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Bryophyllum pinnatum: BOTANICAL DESCRIPTION, VERNACULAR NAMES, PARTS USED, TRADITIONAL USES, PHYTOCHEMICAL AND PHRMACOLOGICAL ACTIVITIES

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ABSTRACT

Bryophyllum pinnatum (Family: *Crassulaceae*) is a traditional herb that has widely been used for removal of kidney stones and is found to possess a number of pharmacological activities such as antiviral, antipyretic, antimicrobial, anti-inflammatory, antitumor, hypocholesterolemic, antioxidant, diuretic, antiulcer, styptic, antidiabetic, astringent, antiseptic, antilithic, cough suppressant, anticancer, antihypertensive, fungitoxic and uterine relaxant. The plant contains flavonoids, tannins, anthocyanins, glycosides, alkaloids, phenols, bufadienolides, saponins, coumarins, carotenoids, sitosterols, quinines, tocopherol and lectins. The flavonoids rutin, quercetin, luteolin and luteolin 7-O-β-d-glucoside detected in the plant might be a responsible factor for the anti-inflammatory effect. Diuretic and antioxidant activity of the plant could be responsible for its wide use against urolithiasis. Anthocyanidines could be responsible for the antimicrobial activity of the plant. Kaempferol 3-O-α-l-arabinopyranosyl (1→2) α-l-rhamnopyranoside) and two other polar flavonoids (quercetin 3-O-α-l-arabinopyranosyl (1→2) α-l-rhamnopyranoside and 4′, 5-dihydroxy-3′, 8-dimethoxyflavone 7-O-β-d-glucopyranoside) are responsible for the antileshmanial activity. Bufodienolides are found to have cytotoxic property and hence might be responsible for the anticancer effect. The present study is undertaken to update and ease the researchers to get a comprehensive summary of the plant regarding its botanical description, common name, parts used, traditional uses, phytochemical evaluation and pharmacological activities.

Keywords: *Bryophyllum pinnatum*; Antileshmanial; Kaempferol; Bufadienolides

INTRODUCTION

Botanical description

Bryophyllum pinnatum is a perennial herb of genus Bryophyllum belonging to family *Crassulaceae*. The family comprises of 25 genera and 450 species. It is erect and grows about 1.5 m height. It belongs to crassula tribe; the leaves and stem of which are fleshy and succulent (Nagaratna and Hedge, 2015). Leaves are alternate/opposite, simple, less commonly pinnately divided and ex-stipulate. Flowers are usually cymose, hermaphrodite/ rarely unisexual and regular. Calyx is free, 4-5 fid/ 4-5 partite. Flowers are pendent, in large spreading panicles with opposite stout branches, pedicels slender. Petals are as many as sepals, and alternate to the monopetalous corolla. Carpels are as many as petals and are opposite to them with a hypogynous gland/scale at the base. Sepals are red striated, green at the base and pale green above. Petals are reddish purple, swollen and octagonal at the base, lobes triangular. Filaments are green at the base, pinkish below the anthers. Anthers are hastate, black. Styles are green. Fruits are follicles and membranous with few seeds. Fruits are enclosed in a persistent papery calyx and corolla. Seeds are small, oblong-ellipsoid, smooth (Nagaratna and Hedge, 2015). The plant flowers in Nov-Mar and fruits in April (Jaiswal and Sawhney, 2006; Kamboj and Saluja, 2009; Paranjpe, 2001).

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It reproduces from seeds and also vegetatively from leaf bubbils (Okwu and Josiah, 2006).

Habitat

It is found naturally in hot and humid tropical regions of the world. It is a native herb of Madagascar.

Vernacular names

The vernacular names of *Bryophyllum pinnatum* is given in Table 1.

Table: 1: Vernacular names of *Bryophyllum pinnatum*

English	Miracle leaf; life plant; Cathedral bells
Nepali	Pattharchhata
Urdu	Zakhm-ayat; Kopata; Kotak; Haem sager
Arabic	Kushnulhayat

Taxonomy

Taxonomy of the plant, *Bryophyllum pinnatum* is given in Table 2.

Table 2 Taxonomy of *Bryophyllum pinnatum*

Kingdom	Plantae
Class	Dicotyledon
Family	Crassulaceae
Genus	Bryophyllum

Parts Used

Almost all parts of the herb have been utilized in the folklore system for the treatment of various ailments. However, the extensive research has been made on leaves.

