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Review Article

Bryophyllum pinnatum: A review

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Abstract

Bryophyllum pinnatum (Lam.) (Crassulaceae) is a perennial herb grows 3-5 feet tall, fleshy dark green leaves that are distinctively scalloped and trimmed in red, and bell like pendulous flowers. It is used in folk medicine in tropical Africa, tropical America, India, China, and Australia. This review covers detailed ethnopharmacology, phytochemistry and bioactivities of *Bryophyllum pinnatum*. A number of active compound groups including alkaloids, triterpenes, lipids, flavonoids , glycosides, bufadienolides, phenols and organic acids has been covered. It is widely used in traditional medicine for the treatment of variety of ailments like anthelmentic, immunosuppressive, hepatoprotective, antinociceptive, anti-inflammatory and antidiabetic, nephroprotective, antioxidant activity, antimicrobial activity, analgesic, anticonvulsant, neuropharmacological and antipyretic. It is well known for its haemostatic and wound healing properties. All these aspects along with available marketed preparations and patents are considered in this review to allow an evaluation of the potential for utilisation of the large biomass of Bryophyllum available focusing on the chemical constituents utilized against variety of pathological conditions.

Keywords: *Bryophyllum pinnatum*, Alkaloids, Bufadienolides, Flavonoids, Phytoconstituents, hepatoprotective, Immunomodulative, tocolysis.

