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Review

A review of the traditional medicinal uses of *Kalanchoe pinnata* (Crassulaceae)

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***Kalanchoe pinnata* (Family: Crassulaceae) is an important plant which has many traditional medicinal uses. The main objective of this literature review was to give advance information for the drug discovery research for *K. pinnata.* It was found that this plant showed various pharmacological activities such as anthelmentic, immunosuppressive, wound healing, hepatoprotective, antinociceptive, anti-inflammatory and antidiabetic, nephroprotective, antioxidant activity, antimicrobial activity, analgesic, anticonvulsant, neuropharmacological and antipyretic. Anthelmentic activity was found due to the presence of tannins of the extract of *K. pinnata* and steroid glycosides such as bufadienolide showed wound healing activity. It was also found that the different flavonoids, polyphenols, triterpenoids and other chemical constituents of the plant were responsible for the antinociceptive, anti-inflammatory and antidiabetic properties. Quercetin had a marked protective effect on cadmium-induced nephrotoxicity and possessed potent oral efficacy against cutaneous leishmaniasis. The two new novel flavonoids such as 5^{I} Methyl 4^{I}, 5, 7 trihydroxyl flavone and 4^{I}, 3, 5, 7 tetrahydroxy 5-methyl 5^{I}-propenamine anthocyanidines could be responsible for the antimicrobial activity of *K. pinnata.* Five bufadienolides (1-5) isolated from the leaves of *K. pinnata* were potential cancer chemopreventive agents. Quercitrin, a flavonoid, is a critical component of *K. pinnata* extract against an extreme allergic reaction. This literature review gave the evidence-based information regarding the phytoconstituents and pharmacological activity of the medicinal plant, *K. pinnata* which could help researchers for more advanced qualitative research.**

Key words: *Kalanchoe pinnata*, phytochemical, nephroprotective, immunosuppressive, neuropharmacological.

INTRODUCTION

Kalanchoe pinnata (Family: Crassulaceae) 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. *K. pinnata* is used in ethnomedicine for the treatment of earache, burns, abscesses, ulcers, insect bites, whitlow, diarrhoea and cithiasis (Okwu and Nnamdi, 2011). In traditional medicine, *Kalanchoe* species have been used to treat ailments such as infections, rheumatism, and inflammation (Nayak et al., 2010) and have immunosuppressive effect as well (McKenzie and Dunster, 1986).

In South-eastern Nigeria, this herb is used to facilitate the dropping of the placenta of new born baby. The lightly roasted leaves are used externally for skin fungus. The leaf infusions are an internal remedy for fever. *K. pinnata* is also used to expel worms, cure acute and chronic bronchitis, pneumonia and others forms of respiratory tract infections such as asthma. The plant is considered a sedative wound-healer, diuretic and cough suppressant. The plant is also employed for the treatment of kidney stones, gastric ulcer and edema of legs (Okwu and Nnamdi, 2011). The plant, *K. pinnata* is also widely used in ayurvedic system of medicine as astringent, analgesic, carminative and also useful in nausea and vomiting (Majaz et al., 2011). It is employed in the African tradition-

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nal medicine as remedies against otitis, headache, inflammations, convulsions and general debility (Nguelefack et al., 2006). In traditional medicine, the leaves of the plant have been used for antifungal (Misra and Dixit, 1979), potent antihistamine and anti-allergic activity (Pal et al., 1999).

PHARMACOLOGICAL ACTIVITIES

Anthelmentic activity

The roots of *K. pinnata* were subjected to petroleum ether, chloroform, methanol and aqueous solvent respectively for extraction and the *in-vitro* evaluation of anthelmentic activity was done against *Pheretima posthuma* (Annelida) and *Ascardia galli* (nematode). The results reveal that chloroform, methanolic and aqueous extract of *K. pinnata* have significant anthelmentic activity while petroleum ether does not show any activity against helminth. Methanolic extract of root of *K. pinnata* was found to be most effective as an anthelmentic as compared to other. The roots extract of *K. pinnata* not only demonstrated paralysis but also caused deaths of worms especially at higher concentrations of 100 mg/ml, in shorter time as compared to the reference drug, Piperazine citrate. Phytochemical analysis of the crude extracts revealed the presence of tannins which were shown to produce anthelmentic activity (Majaz et al., 2011).

Immunosuppressive effect

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).

Wound healing activity

The extract of *K. pinnata* was evaluated for its wound healing activity by using excision wound model in rats. On the 11th day wounding, there was a significant increase in the wound-healing activity in the animals treated with *K. pinnata* ethanolic extract compared to animals which received the control treatment and standard treatment. Significant progressive reduction in the wound area was observed by day 11 (86.3%) when compared to the control (68.0%) and standard (85.5%). The histological analysis showed that *K. pinnata* leaf extract exhibited significant wound healing potential. The wound healing exhibited by the extract may be attributed to the presence of steroid glycosides. The medicinal plant has been shown to have a significant quantity of bufadienolide, a steroidal aglycone which exists in the plant as steroidal glycoside (Nayak et al., 2010).

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 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 CCl_4-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).

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).

Nephroprotective and antioxidant activity

Harlalka et al. (2007) evaluated the aqueous extract of *K. pinnata* 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.

In case of histopathological examination, control rats showed normal glomerular and tubular histology whereas Gentamycin was found to cause glomerular, peritubular and blood vessel congestion and result in the presence of inflammatory cells in kidney sections from the Gentamycin-treated group. Concurrent treatment with the extract was found to reduce such changes in kidney histology induced by Gentamycin. *In-vitro* studies revealed that the *K. pinnata* leaf extract possesses significant antioxidant as well as oxidative radical scavenging activities. Quercetin and kaemferol have been detected in the leaves of *K. pinnata* (Harlalka et al., 2007). Morales et al. (2006) 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.

