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BRYOPHYLLUM PINNATUM (MIRACLE LEAF): A REVIEW OF ITS PHYTOCHEMICAL COMPOSITION AND PHARMACOLOGICAL ACTIVITIES

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Bryophyllum pinnatum, Clinical trials, Toxicological studies, Phytochemistry, Ethnomedicine, Secondary metabolites, Phytopharmaceuticals

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ABSTRACT: *Bryophyllum pinnatum or Kalanchoe pinnata,* commonly known as the air plant, life plant, or miracle leaf, belongs to the Crassulaceae family. Due to its strong nephroprotective (kidney-protecting) and anti-urolithiatic qualities, this prospective medicinal plant is widely used, especially for the treatment of kidney and gall bladder stones. A comprehensive review was conducted through an online study on websites such as Google Scholar, PubMed, ScienceDirect, ResearchGate, and Scopus. Previous studies have reported that *Bryophyllum pinnatum* contains alkaloids, glycosides, tannins, terpenoids, and flavonoids. This plant has demonstrated numerous pharmacological actions, including nephroprotective, hepatoprotective, antioxidant, immunomodulatory, antibacterial, anticancer, antidiabetic, memory-enhancing, cardioprotective, and gastroprotective effects. To provide a foundation for further research in the field of phytomedicine, this study investigated the phytochemical composition, pharmacological activity, and toxicity of *Bryophyllum pinnatum (BP).*

INTRODUCTION: Plants are essential for feeding and subsistence, and nature is an amazing source of medicine. Medicinal plants have been used for thousands of years to treat ailments because they contain bioactive components that can help alleviate various disorders [1]. A large number of people in both urban and rural areas depend on traditional medicine to treat several illnesses, including diabetes. The easy access and affordability of these medicinal plants have increased their demand worldwide. Approximately 25% of the pharmaceutical medications used today are derived from plants, and many synthetic counterparts are based on model compounds originating from plants.

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The fact that plant-based medications have no adverse effects is driving their demand. Studies have demonstrated the significant influence of numerous secondary metabolites, such as lactones, alkaloids, glycosides, terpenes, flavonoids, and saponins, on the therapeutic properties of plants [3]. An example of such a widely plant is *Bryophyllum pinnatum,* which is part of the Crassulaceae family and is also known as the “life plant” and “miracle leaf.” This family is the third largest group of succulent plants worldwide and has substantial economic value. Originating in Madagascar, this perennial herb has successfully spread to various tropical and subtropical regions worldwide.

In these regions, *Bryophyllum pinnatum* is often cultivated for its aesthetic and medicinal value. The plant is characterized by thick, moisture-conserving leaves arranged alternately along its stems [2]. It is well suited to a variety of habitats, including rocky terrain, open forests, and disturbed sites [4]. *Bryophyllum pinnatum* has significant

ethnopharmacological value on a global scale. Traditionally, it has been used to address a wide array of health issues, including conjunctivitis, edema, piles, wounds, eczema, constipation, epilepsy, cholera, asthma, chest colds, menstrual disorders, chickenpox, fever, and other pathological conditions [5, 6].

This review highlights the therapeutic potential of *Bryophyllum pinnatum* by examining its botanical features, phytochemical constituents, ethnomedicinal applications, pharmacological effects of its extracts, and undocumented clinical trials.