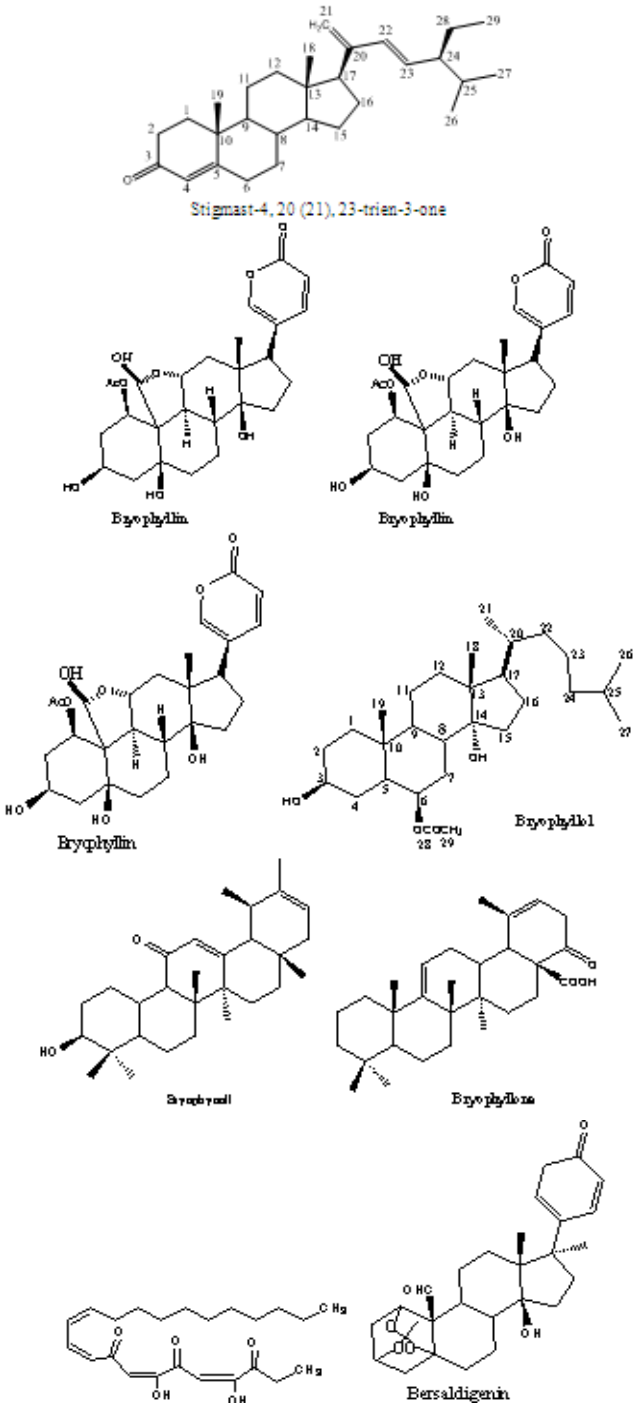
1. Introduction

The plant, Bryophyllum pinnatum (Crassulaceae) is commonly known as air plant, love plant, miracle leaf, life plant, Zakham-e-hyat, panfutti, Ghayamari [26], has been accepted as a herbal remedy in almost all parts of the world [52, 57, 25] etc. It is a crassulescent herb of about 1 metre in height, with opposite, glabrous leaves (with 3–5 deeply crenulated, fleshy leaflets) [53], distributed worldwide but growing primarily in the rain forest [76, 71]. It grows widely and used as folk medicine in tropical Africa, India, China, Australia and tropical America ,Madagascar, Asia and Hawaii [51, 40]

It is astringent, sour in taste, sweet in the post digestive effect and has hot potency. It is well known for its haemostatic and wound healing properties. The plant have considerable attention for their medicinal properties and find application in folk medicine, as well as in the contemporary medicine [33,62].The present review provides detail information of the plant exploring its ethnopharmacological uses, phytochemical and pharmacological studies conducted on *B. Pinnatum* and also pinpoints unexplored potential of it.

2. Ethanopharmacology

The leaves and bark of *B. pinnatum* are bitter tonic, astringent, analgesic and carminative, ethanopharmacologically used for the treatment of diarrhea and vomiting, earache, burns, abscesses, gastric ulcers, insect bites, and lithiasis [9,1,35,80]. The juice from fresh leaves is used to treat smallpox, otitis, cough, asthama, palpitatious, headache, convulsion and general debility [26].The plant has also been employed for the treatment of edema of legs [15]. Leaves powder used as wound dressing and sold as 'Jakhmehayat'. In Southeastern Nigeria, the herb is used to facilitate the dropping of the placenta of newly born baby [12,14]. This is also applied on the bodies of young children when they are ill [1]. It is



Bryophollenone

Fig. 1. Compounds isolated from *Bryophyllum pinnatum*

largely used in folk medicines for the treatment of hypertension and kidney stones, [40] pulmonary infections, rheumatoid arthritis etc [47]. In traditional medicine, the leaves of the plant also have been used for antifungal [65], potent antihistamine and anti-allergic activity[67,17]. *B. pinnatum* is a refrigerant, emollient, mucilaginous, haemostatic, vulneray, depurative, constipating, anodyne, disinfectant, antitonic.The plant proved to be useful in vitiated conditions pitta and vata, epilepsy, piles [45], haematemesis, haemorrhoids, menorrhagia, cuts and wounds, discolourations of the skin, boils, ophthalmia, scalds, corn [58,32]. The plant has hepatoprotective activity and is also used to increase vascular integrity [51].Bryophyllum can reduce fever and does provide anti-inflammatory, and muscle relaxant effects [54]. Its anti-inflammatory effects have been partially attributed to the immunomodulatory and immune suppressant effect [52,69]. Leaf juice is used in the treatment of coughs, bronchial affections, blood dysentery, jaundice and gout [22].

