

Antidiabetic Potential of *Bryophyllum pinnatum*: A Study on Its Pharmacological Effects and Synergistic Action with Glibenclamide

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Abstract

Diabetes is a long-term metabolic disorder that profoundly impacts an individual's overall health, social interactions, and quality of life. While significant progress has been made in diabetes management with the use of medications, such as insulin and oral hypoglycemic agents, the limitations of these existing treatments highlight the need for new therapeutic alternatives. Moreover, the high cost of current diabetes medications makes them inaccessible to many, particularly in rural areas of developing countries. This study investigates the antidiabetic effects of an aqueous extract of *Bryophyllum pinnatum* leaves using diabetic albino rats as experimental models. The effectiveness of the extract was compared to a treatment involving both the extract and the conventional antidiabetic drug, glibenclamide. The rats were administered a specific dose of the aqueous extract, and their blood glucose levels (BGL) were monitored throughout the experiment. The results revealed a significant reduction in BGLs, approaching normal levels within 120 minutes when the aqueous extract was used alone. Additionally, when the aqueous extract was combined with glibenclamide, a more pronounced decrease in blood glucose levels was observed. The results of this study indicate that the aqueous extract of *Bryophyllum pinnatum* leaves exhibits potent antidiabetic properties. Furthermore, the use of this extract appears to enhance the efficacy of the conventional antidiabetic drug, glibenclamide. The plant

has many natural chemicals that can affect the body, such as alkaloids, flavonoids, triterpenes, fats, sugars, phenols, bufadienolides, and organic acids. These chemical constituents contribute to the plant's wide range of pharmacological effects, such as neuropharmacological, nephroprotective, antioxidant, analgesic, antidiabetic, antimicrobial, anticonvulsant, and antipyretic activities. This review explores the various pharmacological effects of *Bryophyllum pinnatum*.

Keywords: *Bryophyllum pinnatum*, hypoglycaemic, insulin, diabetes, hypoglycemic agents, glibenclamide

INTRODUCTION

A metabolic disease known as chronic hyperglycemia may be brought on by insufficient insulin secretion, poor insulin action, or a combination of the two. As an anabolic hormone that controls the metabolism of proteins, lipids, and carbohydrates, insulin is essential. This plant was

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first found in Madagascar and has since spread to portions of Asia, Australia, and New Zealand, among other places [1]. The metabolic abnormalities that characterize diabetes are caused by insulin resistance, which primarily affects tissues like the liver, adipose tissue, and skeletal muscles. Type 1 diabetes is an autoimmune illness that gradually worsens and affects about 1% of people in the developed world. This detrimental immune response is brought on by a confluence of environmental variables and genetic predisposition [2, 3]. The *Bryophyllum pinnatum* (Figure 1) plant is a succulent perennial species with a hollow, four-angled stem that is commonly branched, and a normal height of 1 to 1.4 meters. The opposing, succulent, decussate leaves are 10–21 cm long. *Kalanchoe pinnata* has simple bottom leaves and compound top leaves with three to six leaflets on long petioles. With four to six leaflets per blade, the pinnately compound leaf blades range in length from 11 to 32 cm. The individual leaflets are oblong to elliptic in shape, measuring 6–7 cm by 3–4 cm, while the petioles are 2–3 cm long. The leaves have crenate margins, with a latent bud in each notch. The terminal, panicle inflorescences have a length range of 10 to 42 cm (Table 1). The traditional usage of *Kalanchoe pinnata* leaf extracts in folk medicine can be explained by the presence of several phytochemicals with unique biological activity [4, 5].



Figure 1. Plant of *Bryophyllum pinnatum*.

- *Synonyms:* *Kalanchoe pinnata*, *Crassula pinnata*, *Cotyledon pinnata* [1].
- *Common Names:* Life plant, Miracle leaf, Mother of thousands.
- *Biological Source:* It comes from the dried leaves of the *Bryophyllum pinnatum* plant.
- *Family:* Crassulaceae.

Table 1. Taxonomical classification of *Bryophyllum pinnatum*.

Kingdom	Plantae
Clade	Tracheophytes
Clade	Angiosperm
Clade	Eudicot
Order	Saxifragales
Family	Crassulaceae
Genus	kalanchoe
Species	K.Pinnata

DESCRIPTION

This species' thick, meaty, elliptical, curving leaves have a crenate or serrated edge and are frequently reddish in color. The leaves, which are 10–30 cm long and have three to five pairs of fleshy limb lobes, are simple at the base of the stem and imparipinnate at the top. The ability of the leaves to create bulbils is extraordinary. Adventitious buds that develop into roots, stalks, and leaves sprout at their edge, in between the teeth. When the small plant pieces touch the ground, they take root and can grow into

bigger plants. This characteristic is rather prevalent in the Bryophyllum division. The fruits are small, 10–15 mm long pods found inside the flower's corolla and the lasting calyx [6].