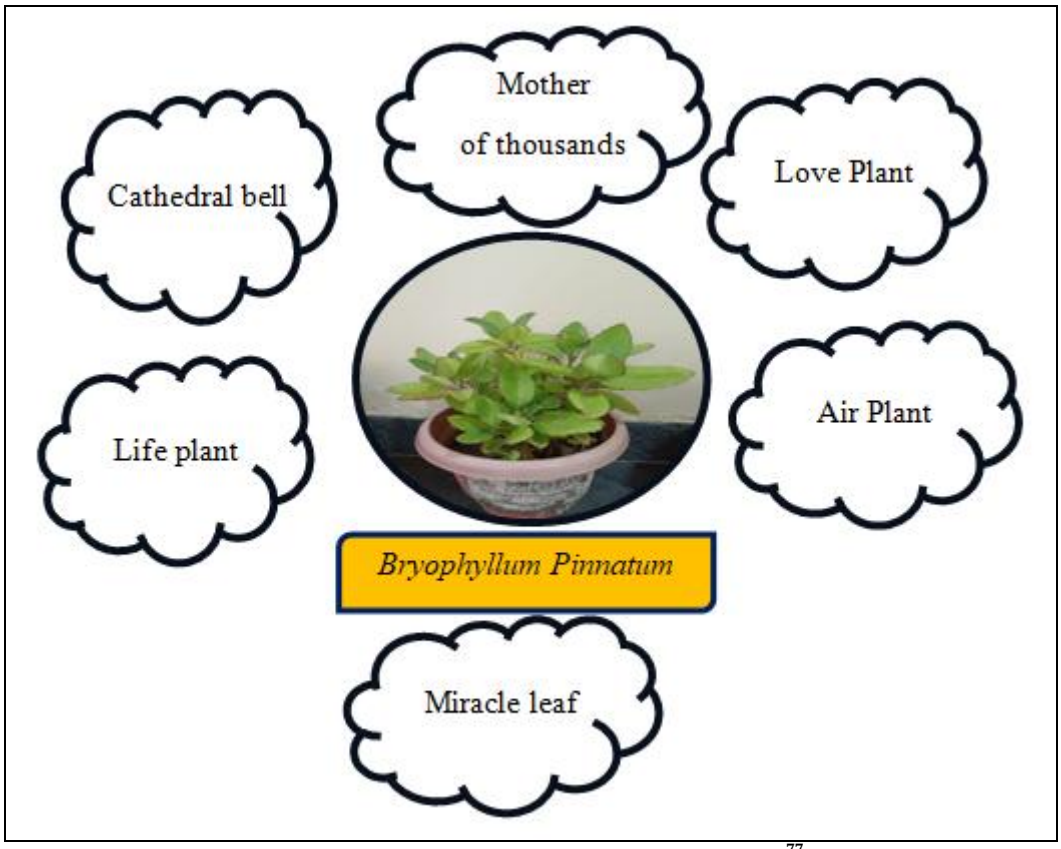

FIG. 1: COMMON NAMES OF *B. PINNATE* [77]

Plant Description [3]:

Plant: The succulent herb *Bryophyllum pinnatum* is short, growing between 0.3 and 1.2 m tall [89].

Stem: Plant stems are dimly quadrangular, with older stems lighter in color and younger stems reddish with a hint of white [89].

Leaves: Characterized by their decussate arrangement, the plant's lower leaves can be simple or complex. The upper leaves are composed of three to seven leaflets, each connected by a long petiole. A ridge, formed where the petioles converge, was evident around the stem. The leaves are elliptical or ovate with serrated or crenate margins [89].

Flower: The plant features large, ostentatious yellowish-green to pastel-green sepals along with pendulous blooms that are approximately 7 cm long and a stem that holds the flower, which is 10–25 mm in length. Reddish-pink dots adorn the tube-like structure formed by the partially joined sepals underneath the flower [89, 90]. The petals were approximately 3–6 cm long and had a reddish-purple hue. At the base, they were octagonal and enlarged with lobe triangles. The anther is black and pinkish-hastate, with green filaments and a green style. The plant flowers most in winter and spring [90, 91].

Fruits: Four cylindrical carpels make up the plant's delicate, membranous follicles, which typically remains enclosed in the flower parts [6, 92].

Seeds: The seeds of *Bryophyllum pinnatum* are tiny, smooth, oblong, brown, and faintly striated [92].

Vernacular Names:

TABLE 1: VERNACULAR NAME OF *BRYOPHYLLUM PINNATUM* [83]

S. no.	Local name	Language/System of Medicine
1.	Pathharchoor, Zakhmhaiyat	Hindi
2.	Air Plant	English
3.	Parnabeeja, Asthibhaksha	Sanskrit
4.	Chubehayat	Urdu and Persian
5.	Gayamari	Marathi
6.	Gandukalinga, Kadu basale	Kannada
7.	Ranapala	Telugu
8.	Malaikalli, Ranakalli	Tamil
9.	Elamarunga	Malayalam
10.	Koppatha, Patharkuchi	Bengali

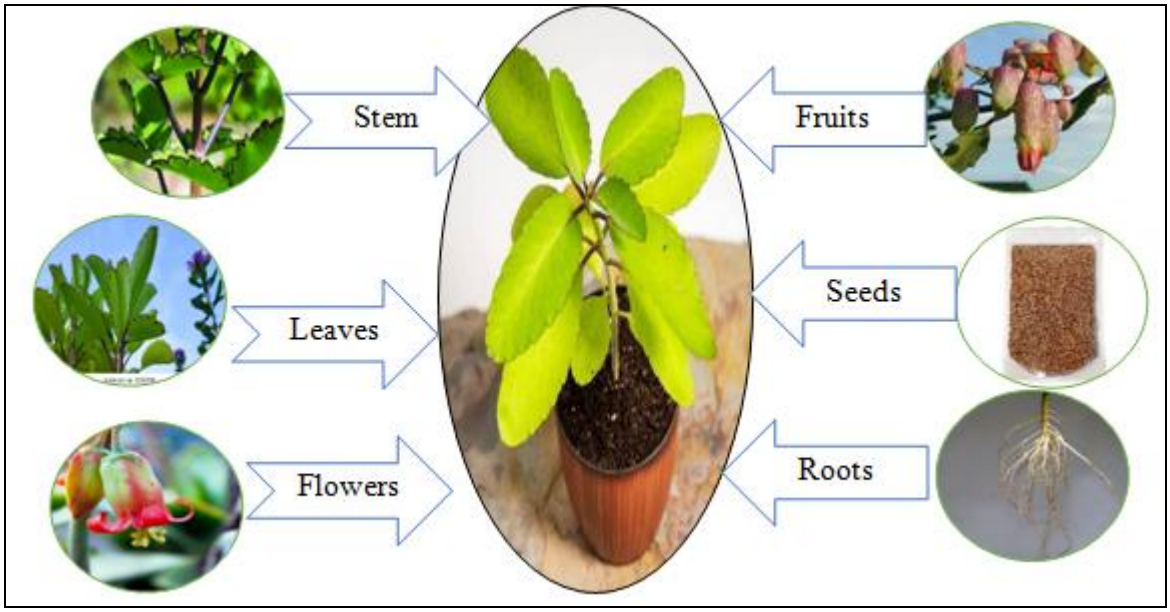

FIG. 2: MORPHOLOGY OF *BRYOPHYLLUM PINNATUM* (PREPARED BY AUTHORS)