3. Phytochemistry

Preliminary phytochemical investigation of different parts of plant extracts of *B. pinnatum* showed the presence of alkaloids, phenols, flavonoids, saponins, tannins, carotenoids, glycosides [34,49,17], sitosterol, anthocyanins, [50] malic acid, quinines, tocopherol [66], lectins [5,49], coumarins [39] and bufadienolides [38,24]. The leaves are found to contain various chemical constituents including 1-octane3-O-α-L-arabinopyranosyl-(1-6)-glucopyranoside [3,64], isorhamnetin-3-O-a-L-1C4-rhamnopyranoside, 40-methoxy-myricetin-3-O-a-L 1C4-rhamnopyranoside and protocatechuic-40-O-b-D-4C1-glucopyranoside [59], 24-epiclerosterol [24(R)-stigmasta-5, 25-dien-3β-ol], 24(R)-5α-stigmasta-7, 25-dien-3β-ol, 5α-stigmast-24-en-3β-ol and 25-methyl-5α-ergost-24 (28)-en-3β-ol [71,56]. A new steroidal derivative, Stigmast-4, 20 (21), 23-trien-3-one was also isolated from the plant leaves extract along with stigmata-5-en-3β-ol , α – amyrin- β-D-glucopyranoside , n-undecanyl n-octadec-9-en-1-oate and n-dodecanyl n-octadec-9-en-1-oate [16]. Different naturally occurring flavanoids from leaves are flavones, falvans, flavanones, isoflavonoids, chalcones, aurones and anthocyanidines [4,75,15], 5^{I} Methyl 4^{I}, 5, 7 trihydroxyl flavone 1 and 4^{I}, 3, 5, 7 tetrahydroxy 5-methyl 5^{I}-propenamine anthocyanidines 2[15]. Compounds with potent biological activity are bersaldegenin- 1, 3, 5-orthoacetate [77] and bufa-dienolide-bryophyllin B [78,56] and Bryophyllin C [74,62],, bryophyllol, bryophollone, bryophollenone, bryophynol [70]are isolated from the aerial part of the plant. Phenanthrene derivatives isolated from the plant extract are 2(9-decenyl)-phenanthrene and 2-(undecenyl)-phenanthrene (II) ,1 -ethanaomino 7 hex-1-yne-5-one phenathrine [63,18], diagremotianin [73]. 18α-Oleanane, ψ-taraxasterol, β-arnyrin acetate was also elucidated along with a mixture of α- and β-amyrins and their acetates [63]

The aqueous leaf extract from the medicinal plant *B. pinnata* (Crasaceae) afforded a kaempferol diglycoside, named kapinnatoside, identified as kaempferol 3-O-a-L-arabinopyranosyl (1! 2) a-L-amnopyranoside known to have anti leishmania activity[64].The major elements, comprising calcium, phosphorus, sodium, potassium malate, magnesium and trace elements (iron and zinc) were also determined in the plant extracts along with vitamins like ascorbic acid (26.42 to 44.03 mg/100 g), riboflavin (0.20 to 0.42 mg/100 g), thiamine (0.11 to 0.18 mg/100 g), and niacin (0.02 to 0.09 mg/100 g) casein hydrlylsate, nicotinamide[61,17,11]. Syringic acid, caffeic acid [37], 4-hydroxy-3-methoxy-cinnamic acid, 4-hydroxybenzoic acid, p-hydroxycinnamic acid, para-coumaric acid, ferulic acid, protocatechuic acid, phosphoenolpyruvate, protocatechuic acid isolated from aerial parts of plants [33,62].

Extract obtained by decoction of the bryophyllum leaves contains various enzymes i.e Phosphoenolpyruate carboxykinase (PCK), Phosphoenolpyruvate carboxylase (PEPC), Pyruvate orthophosphate dikinase (PPDK), ribulose-1, 5-biphosphate carboxylase/ oxygenase (rubisco) [47] along with Phosphoglycerate kinase, Carbonic anhydrase, Glycolate oxidase, Fructosebiphosphate aldolase, DNA topoisomerase which most of having role in metabolism [31].

