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Review Article

KALANCHOE PINNATA: PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE

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Abstract
The main objective of this review is to provide advance information for the drug discovery research from the divine herb *Kalanchoe pinnata*, which contains a wide range of active compounds, including alkaloids, triterpenes, glycosides, flavonoids, steroids, bufadienolides, lipids and organic acids. The pharmacological studies are reviewed and discussed, focussing on activities as immunomodulator, CNS depressant, analgesic, antimicrobial, antiinflammatory, antiallergic, antianaphylactic, antileishmanial, antitumorous, antiulcerous, antibacterial, antifungal, antihistamine, antiviral, febrifuge, gastroprotective, immunosuppressive, insecticidal, muscle relaxant, sedative, anticancer. Now it becomes endangered plant which needs to be conserved as well as explored for its significant green chemistry.
Keywords: Analgesic, antimicrobial, immunomodulator

1. Introduction

Medicinal plants have been known for millennia and are highly esteemed all over the world as a rich source of therapeutic agents for the prevention of diseases and ailments.[1,2,3] This Wonder plant or Divine plant Leaf, Stem and Root portions and its chemicals has high index in therapeutic values.

1.1 Plant description

Botanical Name: *Bryophyllum pinnatum*
Family Name: Crussulaceae
Sanskrit Name: Pashanabheda
Hindi Name: Patharchur
Common Names: Cathedral Bells, Air Plant (USA), Life Plant, Miracle Leaf, Goethe Plant and Katakataka. Also called "Wonder of the World" in the English speaking Caribbean.'Oliwa Ka Kahakai (Hawai'i), Mother Of Thousands, Herbe Mal Tete (Dominica) Never Dead, Parvu, Hoja Del Aire (Bolivia).
Synonym: Bryophyllum calycinum, Bryophyllum pinnatum[4,5,6].

1.2 Taxonomical tree

Kingdom: Plantae
Division: Magnoliophyta
Class: Magnoliopsida
Order: Saxifragales
Genus: Kalanchoe
Section: Bryophyllum
Species: *K. pinnata*

The plant grows all over India in hot and moist areas, especially in Bengal. It is a succulent perennial plant that grows 1-1.5 m in height and the stem is hollow four-angled and usually branched. Leaves are opposite, decussate, succulent, 10-20 cm long. The lower leaves are simple, whereas, the upper ones 3-7 foliate and are long-petioled. They are fleshy dark green that are distinctively scalloped and trimmed in red. Leaf blade pinnately compound with 3-5 leaflets, 10-30 cm; petiolules 2-4 cm; leaflet blades oblong to elliptic, 6-8 X 3-5 cm, margin crenate with each notch bearing a dormant bud competent to develop into a healthy plantlet apex obtuse[8]. The leaves are furnished with rooting vegetative buds. Inflorescences terminal paniculate 10-40 cm. Flowers are many bell-like pendulous. Calyx tubular, 2-4 cm; Corolla reddish to purple, 5 cm, base sparsely ciliate; lobes ovate-lanceolate; stamens inserted basally on corolla; nectar scales oblong; follicles included in calyx and corolla tube. The fruit-pod with four septa and numerous, ellipsoid, smooth striate seeds within. The plant flowers

in Nov-Mar and fruits in April [7,8,9] . It is astringent, sour in taste, sweet in the post digestive effect and has hot potency.

1.3 Habitat: It is a succulent plant native to Madagascar. It is distinctive for the profusion of miniature plantlets that form on the margins of its leaves, a trait it has in common with the other members of the Bryophyllum section of the Kalanchoe genus.It is a popular houseplant and has become naturalized in temperate regions of Asia, the Pacific and Caribbean[4].

1.4 Distribution: Kalanchoe pinnata has become naturalized in temperate regions of Asia, Australia, New Zealand, West Indies, Macaronesia, Mascarenes, Galapagos, Melanesia, Polynesia, and Hawaii. In many of these, such as Hawaii, it is regarded as an invasive species. It is also widely distributed in the Philippines and it is known as katakataka or kataka-taka which is also an adjective meaning astonishing or remarkable[4,5].