METHODOLOGY: A brief review of the literature was conducted to gather scientific evidence on *Bryophyllum pinnatum*. This includes its pharmacognostic properties, traditional uses and chemical compositions, toxicity, and therapeutic effects. We accessed articles from January 2000 to June 2026 through the various databases like Scopus, Elsevier, PubMed, ScienceDirect, Google Scholar, Research Gate, Wiley online library, Bentham Science, CrossRef and SpringerLink. The final search was conducted on June 27, 2026. The search strategy used various types of keywords, including ("*Bryophyllum pinnatum*" OR "*Kalanchoe pinnata*) AND (phytochemistry OR pharmacology OR biological activity OR toxicity OR ethnomedicine), to identify relevant studies. We included only peer-reviewed articles in English. This review covered original research articles, review articles, clinical trials, ethnobotanical information, and *in-vivo* and *in-vitro* investigations, and excluded duplicate publications, conference abstracts, and non-English articles. This article systematically compiles and provides a clear summary of the current scientific knowledge on *Bryophyllum pinnatum*.

Ethnomedicinal Utility: In Brazil, periodontal disease, cracked lips in children, cheilitis, wounds, and boils are treated locally using *B. pinnatum* juice [66]. In Indonesia, rheumatism [67], insect bites in India and Sri Lanka [68], fever, skin conditions, coughing, and cytotoxic action [69], therapy for stomach ulcers, lung infections, and immunomodulatory conditions [70].

In Africa, headaches are relieved by rubbing or tying crushed leaves to the head. Ear infections, dysentery in Nigeria [71, 72], burn injuries, and dermatological conditions have been treated using *B. pinnatum* as a plaster or as a poultice [77].

TABLE 2: ETHNOPHARMACOLOGICAL USES OF *B. PINNATUM*

S. no.	Disease condition	Country	Parts used	Traditional preparation and dose	Route of Administration (ROA)	Reference
1.	Diarrhea and dysentery	Madagascar	Leaves	Decoction of leaves	Oral	[86]
2.	Burns and skin disorders	India	Leaves	Leaves paste	Topical	[87]
3.	Kidney stones	India	Leaves	Fresh leaf juice	Oral	[88]
4.	Cuts and wounds	India	leaves	Leaf paste applied on injured area	Topical	[87]
5.	Joint pain	African countries	Leaves	Heated leaves placed on affected area	Topical	[89]
6.	Insects' bites	Caribbean region	Leaves	Crushed leaves applied on locally	Topical	[90]
7.	Gastric ulcer, gastritis and skin inflammation	Brazil	leaves	Leaves decoction and leaf poultice applied externally	Oral (Gastric ulcer and gastritis) and Topical (Skin disorders)	[91]
8.	Cough, cold and earache	Nigeria	Leaves	liquid from fresh leaves for colds and coughs, as well as liquid applied to ears	Oral and Ear drops	[89]
9.	Diabetes management	Trinidad and Tobago	Leaves	Decoction of leaves	Oral	[90]

Substance Profile: The widespread traditional use of *B. pinnatum* has prompted researchers to investigate its physicochemical and phytochemical compositions, which may be responsible for its therapeutic properties. According to a review of the literature, the physicochemical characteristics of *B. Pinnatum were* discovered in the following values: 5.1 percent for total ash, 1.69 percent for acid insoluble ash, 19.80 percent for water soluble ash and 5.60 percent for alcohol extractive value [73].

Phytochemistry:

Preliminary Phytochemical Screening: Initial phytochemical investigations of various solvent extracts from *Bryophyllum pinnatum* have repeatedly shown the presence of alkaloids, tannins, flavonoids, saponins, terpenoids, steroids, glycosides, organic acids, and phenolic compounds. The phytochemical profile varies depending on the plant part examined and the extraction solvent. Although preliminary screening offers qualitative insights into these groups, it does not verify the specific identities of individual compounds. Consequently, advanced chromatographic and spectroscopic methods are necessary for precise identification and structural analysis [3, 5, 6].

Compounds Identified by Chromatographic and Spectrometric Techniques: Chromatographic profiling has advanced the identification of phytoconstituents in *B. pinnatum*. Abdulrahman (2022) conducted an analysis using GC-MS on extracts from the aerial parts, employing solvents with varying polarities. The study found that the dichloromethane extract contained the most volatile compounds, with 39 identified, while the hexane extract had 25 significant constituents. This highlights the significant impact of solvent polarity on the phytochemical composition [11].

