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Phyto-Chemical and Therapeutic Briefing of Kigelia africana (Lam.) Benth

Asheesh Kumar Gupta*, Anurekha Jain

Department of Pharmacy, Jyoti Vidyapeeth Woman's University Mahela, Jaipur, Rajasthan, India

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ABSTRACT

The present study reveals the medicinal uses, chemical composition and examines recent investigations on the therapeutic activity of extracts and chemicals identified from *Kigelia africana*. The article also presents some of the functions of the chemicals present and attempt to emphasize and create an awareness of the great potential of *K. Africana*. The present review highlights the plant profile, traditional uses as anticancer, antiulcer, anti-aging, antioxidant, and antimalarial and also as genital infections, gynaecological disorders, renal ailments, fainting, epilepsy, sickle-cell anaemia, psoriasis, eczema, central nervous system depression, respiratory ailment, leprosy, worm infestation, athlete's foot, and various cosmetic preparations, etc., the chemical constituents such as iridoids, naphthaquinones, fatty acids, norviburtinal, sterols, lignans, terpenoid, and flavonoids, etc., and various pharmacological activities of *K. Africana* (Lam.) Benth. Examined by various modern scientific researches and from the results of some potent phytoconstituents, this plant has great potential to be developed as drug by pharmaceutical industries for medicinal uses after clinical trials are to be made.

INTRODUCTION

Kigelia africana (Lam.) Benth. Synonym K. pinnata (Jacq.) DC, is a tropical African plant widely grown and distributed in South, Central and West Africa. It belongs to the family of Bignoniaceae and commonly called the sausage tree because of its huge fruits. The tree is evergreen where rainfall occurs throughout the year, but deciduous where there is a long dry season. It is a tree growing up to 20 meters tall or more. The bark is grey and smooth, peeling on older trees thickness 6 mm on a 15 cm branch. The wood is pale brown or yellowish. [1] The leaves are 30-50 cm long, pinnate, with six to ten oval leaflets up to 20 cm long and 6 cm broad; the terminal leaflet can be either present or absent. The flowers (and later the fruit) hang down from branches on long flexible stems (2–6 meters long). Flowers are produced in panicles; they are bell shaped orange to reddish or purplish green and about 10 cm wide. Flowers are bisexual, very large up curved at tip The fruit is a woody berry from 30-100 cm long and up to 18 cm broad; weighs between 5-10 kg hangs down on a long rope-like peduncles.[2] The fruit is indehiscent, with woody wall and heavily marked with lenticels at the surface.

It is grey-brown and many seeded when matured. Seeds are obovoid, 10 mm x 7 mm with leathery testa, embedded in a fibrous pulp.[3]

OCCURRENCE AND DISTRIBUTION

The tree is found on riverbanks, along streams and on floodplains, also in open woodland, from Kwazulu-Natal to Tanzania. The plant is widely distributed in the South, Central, and West Africa.[4] Also found in south Asia (India, Pakistan, Bangladesh, Sri Lanka, etc.

ECOLOGY

K. africana grows along watercourses, in riverine fringes, alluvial and open woodland, high rainfall savanna, shrub land and in rain forest. It occurs on loamy red clay soils, sometimes rocky, damp or peaty, from sea level up to zoom altitude.[5]

TRADITIONAL USES OF KIGELIA AFRICANA

Medicinal Uses

It has a long history of use by rural and African countries particularly for medicinal properties. Several parts of the

*Corresponding Author: Asheesh Kumar Gupta, Department of Pharmacy, Jyoti Vidyapeeth Woman's University Mahela, Jaipur, Rajasthan, India. E-Mail: guptaasheesh01@gmail.com 14



Stem bark

Flower Figure 1: Different parts of the plant *K. africana*

Fruits and Leaves

plant are employed for a variety of purposes, particularly in local medicine, and more recently in commercial applications to treat various skin complaints (Figure 1).[4] Commercially manufactured products are used for symptomatic relief or cure of skin conditions. In the African folk medicine *K. africana* is used against dysentery, venereal diseases and as a topical application on wounds and abscesses. In the area around Nsukka, Nigeria the preferred use of the bark is the treatment of venereal diseases. The stem bark is ground in a mortar and macerated with palm wine (ca 20% alcohol) for two or three days. The macerate is then diluted to 3 L palm wine. 100 mL of the resulting liquid is drunk daily, for 8 days successively.[6]

