ethylene glycol-induced urolithiasis in rats [33].

This study investigated the nephroprotective effects of *Bryophyllum pinnatum* (*B. pinnatum*) extract against ketamine-induced nephrotoxicity in Wistar rats. Rats were divided into six groups: a control group, a ketamine-treated group, and four groups treated with ketamine plus different doses of *B. pinnatum* extract (50, 100, and 200 mg/kg). In the results, ketamine administration significantly increased BUN, creatinine, urea, sodium, and potassium levels compared to the control group.

Treatment with *B. pinnatum* at 100 and 200 mg/kg significantly reduced these biomarkers, with the 200 mg/kg dose showing values near control levels. Histological analysis revealed that *B. pinnatum* treatment attenuated ketamine-induced renal damage and improved tissue architecture. These findings demonstrate that *B. pinnatum* exhibits significant nephroprotective effects against ketamine-induced renal toxicity, suggesting its potential as a therapeutic agent [34].

4.9.4. Wound healing activity

This study focused on isolating and characterizing secondary metabolites from *Bryophyllum pinnatum* (Lam.) and assessing their wound-healing efficacy using an animal model. Leaf extracts were prepared in petroleum ether, ethyl acetate, and ethanol, and phytochemicals were identified using advanced analytical techniques. In the results, an ethanolic extract, which contained a higher concentration of phytochemical constituents, was formulated into 1% and 2% w/w ointments and tested on rat models of acute and burn wounds. The 2% w/w ethanolic ointment significantly stimulated wound healing, as evidenced by an increased wound healing area, hydroxyproline content, and wound index, and a reduced epithelization period compared to the control. The study concluded that the *Bryophyllum pinnatum* leaf ethanolic extract ointment promotes wound contraction, epithelization, and angiogenesis, indicating its potential for wound treatment [35].

4.9.5. Anticonvulsant activity

This study evaluated the anticonvulsant potential of a methanol aerial extract of *Bryophyllum pinnatum* in mice and chicks using the Maximal Electroshock Test (MEST) and pentylenetetrazol (PTZ) test. The extract demonstrated an intraperitoneal LD₅₀ above the tested threshold, suggesting relative safety. It also significantly prolonged the mean onset of PTZ-induced seizures compared to the saline-treated group. The *Bryophyllum pinnatum* extract also significantly reduced the mean recovery time of MEST-induced seizures at 500 and 1000 mg/kg. While the standard drugs, sodium valproate (200 mg/kg) and phenytoin (20 mg/kg), demonstrated a significant ($p \leq 0.05$) delay in the mean onset of seizures in PTZ and MEST, respectively, *Bryophyllum pinnatum* also provided significant anticonvulsant activity. The study concluded that the methanol extract of *Bryophyllum pinnatum* aerial parts possesses anticonvulsant properties [36].

This study evaluated the effects of a hydro-methanol leaf extract of *Bryophyllum pinnatum* on diazepam-induced sleeping time and pentylenetetrazol (PTZ)-induced seizures in mice. Mice were administered the extract at doses of 25, 50, and 100 mg/kg. In the results, the extract significantly ($P < 0.05$) decreased the onset of sleep and prolonged sleep time in a dose-dependent manner. The extract also exhibited biphasic activity, delaying the onset of convulsions and increasing protection against PTZ-induced seizures at doses of 25 and 100 mg/kg. These findings suggest that the hydro-methanol leaf extract of *Bryophyllum pinnatum* possesses central nervous system (CNS) depressant activity, potentially due to the presence of phytochemicals within the plant [37].

4.9.6. Myometrial contractility

This in vitro study investigated the effects of *Bryophyllum pinnatum* press juice (BPJ) on human myometrial contractility, both alone and in combination with atosiban and nifedipine. Myometrial strips were subjected to spontaneous contractions in an organ bath, and the effects of BPJ (2.5 µg/mL), atosiban (0.27 µg/mL), and nifedipine (3 ng/mL) were assessed. In the results,

each substance moderately reduced the strength of contractions. However, the combination of BPJ with either atosiban or nifedipine significantly increased the inhibition of contraction strength compared to the tocolytics alone ($p = 0.03$ and $p < 0.001$, respectively). The enhanced inhibitory effects were concentration-dependent, and no test substance, alone or combined, decreased myometrial cell viability. The study concluded that BPJ enhances the inhibitory effect of atosiban and nifedipine on myometrial contraction strength, suggesting a potential therapeutic benefit for combination treatment [38].

This study investigated the compounds in *Bryophyllum pinnatum* leaves contributing to its tocolytic effect by examining the effects of a flavonoid-enriched fraction, flavonoid aglycon mixture, bufadienolides-enriched fraction and *B. pinnatum* leaf press juice on human myometrial contractility in vitro. Myometrial strips were used to record contraction strength and frequency, and cell viability assays were performed. In the results, repeated addition of each fraction or press juice led to a progressive decrease in contraction strength without affecting myometrium vitality. The bufadienolides-enriched fraction was the most potent, lowering the area under the curve to $40.1 \pm 11.8\%$ of the initial value at $1 \mu\text{g/mL}$, compared to $150 \mu\text{g/mL}$ of the flavonoid-enriched fraction, $6.2 \mu\text{g/mL}$ of the flavonoid aglycon mixture, and 10 mg/mL of the *B. pinnatum* leaf press juice. A progressive increase in contraction frequency was observed, except with the flavonoid aglycon mixture. None of the test substances decreased myometrial cell viability, even at higher concentrations. Given the relative concentrations, the study concluded that bufadienolides may be primarily responsible for the relaxant effect of *B. pinnatum* [39].