Isolated and Structurally Characterized Compounds:

Flavonoids: Several flavonoids have been extracted from *B. pinnatum* using of bioassay-guided fractionation and chromatographic purification. In their research, Fernandes *et al*, identified and described the structures of three key flavonoid glycosides: kaempferol 3-O-alpha-L-arabinopyranosyl-(1→2)-O-alpha-L-rhamnopyranoside (Bp2), quercetin 3-O-L-rhamnopyranoside-(Bp3), and quercetin 3-O-alpha – L – arabinopyranosyl - (1→2) – O - alpha -L-rhamnopyranoside (Bp1). Additionally, the species contains other flavonoids, including quercetin, rutin, luteolin, kaempferol, myricitrin, diosmin, and afzelin [3, 6, 53-57].

Alkaloids: In the study of *B. pinnatum* phytochemistry, many alkaloidal compounds have been investigated, including bryophylline and phenanthrene derivatives such as 2-(9-undecenyl)-phenanthrene, 2-(9-decenyl)-phenanthrene, and 1-ethanamino – 7 – hex – 1 -yne-5-one phenanthrene. These compounds were identified using

spectroscopic and chromatographic techniques [3, 6, 58-61].

Bufadienolides: Bufadienolides are the primary secondary metabolites in *B. pinnatum*. Around 13 compounds structures analyzed and isolated, including Bryophyllin A, Bryophyllin B, Bryophyllin C, Bryotoxin A, Bryotoxin B**,** Diagremontianin, kalantubosides, and Bersaldegenin derivatives. These cardiotonic steroids play a crucial role in the plants cardiotonic, anticancer and anti-inflammatory properties [6, 16, 17].

Major Phytochemical Classes and Biological Importance:

Tannins: Tannins have been investigated in various extracts of *B. pinnatum*, which may be responsible for its role in promoting wound healing and antioxidant effects [5, 6].

Flavonoids: Flavonoids, which are some of the most ubiquitous phytochemicals in *B. pinnatum*, mainly contribute to its neuroprotective, antioxidant, and anti-inflammatory [6, 12, 17].

Saponins: Saponins, which are primarily identified through initial phytochemical screening, are believed to have antimicrobial properties and to protect the kidneys as well [5, 6].

Terpenoids: The anti-inflammatory, antimicrobial, and antioxidant properties of *B. pinnatum* are attributed to the terpenoids found within it [6, 14, 15].

TABLE 3: PHYTOCHEMICAL COMPOUNDS INVESTIGATED FROM *B. PINNATUM*

Class	Part	Compounds	Method	Evidence	Reference
Flavonoid	leaves	Kaempferol	HPLC	Isolated	3
Flavonoid	leaves	Rutin	LC-MS	Identified	54
Bufadienolide	Leaves	Bryophyllin A	NMR/MS	Isolated	17
Bufadienolide	Leaves	Bryophyllin B	NMR/MS	Isolated	17
Alkaloid	Aerial parts	1-Ethanaminophenanthrene	GC-MS	Identified	58

Pharmacological Activities: Research on *B. pinnatum* extracts has extensively explored their potential therapeutic benefits, including antibacterial, antifungal, wound healing, immunomodulatory, antioxidant, anticancer, hemostatic, larvicidal, and anticoagulant properties. Both *in-vitro* and *in-vivo* studies have investigated the pharmacological activities of *B. pinnatum* extracts.

Neuroprotective Effect: The neuroprotective potential of *B. pinnatum* against several forms of chemically induced neurotoxicity is supported by increasing experimental evidence. Neuronal degeneration is primarily *via* oxidative stress, which is defined as an excess of reactive oxygen species (ROS). Methanolic leaf extracts of B. pinnatum reduced the production of hydroxyl radicals caused by the Fenton reaction. *Pinnatum* preserves cellular integrity and neuronal membranes while significantly reducing lipid peroxidation and oxidative biomarkers in iron (Fe^{2+})-induced *ex-vivo* oxidative injury models [18].

In-vivo studies have confirmed its efficacy in reducing heavy metal-induced neurotoxicity. Exposure to lead acetate in Wistar rats caused Purkinje cell degeneration, increased levels of malondialdehyde (MDA), and decreased antioxidant enzyme activities of superoxide dismutase and catalase (SOD and CAT); however, co-administration with *B. pinnatum* retained cerebellar architecture and restored antioxidant defenses [19]. Similarly, the extract reduced acetylcholinesterase (AChE) activity, rectified redox imbalance, and lessened neuronal damage in aluminum-induced neurotoxicity, indicating the regulation of oxidative stress pathways and cholinergic dysfunction [22].

Furthermore, methanolic extract and its flavonoid-rich fraction showed protective benefits against neurotoxicity caused by monosodium glutamate (MSG), with flavonoids playing a major role in antioxidant and neuronal protection [20]. *B. pinnatum* enhances antioxidant status, preserves the histological integrity of brain tissues, and dose-dependently reverses aberrant neurotransmitter levels in ketamine-induced neurotoxicity models [21].

These results highlight the potential of *B. pinnatum* as a treatment for oxidative stress-related neurodegenerative diseases, demonstrating its neuroprotective effects through antioxidant, metal-

chelating, anti-lipid peroxidative, anti-cholinesterase, and neurotransmitter-modulatory mechanisms.