Traditional Uses

The plant is used as traditional as a medicine for treating urinary stones in different parts of world. It has been used in numerous conditions like hypertension, skin disorders, asthma, cold, insect stings, abscesses etc. (Nagaratna and Hedge, 2015).

Ethnobotanical uses

It has been used in the treatment of various diseases including diabetes and heart diseases (Ogbonnia *et al.*, 2008). Leaves of the plant have much higher therapeutic applications than the other parts. The juice of the leaf has traditionally been used for the treatment of ear infections, dysentery and cough. In Southeastern Nigeria, this herb is used to facilitate the dropping of the placenta of newly born baby (Dalziel, 1955). In South West Nigeria, Yoruba tribe, tie and rub the crushed leaves in their head to bring relief for headache (Sofowora, 1982). Igbos of Nigeria, uses decoctions of the leaf or the raw leaves itself for the treatment of hypertension (Ghasi *et al.*, 2009). It has been used with palm oil and shear butter in abscesses and swelling (Okwu and Josiah, 2006). In India, the leaves are used as hepatoprotective herb to treat jaundice (Yadav and Dixit, 2003). In Africa, Latin America, and Asia leaves are used as an antipyretic and for treatment of malaria (Willcox and Bodeker, 2004). The plant has also been used as an antipsychotic agent since 1921.

In traditional medicine, the leaves of this plant have been reported to possess antimicrobial activity antifungal (Salahdeen and Yemitan, 2006) anti-ulcer (Pal and Chaudhuri, 1991) anti-inflammatory and analgesic (Pal and Nag Chaudhuri, 1989) and antihypertensive activities (Ojewole, 2002). The aerial parts of *Bryophyllum pinnatum* has been used against guinea worm. In case of abdominal pain it has been used as a decoction (Agyare *et al.*, 2014).

The Creoles have been using the lightly roasted leaves for cancer, inflammations, and a leaf infusion for fevers. Siona indigenous peoples heat the leaves and apply them topically to boils and skin ulcers. Along the Rio Pastaza in Ecuador, natives use a leaf infusion for broken bones and internal bruises. In Peru, indigenous tribes mix the leaf with aguardiente (sugar cane rum) and apply the mixture to the temples for headaches. They soak the leaves and stems overnight in cold water and then drink it for heartburn, urethritis, and fevers and for all sorts of respiratory conditions. The root infusion has also been used in epilepsy. Other tribes in the Amazon squeeze the juice from fresh leaves and mix it with mother's milk for earaches.

In Mexico and Nicaragua, it has been used traditionally to promote menstruation and assist in childbirth. In Nigeria and other West African countries, leaves are frequently used as herbal remedy for the number of human disorders, including: hypertension, diabetes mellitus, bruises, wounds, boils abscesses, insect bites, arthritis, rheumatism, joint pains, headaches and body pain (Kamboj and Saluja, 2009). Traditionally, the plant seems to have wide applications in different ailments.

Phytochemical studies

Phytochemical study shows that the plant contains, flavonoids, tannins, anthocyanins, glycosides, alkaloids, phenols, bufadienolides, saponins, coumarins, carotenoids, sitosterols, quinines, tocopherol and lectins (Devbhuti *et al.*, 2008; Pal *et al.*, 1999). It also contains steroids, lipids, triterpenes; cardienolides (Gaind and Gupta, 1972; Gaind and Gupta, 1974; Marriage and Wilson, 1971; McKenzie *et al.*, 1987). It contains lipids carbohydrates, proteins vitamins and minerals. The plant

is reported to contain alkaloid (1.24− 1.48 mg/100 g), flavonoids (1.46 − 1.86 mg/100 g), tannins (0.04 − 0.5 mg/100g), saponins (1.46 − 1.72 mg/100 g), and phenols (0.06 mg/100g). The vitamins reported in the plant include ascorbic acid (26.42 − 44.03 mg/100 g), riboflavin (0.20 − 0.42 mg/100 g), thiamine (0.11 − 0.18 mg/100 g), and niacin (0.02 − 0.09 mg/100 g) (Okwu and Josiah, 2006).

The leaves are reported to contain bufadienolides such as bryotoxin A, B, C which are very similar in structure and activity like cardiac glycosides, digoxin and digitoxin (Kamboj and Saluja, 2009; McKenzie *et al.*, 1987; Yamagishi *et al.*, 1989).