2. Chemical constituents: *B.Pinnatum is* rich in alkaloids, triterpenes, glycosides, flavonoids, cardienolides, steroids, bufadienolides and lipids[9,10,11,12]. The leaves contain a group of chemicals called bufadienolides which are very active. Bufadienolides like bryotoxin A, B, C which are very similar in structure and activity as two other cardiac glycosides, digoxin and digitoxin and possesses antibacterial, antitumorous, cancer preventative and insecticidal actions [12,13,14] .

Bufadienolides-Bryophyllin A (bryotoxin)[15]; Bryophyllin B (Fig. 1); Bryophyllol (Fig. 2); Bryophollone (Fig. 3); Bryophollenone (Fig. 4); Bryophynol (Fig. 5) [16].

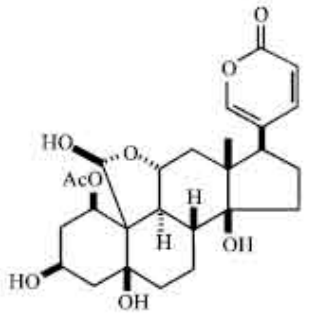

Fig 1. Bryophyllin

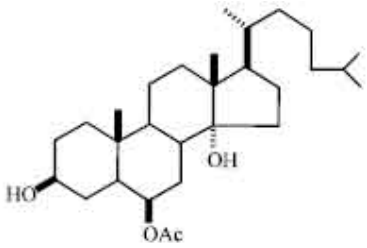

Fig 2 Bryophyllol

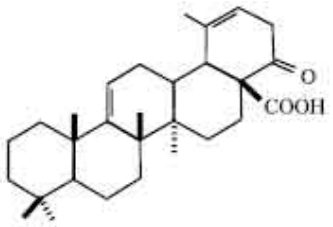

Fig 3 Bryophollone

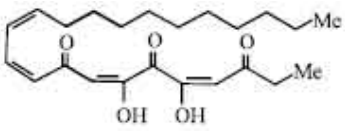

Fig 4 Bryophollenone

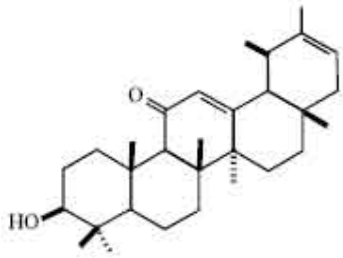

Fig 5 Bryophynol

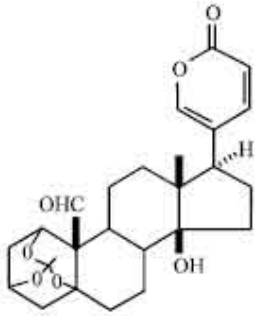

Fig 6 Bersaldegenin

2.1 Phenols, Phenylpropanoids and Flavanoids: Syringic acid, caffeic acid [10] , 4-hydroxy-3-methoxy-cinnamic acid, 4-hydroxybenzoic acid, p-hydroxycinnamic acid, paracoumaric acid, ferulic acid, protocatechuic acid, phosphoenolpyruvate, protocatechuic acid isolated from aerial parts of plants.

Leaves contains astragalin, 3,8-dimethoxy-4, 5, 7trihydroxyflavone, friedelin, epigallocatechin-3-o-syringate, luteolin, rutin**,** kaempferol , quercetin , quercetin-3L-rhamonsido-L-arabino furanoside ; quercetin-3-Odiarabinoside, 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. Because of its restricted occurrence and its abundance in *B. Pinnatum,* flavonoid may be a chemical marker of the plant of high therapeutic potential [4,5,6] .

2.2 Triterpenoids and Steroids: The plant contains α-amyrin, α-amyrinacetate, β-amyrin, β-amyrinacetate, bryophollenone , bryophollone , taraxerol, Ψ-taraxasterol , pseudo taraxasterol, 18-α-oleanane, friedelin, glutinol.

The cardienolide and steroidal contents includes β-sitosterol , bryophyllol, bryophynol , bryophyllin B (Antitumor) , bryophyllin A (bryotoxin C , bufadienolide1, 3, 5-orthoacetate) with potent cytotoxicity, a insecticidal bufadienolide bryophyllin C and bersaldegenin-3-acetate , bryotoxin A, bryotoxin B , bersaldegenin-1, 3, 5-orthoacetate, campesterol , 24-ethyl-25-hydroxycholesterol, isofucosterol , clionasterol, codisterol , peposterol, 22-dihydrobrassicasterol, clerosterol, 24-epiclerosterol, 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, stigmasterol , patuletin , 3-O-(4-O-acetyl-α-L-rhamnopyranosyl)-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 are isolated from aerial parts [17,18] .

