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PHYTOCHEMICAL AND PHARMACOLOGICAL PROFILE OF *KALANCHOE PINNATA*: A REVIEW

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ABSTRACT

Kalanchoe pinnata (Family: Crassulaceae) is an important plant which has many traditional medicinal uses.Traditionally, *Kalanchoe* species have been used to treat ailments such as infections, rheumatism, inflammation, hypertension and for treatment of kidney stones.This plant showed various pharmacological activities such as anthelmentic, wound healing, hepatoprotective, anti-allergic, antiinflammatory, nephroprotective, antimicrobial activity, analgesic, antihypertensive, neuro pharmacological and haematological. The wound healing activity is due to the presence of steroid glycosides. Elevation in haematological parameters is likely due to the presence of tannin, ascorbic acid, phenols, flavonoid, zinc, riboflavin and niacin. Anthelmentic activity was found due to the presence of tannins of the extract of *K. pinnata*. Quercitrin, a flavonoid, is a critical component of *K. pinnata* extract against an extreme allergic reaction. It was also found that the different flavonoids, polyphenols, triterpenoids and other chemical constituents of the plant were responsible for the anti-inflammatory activity.

INTRODUCTION

Kalanchoe pinnata **(**Family: Crassulaceae) is a succulent plant native to Madagascar(Nayak *et al*.,2010).It is a perennial herb growing widely and used in folkloric medicine in tropical Africa, tropical America, India, China and Australia.The plant flourishes throughout the Southern part of Nigeria.This is the only *Kalanchoe* species found in South America, however, 200 other species are found in Africa, Madagascar, China and Java (Kamboj and Saluja,2009).It is an erect,succulent, perennial shrub that grows about 1.5 m tall and reproduces through seeds and also vegetatively from leaf bubils.It has a tall hollow stems, freshly dark green leaves that are distinctively scalloped and trimmed in red and dark bell-like pendulous flowers.This plant can easily be propagated through stems or leaf cutting.It is an introduced ornamental plant that is now growing as a weed around plantation crop (Biswas *et al*.,2011).It's common names are "African never die", "Resurrection plant", "Life plant", "Air plant" etc.(Ufelle *et al*.,2011). In traditional medicine, *Kalanchoe* species have been used to treat ailments such as infections, rheumatism, inflammation, hypertension and for treatment of kidney stones (Nayak *et al*.,2010).

PHYTOCHEMICAL CONSTITUENTS

The plant contain alkaloids, flavonoids, phenolic compounds, tannins, macroelements (magnesium, calcium, potassium, phosphorus, sodium), microelements (iron, zinc), vitamins (ascorbic acid,riboflavine, thiamine, niacin),(Okwu and Josiah,2006).

Syringic acid, caffeic acid, 4-hydroxy-3-methoxycinnamic acid, 4-hydroxybenzoic acid, p-hydroxycinnamic acid, p-coumaric acid, ferulic acid, protocatechuic acid and phosphoenolpyruvate isolated from aerial parts of plants.Leaves contain astragalin, 3,8-dimethoxy 4,5,7-trihydroxyflavone, friedelin, epigallocatechin-3-o-syrigate, luteolin, rutin, kaempferol, quercitin, quercitin-3L-rhamonsido-L-arabino furanoside, quercitin-3-O-di arbinoside and kaempferol-3-glucoside (Kamboj and Saluja,2009).

Three unusual flavonoids isolated from plant are Kaempherol 3-O-α-Larabinopyranosyl(1→2) α-L-rhamnopyranoside, Quercetin3-O- α-Larabinopyranosyl(1→2) α-L rhamnopyranoside, 4′,5-dihydroxy-3′,8-dimethoxyflavone 7-O-β-D-glucopyradinoside and quercetin from Kalanchoe pinnata (Michelle *et.al*.,2006).