Cardioprotective Effect: Research has shown that *B. pinnatum* can protect the hearts of rats from doxorubicin-induced cardiotoxicity. When doxorubicin was administered, there was a marked increase in inflammatory markers (CRP, IL-6, and apolipoprotein-E), a decrease in apolipoprotein-A and nitric oxide levels, and an increase in serum cardiac biomarkers (troponin, myoglobin, CK-MB, and ACE). Additionally, it significantly reduced endogenous antioxidant enzyme levels (SOD, CAT, glutathione peroxidase (GPx), and total antioxidant capacity) and caused structural damage to cardiomyocytes. Simultaneous administration of B's ethanolic extract. Similar to the common medication bisoprolol, pinnatum significantly reduced biochemical and histological changes. The extract preserved myocardial architecture, decreased inflammation, restored antioxidant defense systems, and normalized cardiac biomarkers. These result simply that B has cardioprotective effects. Antioxidants are the main mediators of *B. pinnatum* 23. According to a clinical trial, short-term ingestion of *B. pinnatum* leaf extract dramatically improved lipid profiles and decreased cardiovascular risk indicators, such as low-density lipoprotein (LDL), Atherogenic Index of Plasma, and Castelli risk ratios. However, prolonged intake showed a reversal tendency, with some of these benefits being lost. These findings suggest a potential short-term cardioprotective effect, while highlighting the need for prudence and further long-term safety evaluation [24].

Anti-cancer Effect: Plant-based bioactive compounds are gaining popularity as alternative cancer treatments due to the drawbacks and adverse consequences of conventional cancer treatments such as chemotherapy, radiation, and surgery. Because of its numerous pharmacological effects, *B. pinnatum* has garnered considerable interest. *B. pinnatum* leaf extract has been reported to have significant cytotoxic effects on human colorectal cancer (HCT116) cells using both *in-vitro* and *in-silico* approaches [26]. Mechanistic research revealed that it resulted in G2/M phase cell cycle arrest and increased intracellular ROS, which triggered apoptosis by raising pro-apoptotic markers such as caspase-3, BAX, and p53, while lowering BCL-2. Activation of the p53-dependent apoptotic pathway was further confirmed by enhanced nuclear p53 expression [26].

Ionic gelation has been used to manufacture *B. pinnatum*-loaded chitosan nanoparticles (BPCNPs) to improve their therapeutic efficacy [27]. Compared to the raw extract, this nanoformulation demonstrated enhanced physicochemical stability and increased biological activity, exhibiting notable antioxidant, antibacterial, and anticancer effects. The improved efficacy of BPCNPs was likely influenced by the enhanced bioavailability and cellular absorption of the phytoconstituents [27]. Additionally, the potential of *B. pinnatum* to prevent liver cancer has been studied [28]. Substances such as bryophyllin A and β-sitosterol block important oncogenic pathways, such as PI3K and IGF-1R signalling, which are critical for the development of liver cancer. *B. pinnatum* exhibits promising potential as a natural cancer prevention and therapeutic agent by targeting these molecular pathways [28].

Wound Healing Effect: The skin, the largest organ in the integumentary system, accounts for approximately 15% of an individual's total body weight. It protects the internal organs by acting as a primary barrier against external environmental threats [29]. In this sense, *B. pinnatum (Lam.)* Oken's ability to cure wounds has been extensively studied. Leaf extracts prepared using petroleum ether, ethyl acetate, and ethanol were evaluated *in-vivo* using acute excision and burn wound models. A control and conventional therapy (Cipladine® 1%) were compared to ointment formulations containing 1% and 2% (w/w) extracts. Increased wound contraction, faster epithelialization, and improved angiogenesis demonstrated that the ethanolic extract had the best therapeutic outcome among the evaluated formulations [29]. Further preclinical research revealed that a topical gel containing leaf extract from *B. pinnatum* significantly reduced inflammation in acute edema models and promoted efficient wound healing [30]. Furthermore, hydroalcoholic extracts of *Moringa oleifera* and *B. pinnatum* leaves (MUE and BPE) were rich in phenolics, flavonoids, and other secondary metabolites with antioxidant, cytoprotective, and wound-healing effects. These

bioactive substances may support tissue regeneration, strengthen cellular defense systems, and reduce oxidative stress [31]. Overall, our results support the use of *B. pinnatum* as a promising natural therapeutic option for wound care, highlighting its substantial wound healing capacity.

Hepatoprotective Effect: The liver is crucial for maintaining metabolic homeostasis and is necessary for the biotransformation, detoxification, and elimination of both endogenous metabolites and exogenous substances, such as drugs and environmental contaminants [32]. These essential physiological functions make the liver particularly susceptible to chemical-induced injury. The potential hepatoprotective properties of *B. pinnatum* have been extensively studied in experimental studies. In Wistar rats with paracetamol-induced hepatotoxicity, leaf extract significantly decreased liver damage and improved antioxidant status, with more pronounced effects at higher dosages [33].