2.3 Fatty Acids, Minerals and Others: Fatty acid fraction includes palmitic acid (89.3%), stearic acid (10.7%), traces of arachidic and behenic acid . Plant also contains HCN, oxalic acid , citric acid, isocitric acid, oxaloacetate, malic acid and succinic acid. The plant is rich in vitamins and aminoacids; ascorbic acid, riboflavin, thiamine, niacin, pyridoxine, glycine, cysteine, casein hydrolysate, glutamic acid, protein hydrolysate, methionine, tyrosine, phenylalanine [19].

Food contents are carbohydrates, protein, lipids, acids, iodine. The herb is good source of mineral elements such as Na, Ca, K, P, Mg, Mn, Fe, Cu, Zn. Sugar contents includes raffinose, lactose, sucrose, glucose, galactose, fructose. Plant also contains alkaloids, tannins, phenanthrene derivatives: 2(9-decenyl)-phenanthrene, 2(9-undecenyl)-phenanthrene ,alkanes (C_{25-35}), alkanols (C_{26-34}), n-triacontane, hentriacontane[20].

3. Pharmacological Activities

3.1 Herbal Tonic: The plant is good sources of ascorbic acids, riboflavin, thiamine and niacin. Natural ascorbic acid is vital for the body performance i.e. normal formation of intercellular substances throughout the body, including collagen, bone matrix and tooth dentine [21]. Therefore, the clinical manifestations of scurvy that is hemorrhage from mucous membrane of the mouth, gastrointestinal tract, anemia, pain in the joints can be related to the association of ascorbic acid and normal connective tissue metabolism [21]. This function of ascorbic acid accounts for its normal wound healing property. As a result the plant is used in herbal medicine for the treatment of common cold and other diseases like prostate cancer [13]. In a study an herbal composition comprised of extracts of number of herbs including *B.Pinnatum* acts as a tonic to improve respiration, aid in the elimination of toxins and improves overall vitality [22].

3.2 Antileishmanial activity: Infections caused by protozoa of the genus *Leishmania* are a major worldwide health problem, with high endemicity in developing countries. The incidence of the disease has increased since the emergence of AIDS. L.G. Rocha *et al* refered in a review on a plant extracts that a chemically defined molecules (coumarin, quercetin) of natural origin showing antileishmanial activity [23,24] .

Quercitrin, a flavonoid is responsible for the antileishmanial activity of *B.Pinnatum.* The quercetin aglycone-type structure, as well as a rhamnosyl unit linked at C-3, seem to be important for antileishmanial activity . Da Silva *et al* investigated the antileishmanial properties of three flavanoids

(quercitrin, quercetin and afzelin) of leaf extract in mice against *L. amazonenis* amastigotes and found oral route was more effective than other (i.v. or tropical) routes. The protective effect of plant in leishmaniasis may not be due to a direct effect on the parasite itself but rather activation of the reactive nitrogen intermediates pathway of macrophages.

3.3 Hepatoprotective and Nephroprotective*:* Juice of the fresh leaves is used very effectively for the treatment of jaundice in Bundelkhand region of India. Yadav *et al* studied that the juice of leaves was found more effective than ethanolic extract as evidenced by invivo and invitro histopathological studies for hepatoprotective activity of plant and justifies the use of juice of plant leaves in folk medicine for jaundice. The protective effect on gentamicin-induced nephrotoxicity in rats which may involve its antioxidant and oxidative radical scavenging activities[25]. It is also used for the treatment of kidney stones in India where is goes by the name of Pather Chat or Paan-futti[26].The Quercetin has neproprotective and antioxidant role [25].