From fresh leaves of Bryophyllum pinnatum three new constituents, bryophyllol, bryophollone and bryophollenone have been isolated .Three new compounds, bryophynol and

two phenanthrene derivatives have also been identified in the mixture. 18α-Oleanane, ψ-taraxasterol, β-arnyrin acetate and a new sterol, reported earlier as a hydrolysed product, have also been obtained, along with a mixture of α- and β-amyrins and their acetates (Siddiqui *et.al*.,1989).Two insecticidal bufadienolides were isolated from methanolic extract of leaves of kalanchoe pinnata and identified as bryophyllin A and bryophyllin C (Supratman *et.al*.,2000). 1-octane3-O-α-L-arabinopyranosyl-(1→6)-glucopyranoside, a minor constituent isolated from leaves (Almedia *et.al*.,2006). The cardienolide and steroidal contents includes β-sitosterol, bryophyllol, bryophynol, bryotoxin A, bryotoxin B, campesterol, 24-ethyl-25-hydroxycholesterol, isofucosterol, clionasterol, codisterol, peposterol, 22-dihydrobrassicasterol, clerosterol, 24-epiclerosterol, 24-ethyl- desmosterol, stigmasterol are isolated from aerial parts (Kamboj and Saluja,2009).

Leaf contains amino acids i.e. thiamine, pyridoxine, ascorbic acid, glycine, cysteine, casein hydrolylsate, nicotinamide, Food content i.e. carbohydrate, protein, lipids, Minerals; sodium, calcium, potassium, phosphorus, magnesium, ferrous, copper, zinc, and sugars; raffinose, lactose, sucrose, glucose (Alabi *et.al*.,2005). The plant content various enzymes i.e. Phosphoenolpyruate carboxykinase (PCK), Phosphoenolpyruate carboxylase (PEPC), Pyruate orthophosphate dikinase (PPDK), ribulose-1,5- biphosphate carboxylase/oxygenase (Rubisco) etc enzymes presents in leaf of plant Kalanchoe pinnata (Kondo *et.al*.,1998). Phosphoglycerate kinase, Carbonic anhydrase, Fructosebiphosphate aldolase, DNA topoisomerase, protein in which most of having role in metabolism (Abat *et.al*.,2008).

PHARMACOLOGICAL ACTIONS

WOUND HEALING ACTIVITY

The Ethanolic extract of *K.pinnata* leaves was evaluated for it's wound healing activity by using excision wound model in rats.On day 11,animals treated with the ethanolic leaf extract exhibited 86.33 % reduction in the wound area,compared to petroleum jelly treated control (69.36 %) and mupirocin treated standard (85.49 %).There was significant increase in hydroxyproline content in extract treated animals (22mg/g tissue) as compared to control group (19mg/g tissue) and the standard group was having more hydroxyproline content(35mg/g tissue).Histological analysis also showed that *K.pinnata* leaf extract exhibits significant wound healing potential. The wound healing activity exhibited by the extract may be due to the presence of steroid glycosides (Nayak *et al*.,2010).

HAEMATOLOGICAL PARAMETERS

The crude methanolic leaf extract of *B.pinnatum* was evaluated for some haematological parameters in wistar rats.The results showed significantly increased Haemoglobin(Hb),Packed cell volume(PCV),Total white blood cell count(TWBC) in all the treated groups when compared with the control group.The platelet count was decreased in all the treated groups but was significant only in group A when compared with the control group.The blood film examination revealed normocytic and normochromic red blood cells in both the treated and control groups.The result pattern indicates that some of the phytochemical constituents of the crude methanolic leaf extract of *B.pinnatum* may have stimulatory effect on the bone marrow for leucocyte production and haemoglobin synthesis.This observed effect may be as a result of the tannin, ascorbic acid and phenol content.Other phytochemical constituents of *B.pinnatum* which may have likely affected the haematological parameters in this study include flavonoid, zinc, riboflavin and niacin (Ufelle *et al*., 2011).

NEUROPHARMACOLOGICAL ACTIVITY

Effects of aqueous leaf extracts of *K. pinnata* on some neuropharmacological activities were studied in mice.The extract was found to produce a profound decrease in exploratory activity in a dose-dependent manner. It also showed a marked sedative effect as evidenced by a significant reduction in gross behaviour and potentiation of pentobarbitone-induced sleeping time.It delayed onset in strychnine-and picrotoxin-induced convulsion (seizures) respectively with the protective effect being significantly higher in picrotoxin- than strychnine-induced convulsion.It also decreases the rate of picrotoxin induced mortality in mice with LD50 of 641 mg/kg.The totality of these effects showed that the extract possesses depressant action on the central nervous system (Salahdeen and Yemitan, 2006).