These findings suggest that it can be used therapeutically to alleviate drug-induced liver damage caused by drugs. The ethanolic leaf extract also exhibited notable hepatoprotective and antioxidant properties in adrenaline-induced liver damage models. Superoxide dismutase (SOD), reduced glutathione (GSH), malondialdehyde (MDA), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), and bilirubin levels were among the biochemical parameters that were normalized by treatment, and micronodular cirrhosis was successfully reversed [34, 35]. Moreover, the hepatoprotective effectiveness of the ethanolic leaf extract was validated in Wistar albino rats and hepatotoxicity induced by carbon tetrachloride (CCl_4). The extract exhibited excellent antioxidant activity and considerably reduced the increased levels of serum liver indicators. Flavonoids, phenolic compounds, and other bioactive components were identified through phytochemical screening, which may help elucidate their capacity to lower oxidative stress-induced liver damage [25].

Antidiabetic Effect: Diabetes mellitus is a chronic metabolic disease that diminishes the quality of life, social functioning and general health. Although insulin and other oral hypoglycemic drugs significantly enhance glycemic control, their adverse effects highlight the need for additional therapeutic strategies. An aqueous leaf extract of *B. pinnatum* was evaluated for its antidiabetic potential in a previous study, which found that it considerably lowered blood glucose levels. When combined with glibenclamide, the extract dramatically improved its therapeutic efficacy, suggesting a possible synergistic interaction [36]. The potent ability of the extract to scavenge free radicals, which is linked to its rich phytochemical composition, particularly flavonoids and phenolic components, may contribute to its purported antidiabetic properties. The antioxidant properties of *B. pinnatum* support its conventional use in treating diabetes mellitus by decreasing oxidative stress-induced pancreatic β-cell malfunction and enhancing glucose homeostasis [37].

Nephroprotective Effect: The kidney is a life-sustaining organ that filters blood, removes metabolic waste products from metabolism, controls fluid and mineral balance, and produces hormones such as erythropoietin and renin, which are necessary for blood pressure management and hematopoiesis, respectively [38].

Ketamine is an anesthetic that has been linked to nephrotoxicity. Notable protective effects against ketamine-induced kidney injury were observed in an experimental study evaluating the nephroprotective capacity of *B. pinnatum*. According to these results, *B. pinnatum* may be a good treatment option for treating renal toxicities induced by ketamine [39]. Moreover, a recent study investigated the impact of *B. pinnatum* leaf extract on renal calculi prevention and *in-vivo* dissolution. Treatment with the extract significantly reduced urine oxalate and calcium levels and enhanced kidney histoarchitecture compared to the control group. These results suggest that *B. pinnatum* leaf extract has potent litholytic and nephroprotective properties [40].

Immunomodulatory Effect: A study examined the antifungal and immunomodulatory properties of *B. pinnatum* extracts prepared using ethanol and aqueous solvents against five distinct fungal species. These findings suggest that *B. pinnatum* has strong haematological and immunomodulatory effects, in addition to significant antifungal activity.

These results suggest that the plant may have antibacterial properties and favorable effects on haematological markers [41].

Systemic lupus erythematosus (SLE) is an elaborate autoimmune disease marked by disrupted immune responses. Patients with SLE usually have reduced regulatory T-cell activity and overactive B cells. Pro-inflammatory cytokines, such as tumor necrosis factor-alpha and transforming growth factor-beta (TNF-α and TGF-β), are produced when B cell activity is elevated because it extends the absorption and presentation of autoantigens to T cells. According to reports, the *B. pinnatum* ethanol extract inhibits B-cell maturation, which may lessen autoantigen presentation to T cells and subsequently modify aberrant immunological responses [42]. Further research is required to fully understand *the* immunomodulatory effects of *B. pinnatum* and to determine its safety and effectiveness for human use.

Memory Enhancing Effect: The effects of a methanolic extract of *B. pinnatum* leaves on memory recall and cognitive function in experimental mice, as well as the measurement of phenolic compounds and the capacity of 2,2-diphenyl-1-picrylhydrazyl (DPPH) radicals to neutralize them, have been investigated. The memory-enhancing activity in scopolamine-induced amnesic mice was measured using the elevated plus-maze method with Shankhpushpi, an ayurvedic standard treatment, and piracetam, an allopathic pharmaceutical. This study claims that both herbs have been scientifically shown to enhance memory [43]. Another study examined the effect of *B. pinnatum* (AEBP) leaf aqueous extract on acetylcholinesterase activity in rats with carbon tetrachloride (CCl4)-induced short-term memory impairment [44].

Gastroprotective Effect: Gastric ulcers are one of the most prevalent gastrointestinal conditions affecting people globally. This condition, which is thought to affect 10% of the world's population, is a major health issue that significantly lowers the quality of life of millions of people [46]. Gastric ulcers can pierce the muscular layers of the stomach, causing acute lesions in the gastric mucosa. If left untreated, it can cause chronic inflammation, bleeding, and perforation [47, 48].

A recent investigation indicated that compared to pretreatment with Bp1, treatment with *B. pinnatum* extract contained a higher inhibition percentage. Therefore, this implies that Bp1 has gastroprotective properties [49].

Anthelmintic Activity: An investigation suggested that the methanolic extract of *B. pinnatum* has potential anthelmintic activity [50].