3.4 Neuropharmacological activities: *B.Pinnatum* has been used since 1921 in traditional medicine as an antipsychotic agent. Salahdeen *et al* showed that the aqueous leaf extract possesses depressant action on CNS. The animals treated with 50 -200mg/kg was found to produce quite significant decrease in locomotor's activity in dose dependent manner, with no ptosis at these doses. Similarly in chimney, climbing and inclined screen tests, there was a significant loss of coordination and decrease muscle tone in animals treated intraperitoneally with aqueous extract in a dose dependent fashion. The result indicates significant alterations in general behaviour pattern, reduction in spontaneous mortality , potentiation of pentobarbitoneinduced sleeping time in a dose dependent fashion. Pal *et al* in his study found that the anticonvulsant effect of the aqueous leaf extract observed decrease or no effect compare to methanolic extract. The methanolic fraction possesses a potent CNS depressant action. As alcohol is known to have depressant effect on respiration related hypoglossal nerve output in humans and other mammals. It is possible therefore that the inhibitory effect of methanolic extract on CNS activities may be due to effect of methanol and partly to the constituent of *B.Pinnatum* with its attendant higher dose [27,28,29] .

Radford *et al* investigated that the CNS depressant activity of aqueous leaf extract could be due to the presence of bufadienolide and other water soluble constituents in the extract [30].

Kalanchoe has also shown sedative and central nervous system depressant actions in animal studies. These effects were attributed partially to the leaf extract demonstrating the ability to increase the levels of a neurotransmitter in the brain called GABA (gamma aminobutyric acid)[31].

3.4 Antimutagenic activity: Plant has potent antihistamine and antiallergic activity. The methanol extract of the leaves has also been reported to have histamine receptor (H1) antagonism in the ileum, peripheral vasculature and bronchial muscle and protect against chemically induced anaphylactic reactions and death by selectively blocking histamine receptors in the lungs . Quercetin-3-o-α-L-arabinopyranosyl (1→2)-α-L-rhamnopyrano - side showed anti allergic activity in rats . Obaseiki-Ebor *et al* investigated that organic solvent extracts of leaves had inhibitory activity for His^- to His^+ reverse-mutations induced by ethyl methanesulfonate acting on S. typhimurium TA100 or TA1002 and were also active against reversions induced by 4nitro-o-phenylenediamine and 2-aminofluorene in TA98. The alkaloidal/ water soluble and acid fraction had no appreciable antimutagenic activity [32].

3.5 Anti-ulcer activity: Adesanwo *et al* in his study showed a significant reduction in incidence of ulceration and mean basal and histamine stimulated gastric acid secretion in a dose dependent manner thus justifying its use as an anti-ulcer agent in folklore medicine[33].

3.6 Antibacterial activity: The presence of phenolic compounds indicate that the plant possess anti-microbial activity. Ofokansi *et al*. (2005) reported that 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.* In his study antibacterial activities of the infusion and methanolic extracts against *S. aureusi ATCC 13709, E.coli ATCC 9637, Bacillus, P. aeroginosa, K. pneumonia* and *S. typhi* using the agar diffusion method; also against *S. aureus, E. coli, S.typhi,, Klebsiella spp* and *P.aeruginosa* using a modification of checkerboard method. These 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. Pure isolated alkaloids and their synthetic derivatives are used as basic medicinal agents for their analgesic, antispasmodic and bactericidal effects. Obaseiki-Ebor *et al* investigated the invitro antibacterial activity of leaf juice. The extract at 5% v/v was found to bactericidal to a wide spectrum of gram-positive and gramnegative bacteria such as *B.*

subtilis, S.aureus, S. pyogenes, S.faecalis , E.coli; Proteus spp; Klebsiella spp; Shigella spp; Salmonella spp; S. marcescens; and *P. aeruginosa* including the clinical isolates of these organisms possessing multiple antibiotic resistance . Schmitt *et al* showed the antimicrobial activity of decoct of leaves against gram-positive bacteria by dilution tube method. Akinpelu in a study found that 60% methanolic leaf extract inhibits the growth of five out of eight bacteria used, at a concentration of 25mg/ml. *B. subtilis, E. coli, P. vulgaris, S. dysentriae, S. aureus* were found to inhibited, while *K. pneumoniae, P.aeruginosa* and *C. albicans* were found to resist the action of the extract [34] .