4. Pharmacological activities

4.1. Antimicrobial activity

Two novel flavanoids; 5 methyl 4,5,7 trihydroxyl flavones and 4,3,5,7 tetrahydroxy 5 methyl 5 propenamine anthocyanidines showed potential antimicrobial activities against Pseudomonas aeruginosa, Klebsiella pneumonia, E.coli, Staphylococcus aureus, Candida albicans and Aspergillus niger [15]. When 60% methanolic extract of Bryophyllum pinnatum leaf used to inhibits the growth bacteria, at a concentration of 25 mg/ml it showed good antibacterial effects [19]. Further the Plant is effective in the treatment of typhoid fever and other bacterial infections, particularly those caused *by S. aureus, E. coli, B. subtilis, P. aeruginosa, K. aerogenes, K. pneumoniae and S. typhi* due to the presence of phenolic compounds. Researchers findings supported its use in treating the placenta and navel of newborn baby, which not only heals fast but also prevent the formation of infections [13,16,35]. *Some researchers suggested that the active constituents* Bufadienolides: bryophyllin A and bryophyllin C from *B. Pinnatum* showed strong insecticidal activity against third instar larvae of the silkworm [74].*The* Fungitoxic and phytotoxic effects of extracts on the fungal pathogens have also studied by the researchers [10,81].

4.2. Anti ulcer activity

It also been demonstrated by the investigators that the Methanol-soluble fraction of B. pinnatum leaf extract inhibited the development of a variety of acute ulcers induced in the stomach and duodenum of rats and guinea pigs [68].

4.3. Antihypertensive

The aqueous and methanolic leaf extracts of B. pinnatum decreases in arterial blood pressures and heart rates of anaesthetized normotensive and hypertensive rats [28,69].

4.4. Antileishmanial activity

The flavanoids like Quacertin[43], leuteolin was recently described as a promising antileishmanial drug with low toxity[42].Proanthocyanidins , kaempferol di-glycoside , flavonol and flavone glycosides also show potent antileishmanial activity[36,64].

4.5. Antihelmentic activity

Phytochemical analysis of the crude extracts revealed the presence of tannins which were shown to produce anthelmentic activity. The results reveal that chloroform, methanolic and aqueous extract of *B. pinnata root* not only demonstrated paralysis but also caused deaths of worms and showed significant anthelmentic activity [46].

4.6. Anticancer

Prescreening method for cytotoxic effect showed that the ethanolic extract of bryophyllum pinnatum has anti cancerous activity [29,41]. In BSL bioassay, the ethanolic extract showed lethality against the brine shrimp nauplii. It showed different mortality rate at different concentrations [70]. Five bufadienolides isolated from the leaves of *B. pinnata* were examined for their inhibitory effects on Epstein-Barr virus early antigen (EBV-EA) activation in Raji cells induced by the tumor promoter, 12-Otetradecanoylphorbol-13-acetate. All bufadienolides showed inhibitory activity, and bryophyllin A exhibited the most marked inhibition among the tested compounds. Bryophyllin C, a reduction analogue of Bryophyllin A, and bersaldegenin-3-acetate lacking the orthoacetate moiety were less active. These results strongly suggest that bufadienolides of Bryophyllum pinnatum are potential cancer chemopreventive agents [74]. MTT assay on a highly metastatic human HT-1080 fibrosarcoma cell line showed that metanolic. Methonolic aqueous, aqueous extract have mild antiproliferative activity [30].

4.7. Wound healing activity

The extract of *B. pinnatam* was evaluated for its wound healing activity by using excision wound model in rats. The histological analysis showed that plant leaf extract exhibited significant wound healing potential. The wound healing exhibited by the extract may be attributed to the presence of steroid glycosides [48].

4.8. Antidiabetic activity

The anti-diabetic effect of *Bryophyllum pinnatum* plant extract had been investigated in rats using streptozotocin (STZ)-induced diabetes mellitus. The plant aqueous extract of *B.pinnatum* caused significant reductions in the blood glucose levels of the fasted normal and fasted STZ-treated diabetic rats—via a yet obscure mechanism [27].