Antidiarrheal Effect: An estimated 2.2 million people worldwide die from diarrhea annually. Most of them are young children and infants under the age of five [51]. *B. pinnatum* extracts have been shown to have significant antidiarrheal effects in animal models. Compared to the castor oil-treated negative control, both ethanol and ethyl acetate extracts demonstrated a dose-dependent decrease in intestinal motility and diarrhea. Flavonoids, such as 5-methyl-4,5,7-trihydroxyflavone, extracted from the ethanol extract, may be responsible for the relatively higher activity of the extract at 400 mg/kg [52].

Urolithiatic Effect: Urolithiasis, also referred to as kidney stone disease, is the most excruciating urological condition worldwide. Solid crystal aggregates, including calcium phosphate, calcium oxalate, and ammonium magnesium phosphate, are known as kidney stones. An *in-vitro* study explored the potential of *B. Pinnatum* ethanolic leaf extracts to counteract urolithiasis. In a controlled experiment, researchers synthesized calcium phosphate and calcium oxalate crystals and compared their development with that of the standard drug, cystone, using the nucleation assay method. The findings revealed that the extract significantly hindered the crystallization of calcium oxalate [76] in another study, calcium oxalate crystals were dissolved by the ethyl acetate extract of *B. Pinnatum*, which also showed potent antiurolithiatic effects [75].

Psychoactive Effect: The leaves of *B. Pinnatum* are rich in flavonoids and have been traditionally employed to address inflammation, anxiety, sleep disorders, and infections. Research involving larval zebrafish revealed that an aqueous extract of *B. Pinnatum* leaves induced behavioral changes in a dose-dependent manner, such as diminished movement, reduced anxiety-related behaviors, and

enhanced swimming speed, suggesting possible anxiolytic and psychoactive properties [77].

Antibacterial Effect: A recent investigation revealed the antibacterial potential of *B. Pinnatum* leaf and stem extracts using aqueous and ethanol solvents against *Pseudomonas aeruginosa, Staphylococcus aureus,* and *Micrococcus spp*. at concentration of 60-200 mg/ml. the extract showed no inhibitory his study investigated the *B. pinnatum* live plant fractions' effects on the activities of angiotensin-converting-enzyme (ACE), arginase, blood pressure, and biochemical parameters in sodium fluoride (NaF)-induced hypertensive rats. The results revealed that diastolic blood pressure, systolic blood pressure, mean arterial pressure, heart rate, and arginase activity were reduced, with increased nitric oxide levels, compared to those in hypertensive rats. The aqueous fraction (AQF), n-hexane fraction (NHF), and ethyl acetate fractions (EAF) boosted superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH) levels with a reduction in malondialdehyde (in hypertensive-treated rats activity against the tested bacteria, whereas tetracycline produced significant inhibition zones. These findings indicate limited antibacterial efficacy under the tested conditions, suggesting the need for further studies using different extraction techniques and microbial strains [78].

A study explored the effects of live plant fractions of *B. pinnatum* on angiotensin-converting enzyme (ACE) activity, arginase activity, blood pressure, and biochemical parameters in rats with sodium fluoride (NaF)-induced hypertension. The results showed that administering the aqueous (AQF), n-hexane (NHF), and ethyl acetate (EAF) fractions led to a notable decrease in systolic and diastolic blood pressure, mean arterial pressure, heart rate, and arginase activity, whereas nitric oxide levels increased compared to untreated hypertensive rats. Additionally, these fractions boosted antioxidant defense by elevating the levels of superoxide dismutase (SOD), catalase (CAT), and reduced glutathione (GSH), and by lowering malondialdehyde (MDA) concentrations. These findings suggest that *B. pinnatum* has significant antihypertensive and antioxidant properties, potentially contributing to its cardioprotective effects in management [78].

Anti-hypertensive Effect: An investigation suggested that different fractions of *B. pinnatum* affect arginase activity, blood pressure, (ACE), and biochemical parameters in Sodium Fluoride (NaF)-induced hypertensive rats.

The results demonstrated that treatment with plant fractions significantly lowered Systolic and Diastolic blood pressure, heart rate, mean arterial pressure, and arginase activity. However, nitric oxide levels were compared with those of untreated hypertensive rats [79].

Central Nervous System Depressant Effect: Sleep is characterized as a state of unconsciousness that can be triggered by sensory or other inputs. It is a reversible physiological state marked by reduced mobility and sensitivity to sensory stimuli [81].

The hydro methanol extract of *B. pinnatum* significantly decreased sleep onset and prolonged diazepam-induced sleep duration. The study suggested a dose-dependent central nervous system depressant activity of the plant extract [82].

Anti-convulsant Effect: Epilepsy is a long-term neurological condition with a high morbidity rate [84]. The anticonvulsant effect was studied using the maximal electroshock test (MEST) and pentylenetetrazol on one-day-old chicks and mice at 250,500 and 1000 mg/kg body weight of extract. The findings revealed that the methanolic extract of *B. pinnatum* aerial parts significantly decreased the mean recovery time of seizures caused by MEST at doses of 500 and 1000 mg/kg [84, 85].

Pharmacokinetics and Toxicity: Despite encouraging preclinical data, there have been few pharmacokinetic investigations of *B. pinnatum*. There are data that point to the low bioavailability of flavonoids, which could be enhanced by distribution using nanoparticles.