3.7 Antidiabetic Activity: The presence of zinc in the plants could mean that the plants can play valuable roles in the management of diabetes, which result from insulin malfunction. Ojewole evaluated the antinociceptive effect of the herb's aqueous leaf extract by the 'hot-plate' and 'acetic acid' test models of pain in mice. The anti-inflammatory and antidiabetic effects of the plant extract were investigated in rats, using fresh egg albumin-induced pedal oedema, and streptozotocin -induced diabetes mellitus. The aqueous leaf extract produced significant (P<0.05-0.001) antinociceptive effects against thermally and chemicallyinduced nociceptive pain stimuli in mice. The plant extract also significantly (P<0.05-0.001) inhibited fresh egg albumininduced acute inflammation and cause significant hypoglycaemia in rats. The different flavonoids, polyphenols, triterpenoids and phytosterols of the herb are speculated to account for the observed antinociceptive, anti-inflammatory and antidiabetic properties of the plant. It exert antinociceptive and anti-inflammatory effects probably by inhibiting the release, synthesis and /or production of inflammatory cytokines and mediators, including: prostaglandins, histamine, polypeptide kinins and so on [35].

3.8 Immunosuppressive effect: The fattyacids present in *B.Pinnatum may* be responsible atleast inpart, for its immunosuppressive effect invivo. RossiBergmann *et al* showed the aqueous extract of leaves cause significant inhibition of cell-mediated and humoral immune responses in mice. 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. Treatment with extract also impaired the ability of mice to mount a delayedtype hypersensitivity reaction (DTH) to ovalbumin. The invitro and topical routes of administration were the most effective by almost completely abolishing the DTH reaction. The intraperitoneal and oral routes reduced the reaction by 73% and 47% of controls, respectively. The specific antibody responses to ovalbumin were also significantly reduced by treatment. Thus the aqueous extract of leaves possesses immunosuppressive activities. Almeida *et al* in an investigation also found that leaf extracts inhibited invitro lymphocyte proliferation and showed invivo immunosuppressive activity. An attempt to identify the immunosuppressive substances present in *B.Pinnatum* guided by the lymphoproliferative assays. From the ethanolic extract a purified fraction (KP12SA) found twenty-fold more potent to block murine lymphocyte proliferation than the crude extract. Thus provides evidence that saturated fatty acids present in herb plays an important role on lymphocyte proliferation, which explain its immunosuppressive effect in vivo [36] .

3.9 Antihypertensive activity: Herb possesses hypotensive activity and lend credence to the folkloric use of the herb in the management of hypertension. The plant commonly used in the management of all the types and grades of hypertension by some Yorubas of Western Nigeria.*Kalanchoe pinnata* has been recorded in Trinidad and Tobago as being used as a traditional treatment for hypertension [5] .

3.10 Analgesic, Anti-inflammatory and Wound Healing activity: The high saponin content justifies the use of the extracts to stop bleeding and in treating wounds. Saponin has the property of precipitating and coagulating red blood cells. Some of the characteristics of saponins include formation of foams in aqueous solutions, hemolytic activity, cholesterol binding properties and bitterness .These properties bestow high medicinal activities on the extracts from *B.Pinnatum.* Tannins have astringent properties, hasten the healing of wounds and inflamed mucous membranes. These perhaps, explain why traditional medicine healers in Southeastern Nigeria often use herb in treating wounds and burns . Dra Amalia *et al* investigated the anti-inflammatory activity of the fluid extract of the leaves against the edema caused by carrageen in rats. It was confirmed that the fluid extract with 4.5 % of total solids at doses of 100 mg/kg of weight has an anti-inflammatory effect [37] .

Aqueous extract of *B.Pinnatum* can demonstrate strong analgesic potency comparable in a time and dose-dependent manner to a non steroidal anti-inflammatory drug. Igwe *et al* investigated that the aqueous extract was devoid of severe toxic effects, increased the pain threshold in rats using the hot plate or thermal methods, inhibited or reduced phenylbenzoquinone-induced writhing or abdominal

stretches in mice in a dose-dependent manner, and produced a weak or an inferior anti-inflammatory activity than aspirin. The plant leaf contains Hydroxyproline heals the wounds[38].