4.9. Anti inflammatory activity

Anti inflammatory activity of *Bryophyllum pinnatum* plant extract was investigated on rats using fresh egg albumin-induced pedal (paw) oedema. The plant extract significantly inhibited fresh egg albumin-induced acute inflammation [27]. Moreover antinociceptive effect of aqueous leaf extract of the plant against thermally- and chemically-induced nociceptive pain stimuli in mice has been studied and stated that the plant significantly exhibited antinociceptive effects [27].Further the analgesic and anti-inflammatory activity of a new Stigmast-4, 20 (21), 23-trien-3-one, a steroidal derivative obtained from the leaves extract of the plant has also been evaluated [16].

4.10. Immunomodulatory effect

The aqueous extract of leaves causes significant inhibition of cell-mediated and humoral immune responses in mice [8].The spleen cells of animals pre-treated with plant extract showed a decreased ability to proliferate in response to both mitogen and antigen in vitro as well as the specific antibody responses to ovalbumin were also significantly reduced by treatment. Investigation found that leaf extracts inhibited invitro lymphocyte proliferation and showed invivo immunosuppressive activity, hence it has been proved that the aqueous extract of leaves possesses immunosuppressive activities[8]. It has been stated that the fattyacids present in *B.Pinnatum* may be responsible for its immunosuppressive effect invivo as from the ethanolic extract a purified fraction (KP12SA) of *B.Pinnatum* found twenty-fold more potent to block murine lymphocyte

proliferation than the crude extract[6]. Further the resrachers studied immunomodulatory effect of bryophyllum pinnatum and reported that mice daily treated with oral *B.pinnatum* during hypersensitization with ovalbumin were all protected against death. It was stated that Oral protection was accompanied by a reduced production of OVA-specific IgE antibodies, reduced eosinophilia, and impaired production of the IL-5, IL-10 and TNF- α cytokines. Oral treatment with the quercitrin flavonoid isolated from plant extract prevented fatal anaphylaxis in 75% of the animals. The abovesaid findings indicated that oral treatment with *Bryophyllum pinnatum* effectively downmodulates proanaphylactic inducing immune responses [20]

4.11. Hepatoprotective activity

The hepatoprotectitve activity of *B.pinnatum* was reported by various scientists. It was found very effective hepatoprotective as it significantly lowers the enzyme SGOT, SGPT SALP and SBLN levels as increased level are well known sensitive indicators of liver injury [44]. The juice of its leaves and the ethanolic extract of the marc left after expressing the juice were studied in rats against CCl4-induced hepatotoxicity and found to be potential hepatoprotective [60]. Another findings along with the histopathological studies clearly showed the hepatoprotective activity of *Bryophyllum pinnatam* [51].

4.12. Nephroprotective activity

The investigators reported that the aqueous extract of the leaves of *B.Pinnatum* posses potent nephroprotective activity in Gentamycin-induced nephrotoxicity in rats [21]. It has also stated that Plant extract was found to exert significant diuretic and antiurolithitic activity when Hydroalcoholic extract of leaves of *B.pinnatum* was administered to male wirstar rats by oral and i.p route[55 ,47].

4.13. Anticonvulsant activity

CH2Cl 2/CH3OH extract of *B.pinnatum* were found to reduce seizures induced by pentylenetetrazol, strychnine sulphate and thiosemicarbazide and increases in the latency period of seizures and to reduced the duration of seizures induced by the three convulsive agents. The extract protected 20% of animals against death in seizures induced by TSC and STN [49,24].

4.14. Neurosedative and muscle relaxant activity

The saline leaf extract of *Bryophyllum pinnatum* was investigated for neuropharmacological activities to ascertain ethanopharmacological significance. When tested in mice, it produced a dose-dependent prolongation of onset and duration of pentobarbitone-induced hypnosis, reduction of exploratory activities in the head-dip and evasion tests. Moreover, a dose-dependent muscle in-coordination was observed in the inclined screen, traction and climbing tests [54].