A panicle with several dangling, reddish-orange blooms is the terminal inflorescence. The calyx is a long tube with four small triangular tips at the end. It is deep red at the base and has veins of yellowish-green or green with reddish-brown spots. Four 5 cm-long lobes terminate the tubular corolla, which has a noticeable constriction between the ovoid and subspherical portions. It has streaks of reddish-purple and a yellowish tint (Figure 2). The eight 4 cm long stamens are fused onto the corolla in two whorls. The ovary has four slender carpels that are partially connected at the center [7].



Figure 2. Flowers of *Bryophyllum pinnatum*.

Microscopical Character

1. A thin layer on the abaxial side and a convex surface on the adaxial side are confirmed by the microscopic appearance. Its adaxial side contains tiny, less noticeable cells within a thin layer of epidermis. The ground tissue of the midribs is parenchymatous. Cells are compact, angular, and round.
2. There is only one tiny, hemispherical vascular filament. It is composed of a broad phloem band and a thick horizontal xylem band.
3. The walls of xylem components are thin, angular, and narrow. The vascular bundles are present in both the vertical and horizontal axes. The mesophyll is divided into spongy parenchyma and palisade, while the lamina is flat. The stomata are numerous and amniocytic in type.
4. Spiral vessels can be seen in the longitudinal section of the leaves. Trichomes are absent on the abaxial and adaxial sides, shown in Figure 3 [8].

Chemical Constituents

The plant contains several important chemical components, including: Isocitric as well as citric acids. Buffadienolides include, for example, bryotoxins A, B, and C. Phenolic substances, flavonoids, and phenylpropanoids: These include p-hydroxycinnamic acid, syringic acid, caffeic acid, ferulic acid, paracoumaric acid, 4-hydroxy-3-methoxy-cinnamic acid, 4-hydroxybenzoic acid, p-hydroxycinnamic acid, and protocatechuic acid. Triterpenoids combined with steroids: These include bryophollone, bryophollone, α -amyrin, α -amyrin acetate, β -amyrin, β -amyrin acetate, 18- α -oleanane, friedelin, taraxerol, and pseudo-taraxasterol (Figure 4) [9, 10].

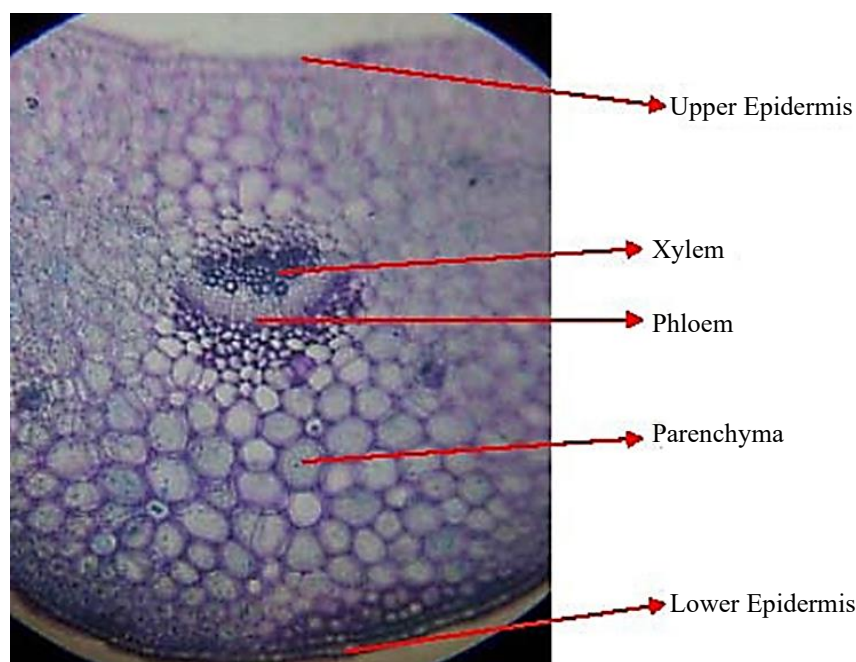


Figure 3. Ts of midrib portion of leaf.