3.11 Uterine Contractility: B. Gwehenberger *et al* characterise the phytotherapeutic tocolytic effect of *B.Pinnatum* in vitro versus the conventional betamimetic, fenoterol, in human myometrium. Contractility was measured in strips of term myometrium biopsied at caesarean section in 14 women and exposed to increasing concentrations of *B.Pinnatum* versus +/- oxytocin 1 U/l. Result state inhibition of spontaneous contraction was concentration dependent. *B.Pinnatum* increased contraction frequency by 91% at constant amplitude and inhibited oxytocin stimulated contractions by 20% at constant amplitude with slightly decreased frequency. Fenoterol decreased contraction by 50% with a significant decrease in frequency [39] .

3.12 Toxic to cattle: Mckenzie *et al* investigated that cardiac glycoside poisoning was produced in calves given flower heads of the hybrid *Bryophyllum Species* and found that for each plant (except *B. tubiflorum),* 2 calves were each given a single dose of 20 g wet weight per kg bodyweight. The results of the calf toxicity experiment with the amounts of bufadienolide measured in the plants suggests that bryotoxins A, B and C probably account for the observed disease [4,40] .

3.13 Insecticidal, Fungitoxic and Phytotoxic activity: Alabi *et al* studied to evaluate the fungitoxic and phytotoxic effects of extracts on the fungal pathogens inducing wilting on cowpea grown in Ago-Iwoye, South Western Nigeria. The extract reduces the Disease Infection Rate (DIR) in treated plants. *Sclerotium rolfsii sacc* induced wilting of between 4 and 12% on cowpea seedlings treated with plant extract under field conditions while about 39.6% incidence of cowpea seedlings wilting was observed under control experiment on the same experimental plot. The extracts increased significantly the plant height, shelf life, relative water content and chlorophyll contents of the cowpea seedlings during both the wet and dry season. On the other hand, the extracts significantly reduced transpiration rate and stomata aperture of treated plant in both seasons. Furthermore, application of these extracts on the cowpea plants significantly enhanced the Leaf Area Index (LAI), number of branches and pods per plant, total dry matter per plant, weight per pod, 100 grains weight and grain yield in both season. 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[41].

3.14 Anticancer: Bryophyllin compounds have marked anticancer therapeutic value against cancer cells[15]. Bersaldegenin-1, 3, 5-orthoacetate inhibited cancer cell growth on several cancer lines.

3.15 Clinical usage

- The leaves are useful in burns, boils, bites of insects, congestive othalmia dysuria, diarrhoea, dysentery, impetigo, polyuria, plegmon, swellings, tuberculosis, ulcers and wounds
- The leaf juice 3 g, jeera 3 g and ghee 6 g is mixed and given for blood mixed diarrhoea
- The leaf poultice is applied on wounds, sprains, swellings and inflammations
- The leaf juice is useful in cholera
- The leaf juice mixed with Kali Mirch is useful in blood oozing piles and haemorrhoids
- The leaf powder with Kali Mirch is also useful in inflammation, burning in urination and blocked urination and leprosy
- The leaves roasted over fire are applied to places of wounds and surgical sutures in the skin to prevent discoloration of the skin[42].

4. Caution

Contraindicated in cases of impaired digestive function. Topical treatment may produce severe skin blisters.Avoid long-term use because of its immune suppressant effects[26].*Kalanchoe pinnata* has been found to contain bufadienolide cardiac glycosides.These can cause cardiac poisoning, particularly in grazing animals[5].

5. Preparation

Collect all year round. Use fresh and squeeze the juice, or prepare as decoction
Dosage: 30 - 60 gm[3].

Conclusion

It is believed that detailed information as presented in this review on its phytochemical constituents and various biological properties of extracts and the constituents might provide incentive for evaluation of the use of the plant in medicine and in agriculture. Some small companies in India and

Amazon are using *B. Pinnatum* as raw materials for phytochemicals. The pharmacological studies so far have mostly been performed *in vitro* and *in vivo* with animals. In future study, the isolated principles and *B.Pinnatum* needs to be evaluated in scientific manner using specific animal models and clinical studies are urgently needed in order to confirm traditional wisdom in the light of a rational phytotherapy on the toxicity of plant and especially on bufadienolides and its use during pregnancy. The present review shows the pharmacological potentials of *K. pinnata* which is very helpful to researcher to explode more about this valuable plant.

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