Neuropharmacological effects of ethanolic leaf extract of *B.pinnatum* in mice. The ethanolic extract of *B.pinnatum* leaves produced significant reduction in spontaneous locomotor activity, potentiation of pentobarbitone induced sleeping time in dose dependent manner.Results reported that the enhancement of barbital hypnosis is a good index of CNS depressant activity.Ethanolic extract produced significant decrease in exploratory behaviour as evident from the results of head dip, climbing and evasion test.The extract also produced significant decrease in exploratory behavior pattern as evident from the results of head-dip, climbing and evasion tests.Furthermore

the ethanolic extract produced minor anticonvulsant effect by delaying seizure produced by strychnine and picrotoxin.The CNS depressant activity of ethanolic extract may due to the presence of glycosides and flavanoids.One of the major phytoconstituent isolated from the leaves of *B.pinnatum* is bufadienolide, a cardiac glycoside reported to possess significant CNS depressant property (Shetty *et al*., 2009).

ANTI-INFLAMMATORY ACTIVITY

The various extracts/fractions of leaves of *Bryophyllum pinnatum* were investigated in chemically-induced inflammation rodents model.Indomethacin showed more or less uniform inhibition of edema in early intermediate and later phases.Methanolic fraction showed also more or less significant inhibition of formaldehyde induced edema in early phases while significant inhibition at later phases.Out of Pet-ether, Chloroform, Acetone and Methanol fractions from *B.pinnnatum* leaves, Methanol fraction was more significant than the other fractions in percentage inhibition of paw edema (Gupta *et al*., 2010).

CYTOTOXICITY AND ANTIMICROBIAL ACTIVITY

Ethanolic extract of leaves and stem of *K.pinnata* was evaluated for cytotoxicity by using Brine shrimp lethality (BSL) bioassay.The ethanolic extract showed lethality against the brine shrimp nauplii. It showed different mortality rate at different concentrations.

The antibacterial test was performed using the disc diffusion method.The antibacterial activity of the extract was assessed against eight bacterial strains (both gram positive and gram negative) at the dose of 0.5gm/disc and the results were compared with the activity of the standard drug, Amoxycillin (0.1gm/disc). In this experiment, the ethanolic extract of *Kalanchoe pinnata* Linn. showed significant sensitivity to the five of the test organisms both gram positive and gram negative type of bacteria except *B. Megaterium, S. typhi* and *Vibrio cholerae.*The zone of inhibition varies within the range of 6.0±0.35 and 8.2±0.22 mm.The highest zone of inhibition (8.2±0.22 mm) was recorded against *E. coli* (Biswas *et al*., 2011).

ANTIHYPERTENSIVE ACTIVITY

The effects of aqueous leaf extract of *K. pinnata* on the blood pressure of anaesthetized cats as well as on the liver and kidney status of the rabbit were investigated in this study.The results revealed that the extract produced a small fall in the blood pressure of the anaesthetized cat and also reduced the effect of adrenaline-induced elevation of blood pressure.It was concluded that

the pharmacological basis for the use of *K. pinnata* among the Igbos of Nigeria to lower blood pressure was established by this study.However, the facts that the reduction in blood pressure produced is slight and the *K.pinnata* leaf extract is potentially organotoxic which negates its use as a blood pressure lowering agent (Ghasi *et al*., 2011).

HEPATOPROTECTIVE ACTIVITY

Juice of the fresh leaves of *K.pinnata* is used very effectively for the treatment of jaundice in folk medicines of Bundelkhand region of India. The juice of the leaves and the ethanolic extract of the marc left after expressing the juice were studied in rats against CCl4-induced hepatotoxicity.The test material was found effective as hepatoprotective as evidenced by *in vitro*, *in vivo* and histopathological studies.The juice was found to be more effective than ethanolic extract (Yadav and Dixit, 2003).

ANTHELMENTIC ACTIVITY

The roots of *K.pinnata* were extracted successively with petroleum ether, chloroform, methanol and aqueous solvent respectively.The results reveal that chloroform, methanolic and aqueous extract of *K.pinnata* was having significant anthelmentic activity.While petroleum ether extract does not show activity against helminth.Tannins were shown to produce anthelmentic activity (Majaz *et al*., 2011).

ANTI-ALLERGIC ACTIVITY

Aqueous extract of *K.pinnata* was evaluated for it's protective effect in fatal anaphylactic shock, likewise a Th2-driven immunopathology and the identification of its active component. *In vitro*, *K.pinnata* prevented antigen-induced mast cell degranulation and histamine release.Oral treatment with the quercitrin flavonoid isolated from the plant prevented fatal anaphylaxis in 75% of the animals.These findings indicate that oral treatment with *K. pinnata* effectively down-modulates pro-anaphylactic inducing immune responses.Protection achieved with quercitrin, although not maximal, suggests that this flavonoid is a critical component of *K.pinnata* extract against this extreme allergic reaction (Cruz *et al.,* 2008).