B. pinnatum contains bufadienolides, which raise toxicity concerns because they can cause cardiotoxicity in high quantities. Safety evaluations and reproducibility of results are typically complicated by variations in the chemical levels in plant extracts caused by extraction techniques, environment, and climate [6].

TABLE 4: PHARMACOLOGICAL ACTIVITIES OF *B. PINNATUM*

S. no.	Pharmacological effect	Extract	Model	Reference
1.	Neuroprotective	Methanolic	Ketamine induced neurotoxicity	21
		Leaf extract	Aluminium induced neurotoxicity model	22
			Lead Acetate induced neurotoxicity in Wistar rats	19
		Methanolic extraction and flavonoids rich fraction	MSG- induced neurotoxicity	20
2.	Cardioprotective	Ethanolic leaf extract	Doxorubicin induced cardiotoxicity in rats	23
3.	Cardioprotective /Hypolipidemic	Leaf extract	Clinical trials	24
4.	Hepatoprotective	Leaf extract	Paracetamol-induced hepatotoxicity in Wistar rats	33
		Ethanolic	Carbon tetra chloride induced hepatotoxicity in Wistar albino rats	25
			Adrenaline-induced liver injury model	34,35
5.	Anticancer (Cytotoxic)	Leaf Extract	Human colorectal cancer HCT116 cells	
	Anticancer/ Antioxidant/ Antimicrobial	*B. Pinnatum* loaded chitosan nanoparticles	*In-vitro* biological evaluation	27
6.	Anticancer (Hepatocellular carcinoma prevention)	Bioactive compounds (beta-sitosterol, bryophyllin A)	Molecular pathway analysis	28
7.	Wound healing	Petroleum ether,ethyl acetate and ethanolic acetate extract (ointment formulation)	Acute excision and burn wound model	29
8.	Wound healing and Anti inflammatory	Topical gel containing leaf extract	Acute edema and wound models	30
9.	Wound healing and antioxidant	Hydroalcoholic leaf extract (single and with moringa oleifera)	Preclinical evaluation	31
10.	Antidiabetic	Aq. Leaf extract	-	36
11.	Antidiabetic/ Antioxidant	Leaf extract	Oxidative stress related pancreatic dysfunction model	37
12.	Nephroprotective	Leaf extract	Ketamine induced nephrotoxicity model	39
13.	Nephroprotective/ Litholytic	Leaf extract	*In-vivo* renal calculi model	40
14.	Neuroprotective/ Memory enhancing	Methanolic leaf extract	Scopolamine induced amnesic mice	43
15.	Neuroprotective/ AChE modulation	Aq. Leaf extract	Carbon tetra chloride induced short term memory impairment in rats	44
16.	Gastroprotective effect	Quercetin derivatives	Ethanol and indomethacin induced gastric lesion models	49
17.	Antidiarrheal effect	Ethyl acetate and ethanolic extract of leaf's	Castor oil induced diarrhoea model in mice	52
18.	Urolithiatic effect	Ethanolic and ethyl acetate leaf extract	*In-vitro* calcium oxalate and calcium phosphate crystallization and *in-vitro* calcium oxalate crystal dissolution model	75,76
19.	Antihypertensive effect	Aqueous fraction, n-hexane fraction, and ethyl acetate fraction	NaF (Sodium fluoride) induced hypertensive in rats	79
20.	Central nervous system depressant effect	Hydromethanolic leaf extract	Diazepam induced sleep model	82
21.	Anticonvulsant effect	Methanolic extract of aerial parts	Maximal electroshock test and pentylenetetrazol seizure model in one day old chicks and mice	85
22.	Psychoactive effect	Aqueous leaf extract	Larval zebrafish behavioral model	77

Nutritional Composition of *B. pinnatum* [45]: *B. pinnatum* contains minerals and bioactive substances, such as terpenoids, flavonoids, glaucidanes, and alkaloids.

TABLE 5: NUTRIENTS COMPOSITION

Composition	Percent (%)	Composition	Percent (%)
Fats and oils	1.28	Fibre	6.02
Protein	5.38	Carbohydrate	72.92
Iron	0.18	Copper	0.03
Zinc	3.49	Potassium	3.49
Nickel	0.08	Calcium	4.99
Sodium	0.32	Lead	0.03

CONCLUSION: Communities in several countries, including Indonesia, use the herb *B. pinnatum* for ethnomedical purposes. As previously mentioned, *B. pinnatum's* biochemical peculiarity is its unique bioactive chemicals, which may lead to the development of semi-synthetic medications and herbal cures. This review emphasizes the anticancer, antibacterial, antidiabetic, anti-inflammatory, and antioxidant properties of *B. pinnatum* leaf extracts, which support its biomedical applications.

Therefore, significant research and scientific confirmation are still needed to explore new possibilities for the phytochemical potential of *B. pinnatum*. The pharmaceutical sector could greatly benefit from research discoveries in this field by developing novel therapeutic medicines. In addition to strengthening medical sovereignty, using *B. pinnatum* as a natural treatment can help farmers by promoting the production of medicinal plant.

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