Antimicrobial activity

The roots of *K. pinnata* were subjected to petroleum ether, chloroform, methanol and aqueous solvent respectively for extraction and *in vitro* evaluation of antimicrobial activity was done against *Staphylococcus aureus, Escherichia coli, Pseudomonas aeruginosa* and *Candida albicans*. Methanolic extract of roots of *K. pinnata* was found to be most effective as antibacterial as compare to others while none of extract showed the activity against *C. albicans* (Quazi et al., 2011). Akinpelu (2000) in a study found that 60% methanolic leaf extract inhibits the growth of five out of eight bacteria used at a concentration of 25 mg/ml. *Bacillus subtilis, E. coli, Proteus vulgaris, Shigella dysenteriae, S. aureus* were found to be inhibited while *Klebsiella pneumoniae, P. aeruginosa* and C*. albicans* were found to resist the action of the extract. Chemical investigation of the bioactive constituents from the leaf of *K. pinnata* resulted in the isolation of two new novel flavonoids; 5^{I} Methyl 4^{I}, 5, 7 trihydroxyl flavone and 4^{I}, 3, 5, 7 tetrahydroxy 5-methyl 5^{I}-propenamine anthocyanidines. The antimicrobial observation of the aforementioned compounds could be responsible for the activity of *K. pinnata* and its use in herbal medicine in Nigeria (Okwu and Nnamdi, 2011).

Analgesic and anticonvulsant effects

The analgesic effect of methylene chloride/methanol (1:1) (CH_2Cl_2/CH_3OH) extract and its hexane, methylene chloride (CH_2Cl_2), ethyl acetate, *n*- butanol fractions and aqueous residue was evaluated using acetic acid, formalin and pressure test. The anticonvulsant effects of the CH_2Cl_2/CH_3OH extract were also investigated on seizures induced by pentylenetetrazol (PTZ), strychnine sulphate (STN) and thiosemicarbazide (TSC). CH_2Cl_2/CH_3OH extract and its fractions administered orally exhibited protective effect of at least 30% on the pain induced by acetic acid. The CH_2Cl_2 fraction at 300 mg/kg showed a maximal effect of 78.49%. The CH_2Cl_2/CH_3OH extract and its CH_2Cl_2 fraction at the doses of 150 and 300 mg/kg significantly reduced the first phase of pain induced by formalin while the second phase was completely inhibited. The CH_2Cl_2 fraction produced more than 45% reduction in the sensitivity to pain induced by pressure. The CH_2Cl_2/CH_3OH extract of *K. pinnata* significantly increased the latency period in seizures induced by PTZ and significantly reduced the duration of seizures induced by the three convulsant agents. The extract protected 20% of animals against death in seizures induced by TSC and STN. These results suggest a peripheral and central analgesic activities as well as an anticonvulsant effect of the leaves of *K. pinnata* (Nguelefack et al., 2006).

Leishmaniasis activity

Muzitano et al. (2009) carried out an investigation to study the effect of *K. pinnata* on cutaneous leishmaniasis.

In order to demonstrate the safety and oral activity of *K. pinnata,* different flavonoids were extracted from the plants and were evaluated *in vivo* in murine model of cutaneous leishmaniasis. Daily oral doses of quercetin 3-O- -L-arabinopyranosyl, -L-rhamnopyranoside, quercetin 3-O- -L- rhamnopyranoside and free quercetin (16 mg/kg body weight) were administered. It was observed that they were able to control the lesion growth caused by *Leishmania amazonensis* and significantly reduce the parasite load. These flavonoids were as effective as the crude *K. pinnata* aqueous extract given at 320 mg/kg body weight. HPLC-DAD-MS analysis of the plasma of extract-treated mice suggested that quercetin and quercetin glucuronides are the main metabolites of *K. pinnata* quercetin glycosides. These results indicate that quercetin glycosides are important active components of the aqueous extract and that they possess potent oral efficacy against cutaneous leishmaniasis.

Diuretic and anti-urolithiatic activity

Patil et al. (2009) studied the diuretic and anti-urolithiatic activity of *K. pinnata*. Hydroalcoholic extract of leaves of *K. pinnata* was administered to male Wistar rats orally and intraperitonially. The effect of the extract on urine output was determined by comparing the urine volume collected by keeping the individual animals in metabolic cages. Calcium oxalate urolithiasis was induced in rats by giving ethylene glycol orally for 7 days and the effect of the extract was observed by its concurrent administration. The extract was found to have significant diuretic and anti-urolithiatic activity and the intraperitonial administration of the extract gave more potent diuretic effect.

Anti-tumor activity

Five bufadienolides (1-5) isolated from the leaves of *K. 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-O-tetradecanoylphorbol-13-acetate. All bufadienolides showed inhibitory activity, and bryophyllin A (1) exhibited the most marked inhibition (IC50 = 0.4 microM) among the tested compounds. Bryophyllin C (2), a reduction analogue of 1, and bersaldegenin-3-acetate (3) lacking the orthoacetate moiety were less active. These results strongly suggest that bufadienolides are potential cancer chemopreventive agents (Supratman et al., 2001).

Anti-allergic activity

Cruz et al. (2008) reported on the protective effect of *K pinnata* 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.

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).

CONCLUSION

The plants are well known and have possible source of curing ailments from time immemorial. In recent year, ethnobotanical and traditional uses of natural compounds especially of plant origin received much more attention as they are well tested for their efficacy and generally believed to be safe for human use. 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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