Aerial parts of the plant contain varying amount of phenol acids such as caffeic acid, synergic acid, p-hydroxycinnamic acid, ferulic acid, para-coumaric acid, 4-hydroxy-3-methoxy-cinnamic acid, protocatechuic acid, 4-hydroxybenzoic acid, phosphoenolpyruvate and protocatechuic acid (Gaind and Gupta, 1972). Flavonoids found in the plants include friedelin, astragalin, epigallocatechin-3-o-syringate,luteolin, kaempferol, rutin, quercetin 3, 8-dimethoxy-4, 5, 7 trihydroxyflavone, quercetin-3-Odiarabinoside, quercetin-3L-rhamonsido-L-arabino furanoside; kaempferol-3-glucoside, kaempferol-3-O-α-L-arabinopyranosyl (1→2)α -L-rhamno pyranoside, quercetin-3-O-α-L-arabino pyranosyl (1→2)α -L-rhamno pyranoside and 4',5-dihydroxy-3',8-dimethoxy flavone-7O-β-D-glucopyranoside. Three unusual flavonoids kaempferol 3-O-α-l-arabinopyranosyl (1→2) α-l-rhamnopyranoside , quercetin 3-O-α-l-arabinopyranosyl (1→2) α-l-rhamnopyranoside and 4′,5-dihydroxy-3′,8-dimethoxyflavone 7-O-β-d-glucopyranoside (Muzitano *et al.*, 2006).

The cardienolide and steroidal contents in the aerial parts of the plant includes: β-sitosterol, bryophyllol, bryophynol, bryophyllin B, bryophyllin A, bryophyllin C and bersaldegenin-3-acetate, bryotoxin A, bryotoxin B, bersaldegenin-1, 3, 5-orthoacetate, 24-ethyl-25-hydroxy-cholesterol, campesterol, clionasterol, isofucosterol, peposterol, codisterol, 22dihydrobrassicasterol, 24-epiclerosterol, clerosterol, 24ethyl- desmosterol, 25-methyl-5α-ergost-24 -en-3-β-ol, ergosta-5-24 -dien-3-β-ol, 25-methyl-ergosta-5-24 -dien3-β-ol, 5α-stigmast-24-en-3-β-ol, (24s)-stigmast-25-en-3-β-ol, (24r)-5α-stigmasta-7-25-dien-3-β-ol, (24s)-5α-stigmasta-7,25 dien-3-β-ol, 24(R)-stigmasta-5,25-dien-3β-ol, stigma-sterol, patuletin], 3-O- (4-O-acetyl-α-L-rhamno-pyranosyl) -7O- (2-O-acetyl-α-L-rhamno pyranoside) patuletin, 3-O-α-L-rhamno pyranosyl-7-O-(2-O-acetyl-α-L-rhamno pyranoside) patuletin, 3-O-(4-O-acetyl-α-L-rhamno pyranosyl)-7-Orhamno pyranoside patuletin.

The triterpenes present in plant includes α-amyrin, α-amyrinacetate, β-amyrinacetate ,β-amyrin, bryo-phollenone, bryophollone, taraxerol, γ-taraxasterol, pseudo taraxasterol, , friedelin, glutinol and 18-α-oleanane (Kamboj and Saluja, 2009).

The plant contains amino acids such as thiamine, pyrodoxine, glycine, ascorbic acid and cysteine and casein hydrolysate nicotinamide in its dry and fresh leaves. Minerals present in plant leaves include sodium, calcium, phosphorus, copper, potassium, magnesium, zinc and ferrous.

Fatty acids such as palmitic acid, steric acid, behenic acid, malic acid, oxalic acid, citric acid, succinic acid hydrocyanic acid isocitric acid are found in plants. Sugars found in plants include raffinose, lactose, sucrose, glucose, galactose fructose, maltose and arabinose which justify its uses in diarrhea (Alabi *et al.,* 2005).

Pharmacological activities

Antihelminthic activity

Ether, chloroform, methanol and aqueous extracts of the plant were tested against Pheritima posthuma, wherein methanolic extract of the leaves had profound effect on paralyzing and killing these worms (Lunkad *et al.*, 2016). The tannins present in leaves were the reason for antihelmentic activity (Majaz *et al.*, 2011).

Antihypertensive activity

Methanolic and aqueous leaf extracts of arterial parts of the plant were investigated for their effect on blood pressure and heart rate of normal and hypertensive rats using invasive and noninvasive technique. Both the extracts given through intravenous and intraperitoneal route produced a significant decrease in blood pressure and heart rate of anaesthetized rats. The effect was more on the hypertensive rats. Similarly, these extracts showed the measurable decrease in rate and force of contraction in atrium isolated from guinea pig. Cardiodepression and vasodilation might be the reason behind its antihypertensive effect (Ojewole, 2002).