4.15. Uterine relaxant and uterine contractility

B. pinnatum showed its relaxant effect invitro on the contractility of human myometrium on oxytocin-stimulated contraction at a minimum concentration almost 100-fold lower than in the case of spontaneous contraction [2].

4.16. Antihistaminic and antiallergic activity

The methanol extract of *B. Pinnatum* leaves has also been reported to have histamine receptor (H1) antagonism in the ileum, peripheral vasculature and bronchial muscle [67].

4.17. Antioxidant activity

Physiological burden of free radical causes imbalance in homeostatic phenomenon between oxidants and antioxidants in the body. The imbalance leads to oxidative stress that is being suggested as the root cause of aging and various human diseases like arteriosclerosis, stroke, diabetes, cancer and neurodegenerative diseases such as Alzheimer's and Parkinson's disease. The DPPH and Nitric oxide free radical scavenging method were used to detect oxidative activity by Jain C.Vineet. The results of DPPH method showed 50% inhibition rate at the 144.23µg/ml and 117.42µg/ml with aqueous and alcoholic extract, respectively. Nitric oxide scavenging inhibition showed 50% inhibition rate at the 525.92µg/ml and 460.48µg/ml with aqueous and alcoholic extract, respectively. The researchers stated after screening that the extract from leaves have interesting potential free radical scavenging activity for treatment of diseases. [23,7,26, 21]. Morales and colleagues suggested that quercetin has a marked protective effect on cadmium-induced nephrotoxicity that results from an increase Metallothionein, a small cysteine-rich protein and eNOS (endothelial nitric oxide synthase) expression and the inhibition of COX-2 (cyclooxygenase-2) and iNOS (inducible nitric oxide synthase) expression [79].

5. Marketed Prepration

1. Amantol Cream: Its indications are respiratory disorders, Sinusitis, bronchitis, allergic reactions, blocked nose. Ingredients are Mentha Viridist extract (mint.), Iresine difusa (escanel) extract, Lippia alba extract (yantria), Zingiber officinalis extract (ginger),Bryophyllum pinnata extract (Pakipanga),Mansia alliacea extract (ajode monte),mentol, alcanfor, water cream base, external use only.
2. Parnabija savarasa: anti obesity [47].

6. Patents

Dr. Tejal Gandhi, Dr. Kirti Patel applicant from Anand Pharmacy College, Gujarat have Indian patent on novel process for the isolation of flavonoids and saponins from *Bryophyllum pinnatum* fresh leaves, Filed on 2011-09-29,Publication date 2011-12-09 [82].

A Chinese medicine having emulsifying property got US Patent comprising *Akebia trifoliata, Polygonum perifoliatum, Euodia rutaecarpa, Stemona tuberose, and Bryophyllum pinnatum* [83].

7. Conclusion

Bryophyllum pinnatum (Lam.) Synonym Kalanchoe pinnata (Lam.) is a perennial herb growing widely and used in folkloric medicine in tropical Africa, India, China, Australia and tropical America. Classified as a weed, the plant flourishes throughout the Southern part of Nigeria. A number of active compounds, including flavonoids, glycosides, steroids, bufadienolides and organic acids, have been identified in *Bryophyllum pinnatum*. Its bufa-dienolides are structurally similar to Cardiac glycosides and have demonstrated in clinical research to posses antimicrobial, antifungal, anticancer, anti tumour, insecticidal actions. It also possess other activities like anti ulcer, anti-inflammatory and analgesic, antihypertensive,

hepatoprotective, Nephroprotective, diuretic,anti diabetic, anticonvulsion, antioxidant, uterine relaxant,muscle relaxant and neurosedative activity and tocolysis activity. The methanol extract of the leaf of the plant has also been reported to have histamine receptor (H1) antagonism in the ileum, peripheral vasculature and bronchial muscle. The present review shows the pharmacological potentials of *Bryophyllum pinnatam* which is very helpful to researcher to explode more about this valuable plant

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