ANALGESIC ACTIVITY

The analgesic potency of aqueous extract of *B.pinnatum* was investigated using models. Results showed that the aqueous extract of *B.pinnatum* was devoid of severe toxic effects. It is concluded that the aqueous extract of *B.pinnatum* can demonstrate analgesic potency (Igwe, 2005).

NEPHROPROTECTIVE ACTIVITY

The aqueous extract of *K.pinnata* was evaluated for its protective effects on Gentamycin-induced nephrotoxicity in rats.It was observed that the aqueous extract of *K.pinnata* leaves significantly protects rat kidneys from Gentamycin-induced histopathological changes. Gentamycin-induced glomerular congestion, peritubular and blood vessels congestion, epithelial desquamation, accumulation of inflammatory cells and necrosis of the kidney cells were found to be reduced in the group receiving the leaf extract of *K.pinnata* along with Gentamycin.Urine creatinine, serum creatinine, blood urea, blood urea nitrogen and the weights of the kidneys were found to be significantly increased in rats treated with only Gentamycin; whereas the treatment with the aqueous extract of *K.pinnata* was found to protect the rats from such effects of Gentamycin.The volume of urine was found to be significantly increased in the rats treated with *K.pinnata* leaf extract (Harlalka *et al*., 2007).

ANTINOCICEPTIVE, ANTI – INFLAMMATORY AND ANTIDIABETIC ACTIVITY

In order to scientifically appraise some of the ethnomedical uses of *K. pinnata* leaves, a study was undertaken to investigate the antinociceptive, anti-inflammatory and antidiabetic properties of the plant's leaf aqueous extract in experimental animal models. *K.pinnata* leaf aqueous extract (BPE, 25 to 800 mg/kg i.p.) produced significant ($P < 0.05$ to 0.001) antinociceptive effects against thermally- and chemically-induced nociceptive pain stimuli in mice. The plant extract (BPE, 25 to 800 mg/kg p.o. or i.p.) also significantly ($P < 0.05$ to 0.001) inhibited fresh egg albumin-induced acute inflammation and caused significant ($P < 0.05$ to 0.001) hypoglycaemia in rats. The results of this experimental animal study suggest that *K. pinnata* leaf aqueous extract possesses antinociceptive, anti-inflammatory and hypoglycaemic properties. The different flavonoids, polyphenols, triterpenoids and other chemical constituents of the herb are speculated to account for the observed antinociceptive, anti-inflammatory and antidiabetic properties of the plant (Ojewole, 2005).

ANTI – ULCER ACTIVITY

A methanolic fraction from an extract of *Bryophyllum pinnatum* leaves was found to possess significant anti-ulcer activity in nine different experimental animals models.. Premedication tests in rats revealed that the extract possessed significant protective action against the gastric lesions induced by aspirin, indomethacin, serotonin, reserpine, stress and ethanol. Significant protection

with extract treatment was observed to occur for aspirin-induced ulcer in pylorus-ligated rats and for histamine-induced duodenal lesions in guinea pigs. Significant enhancement of the healing process was also found to occur in acetic acid-induced chronic gastric lesions in rats(Pal and Chaudhary, 1991).

IMMUNOSUPRESSIVE ACTIVITY

The aqueous extract of *K. pinnata* leaves was found to cause significant inhibition of cell-mediated and humoral immune responses in mice. The spleen cells of animals pre-treated with *K. pinnata* showed a decreased ability to proliferate in response to both mitogen and to antigen *in vitro.* Treatment with *K. pinnata* also impaired the ability of mice to mount a delayed-type hypersensitivity reaction (DTH) to ovalbumin. The intravenous 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. Together, these observations indicate that the aqueous extract of *K. pinnata* possesses an immunosuppressive activity (Bergmann *et al*., 2006).

CONCLUSION

The plant *K.pinnata* is a succulent plant which has been introduced to many temperate and tropical regions of the world as an ornamental plant.Kalanchoe is rich in alkaloids, triterpenes, glycosides, flavonoids, steroids and lipids.The leaf contains a group of chemicals called bufadienolides which are very active and similar in structure and activity to cardiac glycosides, digoxin and digitoxin.As we find that clinical trials on the plant is yet not done hence the plant can be explored for the clinical study.

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