Neuropharmacological activity

Aqueous extract of the leaves produced CNS depressant effect in mice at (50,100 and 200mg/kg). The exploratory activity was decreased with the extract in a dose dependent manner. It delayed the onset of seizures induced by picrotoxin and strychnine. The effect was more protective on picrotoxin induced seizure. It also showed the significant sedative effect and increased the phenobarbitone induced sleeping time (Salahdeen and Yemitan, 2006).

The methanolic leaves extract also produced CNS depression as aqueous extract in rats and mice,

potentiating the phenobarbitone induced sleeping time. It was found to reduce the exploratory behavior. The extract also produced an analgesic effect (Pal *et al.*, 1999). The saline leaf extract of this plant produced similar effect on CNS as the aqueous and methanolic and extracts. It reduced the exploratory activity in head dip extracts. It reduced the exploratory activity in head dip evasion tests. It also showed muscle relaxant property (Yemitan and Salahdeen, 2005).

Hepatoprotective activity
Yadav and Dixit (2003) evaluated the in vitro, in vivo and histopathological studies on hepatoprotective activity of the juice of the plant and concluded that the juice is effective in jaundice. The juice of the leaves was found to be more effective than the ethanolic extract to protect the hepatocytes damaged by CCl_4 (Yemitan and Salahdeen, 2005).

Wound healing property
Petroleum ether, alcohol and water extracts of the plant were investigated on albino rats, and these extracts increased the breaking strength of incision wound, granuloma breaking strength and hydroxyproline content of granulation tissue. Water extract increased the wound contraction and formation of scars (Khan *et al.*, 2004). Because tannins have astringent properties, it fastens the healing of wounds and inflamed mucous membranes (Agoha, 1974). The plant also contains ascorbic acid, which also helps in wound healing process (Okwu and Josiah, 2006).

Antidiabetic and hypolipidemic activity
The extract of the plant caused the measurable reduction in both postprandial and STZ-induced diabetes blood glucose levels. The extract increased high density lipoprotein (HDL) level and decreased the low density lipoprotein LDL and triglycerides in rats. The research justifies its traditional use in diabetes and risk of cardiovascular diseases (Ojewole, 2005). The role of the plant to treat diabetes resulting from insulin malfunction might be because of the presence of zinc (Okwu and Josiah, 2006).

Uterine contractility
The plant was found to possess the tocolytic activity on human myometrium (Gwehenberger *et al.*, 2004). The extract was found to show similar result in pregnancy and newborn outcomes in preterm labor as beta agonists with comparatively less adverse effects and was better in Apgar scores, oxygen use and neonatal morbidity. The H1 receptor antagonist present in leaf juice may be responsible for the relaxant effect (Plangger *et al.*, 2006).) Further investigation showed that juice in concentrations of 1–10% lead to an inhibition of electrically induced contractions less than oxybutynin (Schuler *et al.*, 2012).

Antileshmaniasis
Muzitano *et al.* (2009) investigated the effect of plant on cutaneous leishmaniasis. The activity was compared with three compounds such as quercetin, quercitrin and afzelin (Muzitano *et al.*, 2006).

Antimicrobial activity
The 60% methanolic extract of the leaves was found to be effective against different microorganisms. These include Bacillus substilis, Escherichia coli, Proteus vulgaris, Shigella dysenteriae and Staphylococcus aureus at concentration of 25mg/ml. Pseudomonas aeruginosa, Candida albicans and Klebsiella pneumonia were found to be resistant to the extract (Akinpelu, 2000).

Antiulcer and anti-inflammatory activity
The methanolic extract of the leaves was found to have an antiulcer activity against aspirin induced ulcer in pylorus ligated rats. It showed healing effect in acetic acid induced chronic gastric lesions in rats and histamine induced duodenal lesions in guinea pigs (Pal and Chaudhuri, 1991). Adesanwo et al. (2007) justified the use of plant as antiulcer, where methanolic extract was found to have significant reduction in incidence of ulceration and mean basal and histamine stimulated gastric acid secretion in a dose dependent manner. The extract of leaves showed healing effects in gastric ulcer at two distinct ulcer models in rats; in acidified ethanol model and in acid acetic model at 200 and 400 mg/kg. The healing effect was better at 400mg/kg (Sobreira, 2013). Chibli et al. (2014) investigated the anti-inflammatory activity of the ethanolic extract of leaves on acute and chronic cutaneous inflammation. Significant reduction ($P<0.001$) of the ear edema was noticed after the topical application of the extract.