4.9.7. Uterine contractility

This study compared the tocolytic effects of *Bryophyllum pinnatum* and fenoterol on human myometrial contractility in vitro. Term myometrium strips, obtained from caesarean sections, were exposed to increasing concentrations of *B. pinnatum* or fenoterol in the presence of oxytocin. In the results, *B. pinnatum* inhibited spontaneous contractions in a concentration-dependent manner, achieving a 16% reduction in area under the curve (AUC) at its maximum concentration (10^4 mg/L), which was 53% of the inhibition achieved by fenoterol ($5 \times 10^{-8} \text{ mol/L}$). *B. pinnatum* increased contraction frequency by 91% while maintaining constant amplitude and inhibited oxytocin-stimulated contractions by 20% (AUC) with a slight decrease in frequency. Conversely, fenoterol decreased contraction AUC by 50% with a significant decrease in frequency.¹ The study concluded that *B. pinnatum* exhibits tocolytic activity in vitro, confirming observations from alternative medicine centers and suggesting the need for further clinical studies [40].

4.9.8. Antibacterial activity

This study investigated the antibacterial activities of *Bryophyllum pinnatum* leaf extracts against multidrug-resistant bacterial pathogens. Aqueous and ethanol extracts were prepared from air-dried leaves. In the results, using agar well diffusion, the aqueous extract showed mean zone diameters of inhibition ranging from 9.20 ± 0.17 to $10.50 \pm 0.50 \text{ mm}$ against *Escherichia coli* and 9.30 ± 0.33 to $10.33 \pm 0.89 \text{ mm}$ against *Staphylococcus aureus* at concentrations of 25-100 mg/ml. The ethanol extract exhibited mean zone diameters of inhibition ranging from 9.50 ± 0.28 to $13.33 \pm 0.88 \text{ mm}$ and 10.67 ± 0.67 to $19.00 \pm 0.58 \text{ mm}$ at concentrations of 6.25-100 mg/ml. Minimum inhibitory concentrations (MICs) for the ethanol extract ranged from 6.25-100 mg/ml, while those for the aqueous extract ranged from 25-100 mg/ml. Minimum bactericidal/fungicidal concentrations (MBCs/MFCs) for the ethanol extract were 25-50 mg/ml, and for the aqueous extract, 50 mg/ml. The test bacterial pathogens

exhibited multidrug resistance, with multidrug resistance indices ranging from 0.3 to 0. The study concluded that multidrug-resistant clinical bacterial pathogens are sensitive to the aqueous extract of *Bryophyllum pinnatum* [41].

4.9.9. Urolithic activity

This study investigated the anti-urolithiatic activity of *Bryophyllum pinnatum* Lam. hydroalcoholic extract (BPHE) in sodium oxalate (NaOx)-induced urolithiasis in rats. Rats with NaOx-induced renal calculi were orally administered BPHE at doses of 50 and 200 mg/kg for 14 days, with Cystone (500 mg/kg) as a reference standard. In the results, oral administration of BPHE demonstrated dose-dependent, substantial ($P < 0.05$) anti-urolithiatic potential, notably reversing NaOx-induced ion excretion and urinary CaOx concentration. The study concluded that these findings support the traditional use of *Bryophyllum pinnatum* hydroalcoholic extract in the treatment of renal calculi [42].

This study investigated the anti-urolithiatic effect of an ethanolic extract of *Bryophyllum pinnatum* (Lam) against chemically induced renal calculi in rats. Two models were used: ethylene glycol-induced and sodium oxalate-induced urolithiasis. In the results, in both models, treatment with *Bryophyllum pinnatum* extract (50, 100, and 200 mg/kg) significantly decreased the concentrations of calcium, uric acid, magnesium, urea, and creatinine in blood serum, as well as oxalate, calcium, uric acid, magnesium, urea, and creatinine in urine, compared to the lithiatic control groups. The study concluded that the ethanolic extract of *Bryophyllum pinnatum* exhibits favorable action against urolithiasis by inhibiting kidney crystal deposition [43].

5. Conclusion

Bryophyllum pinnatum, the plant exhibits significant therapeutic potential across a wide range of ailments, including wound healing, inflammation, infections, and metabolic disorders, attributed to its diverse phytochemical constituents like flavonoids, alkaloids, saponins, and triterpenoids. While in vitro and in vivo studies have validated traditional uses and demonstrated promising pharmacological activities, including analgesic, anti-inflammatory, and antimicrobial effects, further clinical trials are essential to confirm safety and efficacy in humans, particularly regarding potential toxicity, especially bufadienolides, and use during pregnancy. Therefore, this review critically examines recent progress to validate the plant's diverse medicinal applications.

Author contribution

Pratiksha Sukumar Magdum conceptualized, investigated, collected data, and wrote the original draft. A. M. Krupanidhi reviewed and edited the manuscript. Prakash Dabadi supervised the manuscript. All authors reviewed and finalized the manuscript for submission.

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Declaration of Competing Interest

The authors declare no conflict of interest, financial or personal, that could have influenced the work presented in this paper.

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