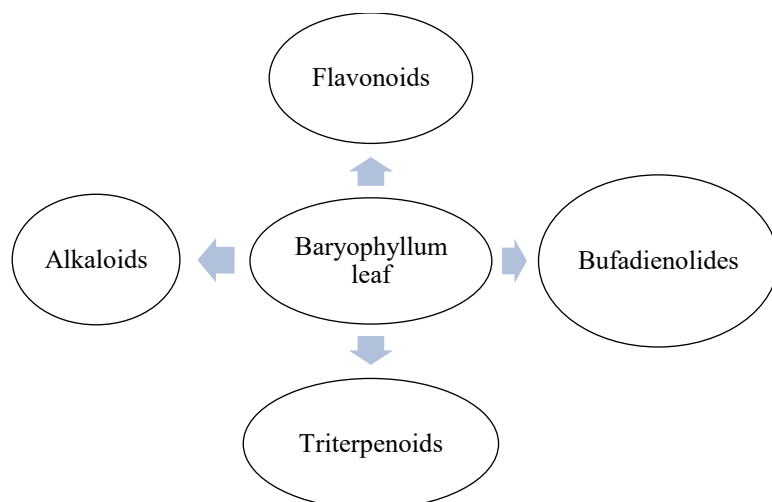


Figure 4. Bioactive constituents of *Bryophyllum* leaf: Highlighting Flavonoids, Alkaloids, Bufadienolides, and Triterpenoids.

Alkaloids

The pharmacological activities of the plant's alkaloids are diverse. The diuretic properties of some alkaloids can aid in the removal of specific kidney stones. However, the specific alkaloids found in *Bryophyllum pinnatum* and how they affect kidney stones [11].

Flavonoids

Bryophyllum pinnatum has flavonoid compounds that act as antioxidants. Flavonoids have been studied for their potential to reduce oxidative stress, which may be a factor in kidney stone production [12].

Triterpenoids

Squalene, an acyclic C₃₀ hydrocarbon, is the biosynthetic precursor of triterpenoids, which are molecules with a carbon skeleton composed of six isoprene units. Their cyclic formations are rather intricate.

Bufadienolide

According to reports, the genus *Kalanchoe* contains plant cytotoxic bufadienolides [13, 14]. It has been reported that bufadienolides have been isolated from the leaves and the aerial portions of various *Kalanchoe* species. The leaves of *K. lanceolata* contain hellibrigenin-3-acetate [15]. Bersaldegennin-1,3,5-oracetate from the leaves of *K. daigremontiana* [16]. The leaves of *Bryophyllum pinnatum* contain bryophyllin B. [17], and Bryophyllin A (Bryotoxic C) from *K. pinnata* leaves [18].

Medicinal Benefits of the *Bryophyllum pinnatum* Plant

- **Antiviral activity:** The antiviral effects of the juice from eight *Kalanchoe* species – *K. daigremontiana*, *K. petersii*, *K. prolifera*, *K. marnieriana*, *K. blossfeldiana*, *K. beharensis*, *K. waldheimii*, and *K. pinnata* – were studied [19].
- **Antidiabetic Activity:** The current study found that in diabetic-induced rats, 800 mg/kg + 2 mg/kg of glibenclamide and four different doses of *Bryophyllum pinnatum* aqueous leaf extract (200, 400, 800, and 800 mg/kg) have anti-diabetic effects. In these four situations, the 800 mg/kg aqueous extract plus 2 mg/kg glibenclamide combination works better and more efficiently than the other extracts [20]. Glycosides and reducing sugar were identified in modest amounts in rats, whereas flavonoids and alkaloids were found in substantial concentrations in contrast to the trace amounts of steroids and terpenoids. For 21 days, albino rats were split up into three groups and fed equal doses of ethanol extracts of *T. africana* leaves and a mixture of Bry. pin (Lam.) Oken plants. Different percentages of the above plant extract mixture were given to the groups, and their plasma sugar levels, glycaemic state, and serum lipid profiles of streptozotocin and normal were assessed – induced diabetic mice from tail vein blood at various 30-, 60-, and 120-minute intervals, which showed a significant ($P < 0.05$) drop in glucose, density compound protein, and high density compound protein levels brought on by STZ – caused diabetes [21, 22]. Bry. pin (Lam.) Lorenz Okenfuss plant leaf liquid extract was also utilised to investigate the medicinal medication activity of rats with diabetes mellitus induced by streptozotocin (STZ) and rats with diabetes induced by modern egg albumin. Rats treated with 25–800 mg/kg p.o. experienced considerable ($P < 0.05$ – 0.001) hypoglycemia. Therefore, the results of this animal study showed that a micronutrient, zinc in particular, with hypoglycemic activity was present in the aqueous extract of Bry. pin (Lam.) Oken leaves (Figure 5) [23].
- **Antimicrobial Activity:** As bacteria grow increasingly resistant to artificial drugs, new and safer antimicrobials – mostly derived from natural sources, like plants – must be developed. Bacterial infections, mainly caused by *S. aureus*, *E. coli*, *B. subtilis*, *P. auroginosa*, *K. aerogenes*, *K. pneumoniae*, and *S. typhi*, are treated using the herb *Bryophyllum pinnatum*. Typhoid fever is also treated with it. Additionally, its leaves prevent pathogens from growing. The compounds bryophyllin A and bryophyllin C show potent insecticidal effects when administered to silkworm larvae in their third instar. The new substances 4,3,5,7-tetrahydroxy-5-methyl-5-propenamine anthocyanidines and 5-methyl-4,5,7-trihydroxy flavones may have antimicrobial properties against bacteria, such as *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, and *Escherichia coli*. Used *Bryophyllum pinnatum* leaf 60% methanolic extract, which has potent antibacterial action at 25 mg/ml [24].
- **Anticancer Activity:** An in vitro study found that some chromatographic fractions and crude extracts from *B. pinnatum* leaves prevent the proliferation of human cervical cancer cells [25].
- **Antihypertensive activity:** According to the study's findings, rats with normotensive and spontaneously hypertensive arterial blood pressure and heart rates responded favorably to *B. pinnatum* aqueous and methanolic leaf extracts. The hypertensive rats showed a more pronounced hypotensive effect than the normotensive rats. The guinea pig isolated atria's contraction force and rate decreased in a dose-dependent manner even with the leaf extracts [26].
- **Wound healing Activity:** The study's findings demonstrated that after 10 days of oral treatment of *B. pinnatum* leaf extracts (petroleum ether, water, and alcohol) had a wound-healing impact on dead space wound models, re-sutured incisions, and excision wounds in Albino rats. Furthermore, the excision wound model was treated with a tropical water extract for 21 days, or until eschar