Antiurolithic activity
Administration of the aqueous extract of the leaves was found to reduce the urine oxalate level, decreased the deposition of calcium oxalate crystals. It also decreased the relative kidney weight and improved the serum creatinine and blood urea level in Wistar male rats. It was found to be effective in preventing and treating ethylene glycol induced preclinical model of urolithiasis. Renal function test was found to be improved with no significant effect in urinary volume. The improved serum creatinine level and blood urea level is might be due to the antioxidant activity of the plant by preventing the

lipid peroxidation induced oxidative stress (Shukla *et al.*, 2014). Similarly the hydroalcoholic leaf extract was found to inhibit the calcium oxalate crystals growth and found to protect the kidney against oxidation stress and renal cell injury induced by calcium oxalate crystals. It was possibly because of the diuretic and antioxidant activity of the plant (Ahmad *et al.*, 2007).

Antitussive and Anasthmatic property

Aqueous extract demonstrated antitussive and antihistaminic properties in guinea pigs. Ovalbumin sensitized guinea pigs were treated with doses of 200 and 400 mg/kg/day aqueous extract for 21 consecutive days and were exposed to 0.2% histamine aerosol in glass chamber. Treated group significantly increased the time to experience preconvulsive dyspnoea. Bouts of cough were reduced with both doses however amount of secretion of phenol red was reduced significantly with 400 mg/kg/day. The extracts reduced the mucus viscosity in the sensitized group to values comparable with controls as that of salbutamol (5 mg/kg/day) There was so significant change in parameters such as white blood cell, tracheal morphometry and lymphocyte counts (Salami *et al.*, 2013).

Anticancer and antiviral property

The inhibition of the growth of cervical cancer cell was noted with the extracts. The IC_{50} of crude extract was at 552 µg/ml and IC_{50} for the fraction collected from the column was at 91 µg/ml. It also strongly induced apoptosis as evidenced by an increased expression of the pro-apoptotic protein Bax, suppression of the anti-apoptotic molecules Bcl-2, and activation of caspase-3 and cleavage of PARP-1 (Yamagishi *et al.*, 1989).

A specific anti-HPV activity on cervical cancer cells was evidenced by down regulation of constitutively active AP1 specific DNA binding activity and suppression of oncogenic c-Fos and c-Jun expression which was accompanied by inhibition of HPV18 transcription with the crude extract and that of the fraction (Mahata *et al.*, 2012).

Antioxidant activity

Antioxidant activities were carried out on aqueous and methanolic extracts of leaves stem and whole plant using different models such as hydroxyl radical scavenging activity, superoxide radical scavenging activity and iron chelating power. The results indicated that the plant possessed antioxidant properties and could serve as free radical inhibitors (Sharma *et al.*, 2014). The methanolic extract of the plant showed an antioxidant property with an IC50 value of 52.48 µg/ml.

Insecticidal activity

Methanolic extract of the leaves showed insecticidalactivity against third instar larvae of the silkworm (Bombyx mori) (Supratman *et al.*, 2000).

Fungitoxic Phytotoxic activity

A fresh and dried leaf of the plant was found to protect cowpea seedlings and increased the yield. Cowpea seedlings are attacked mostly by fungus Sclerotium rolfussi in wet season in Nigeria. The extracts significantly reduced disease infection rate, transpiration rate and stomatal aperture, when compared with the values of the control. The extract significantly increased plant height, plant, shelf life, relative water content and chlorophyll when compared to control. The extracts also inhibited the release of current photosynthethates from treated plants thus maintaining the water status of plant and also making photosynthethates which can be oxidized to release energy needed for growth available to treated plants (Alabi *et al.*, 2005).

Toxic to cattle

Cardiac glycosides toxicity was observed in calves after eating flower head of different species of the plant (*B. fedtschenkoi, B. proliferum* and *B. pinnatum)*. The toxicity was due to bufadienolide which was detected in through HPLC (McKenzie *et al.*, 1987).

Conclusion

The leaves and leaf juice of the plant have been extensively investigated for a number of pharma-cological activities. The comprehensive summary of this plant signifies the importance and rationale behind its traditional uses. The important phytochemicals found in the plant include flavonoids, tannins, anthocyanins, glycosides, alkaloids, phenolic acids and bufadienolides. This literature review would be helpful for researchers to know about the work that has been completed till date and to plan for future.

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