developed. All three extracts – water, alcohol, and petroleum ether – significantly strengthened the incision site compared to the control group [27].

- **Antihelmintic Activity:** Parasitic worm infections are among the most common health issues in humans, affecting a large portion of the population. *Bryophyllum pinnatum* tannins have antihelmintic properties; worms are killed by chloroform, methanol, and an aqueous extract of *Bryophyllum pinnatum* root, which also exhibits strong antihelmintic activity; the action taken against *Pheretima posthuma*, the Indian soil worm, is also investigated; various extract concentrations (30 and 50 mg/ml) are tested, and the paralysis and death time of the worms are noted. The entire plant of *Bryophyllum pinnatum* shows anthelmintic action, which may be beneficial [28].
- **Neuroprotective Activity:** Aqueous leaf extract from *Bryophyllum pinnatum* has neuropharmacological effects on mice. The *Bryophyllum pinnatum* extract exhibited a strong sedative effect, reducing overall activity and extending the duration of pentobarbitone-induced sleep. It also helped delay seizures triggered by strychnine and picrotoxin. It also lowers the rate of picrotoxin-induced death in mice with an LD50 of 641 mg/kg. Together, these studies show that *Bryophyllum pinnatum* has CNS depressant qualities [29].
- **Immunosuppressive Activity:** *Bryophyllum pinnatum* leaf aqueous extract dramatically suppresses humoral and cell-mediated immune responses in mice. Similarly, the mice's spleen cells pretreated with plant extract showed a decreased ability to multiply in response to both antigen and mutagen in vivo [30].
- **Hepatoprotective Activity:** The liver, the biggest and most important organ in vertebrates, helps the body metabolise food and flushes out toxins. The chemicals and drugs used damaged the liver and disrupted its metabolism. Liver problems are treated with a variety of medicinal plants. Similarly, ethanolic extracts of *Bry. pin* (Lam.) Oken leaves were utilized to treat liver cirrhosis, liver cancer, and other liver diseases in rats. An aqueous and ethanolic extract of *Bry. pin* (Lam.) was administered orally to rats wounded by induced N-diethyl nitrosamine at doses of 250 and 500 mg/kg, and the researchers discovered that the extract greatly protected the rats [31].
- **Analgesic Activity:** Analgesics work on the central nervous system's peripheral pain mechanism to lessen pain without impairing awareness. Some steroid derivatives, which were extracted from the leaves of *Bry. pin* (Lam.), are also phytoconstituents [32].



Figure 5. Leaf of plant *Bryophyllum pinnatum*.

CONCLUSIONS

This review highlights that *Bryophyllum pinnatum* is one of the most commonly available medicinal plants in India, containing a variety of beneficial chemical compounds. It primarily contains bufadienolides, alkaloids, flavonoids, glycosides, and organic acids. These constituents show various pharmacological activities, such as antimicrobial, antidiabetic activities, anthelmintics, neuroprotective, diuretics, immunosuppressive and show muscle relaxant, antioxidant, anticonvulsant activity. This review highlights the pharmacological potential of *Bryophyllum pinnatum*, providing valuable insights for researchers to explore the plant further.

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