In addition *K. africana* has a reputation for the treatment of dysentery, and in contradiction to it as a purgative. For these reasons it is sold in markets. In Togo, the stem bark is the component of a prescription against cancer: 100 grams stem bark of *Kigelia africana* and 25 grams fruits of *Xylopia aethiopica* are cooked in one liter of water. Then three tablespoons of this mixture are drunk three times daily during two months. The fruit pulp also has internal applications in treatment of dysentery, ringworm, tape-worm, post-partum hemorrhage, malaria, diabetes, pneumonia, and toothache.[7] Most commonly traditional healers used it to treat a wide range of skin ailments like fungal infestations such as ringworm, mycosis, boils, psoriasis, and eczema. among others sunburn, chafing, psoriasis, itchy scalp, and nappy rash.[7]

A broad-spectrum antimicrobial cream, reputedly effective against a number of common microbial infections,

is produced from the stem bark. Fungal infestations such as ringworm, mycosis, and athlete's foot are washed with the water in which bark has been macerated, and preparations containing the leaves and fruits applied locally. *K. africana* is used in both traditional and orthodox medicines to treat malignant neoplasm such as skin melanoma, tumors and breast cancer.[7]

MISCELLANEOUS USES

Leaves and ground wood soaked with water and pressed through a sieve were mixed with Strophanthus gratus seeds. The concentrated syrup is then used as a hunting poison by the Gbaya in the Southwest of the Central African Republic. In order to enlarge the penis young males enrub the sap of the fruit into cuts of the penis skin. Young females do the same with the flesh of ripe fruits for enlarging their bosom. The African tonga woman regularly apply cosmetic preparation of Kigelia fruits to their faces to ensure a blemish free complexion.[8] Great Kigelia fruits are used as a fetish against whirling winds by hanging one of it in the houses. In Malawi, during famine the seeds are roasted to eat, baked fruits are used to ferment beer and boiled ones yield a red dye. Traditional preparations include extracts, poultices and powders of the bark or fruits; topical creams containing extracts of the fruits are produced commercially.

PROPERTIES

The use of *K. africana* in traditional African medicines is in some cases verified by corresponding pharmacological properties of the photochemicals elucidated in extracts of *K. africana*, the compound groups to which activity is

most frequently attributed are naphthoquinones, flavonoids, and iridoids. Extracts of the bark, wood, roots and fruits possess antibacterial and antifungal properties. These extracts exhibit significant inhibitory effects in vitro against common gram-negative and gram-positive bacteria, and the yeast Candida albicans. Of the naphthoquinones isolated in fruit and root extracts, kigelinone has shown notable antimicrobial activity. Iridoids and dihydroisocoumarins in extracts of the bark, fruits, and roots may enhanc the antimicrobial activity of naphthoquinones. Other active antimicrobial compounds present in the bark and are the phenylpropanoids caffeic acid, p-coumaric acid and ferulic acid. The naphthoquinones are responsible for the antiprotozoal activity. K. africana is renowned for anticancer properties, and laboratory screening has confirmed in vitro anti-cancer activity. Fruit extracts exhibited significant effects against induced tumours in mice. Fruit and bark extracts have shown moderate efficacy against melanotic cell lines. Of dried fruit elicited lower cytotoxic responses than those of fresh fruit, indicating that the active principles may be thermolabile. The naphthoquinones lapachol and isopinnatal, in some extracts of bark, wood, fruits and roots, exhibit antineoplastic activity against melanoma cell lines. Sterols and iridoids are ubiquitous in the plant and may be a factor in the activity against melanoma. Naphthoquinones and sterols isolated in root extracts suggest anti-cancer potential, although in vitro activity is not confirmed. The reported cytotoxicity of the root in the brine shrimp assay was attributed to the presence of beta-sitosterol. Cinnamic acid derivatives are thought to be responsible for anticonvulsant properties for which K. africana is used to prevent epileptic fits. The leaves and fruits contain flavonoids. A high concentration of flavonoids may be responsible for antidiarrhoeal properties, increased by antimicrobial constituents. The bark and leaves are bitter tasting, and the bark is reported to contain a bitter principle. Acute toxicity tests of the fruits indicate they are non-toxic.[4,9]

CHEMICAL CONSTITUENTS AND PHYTOCHEMISTRY

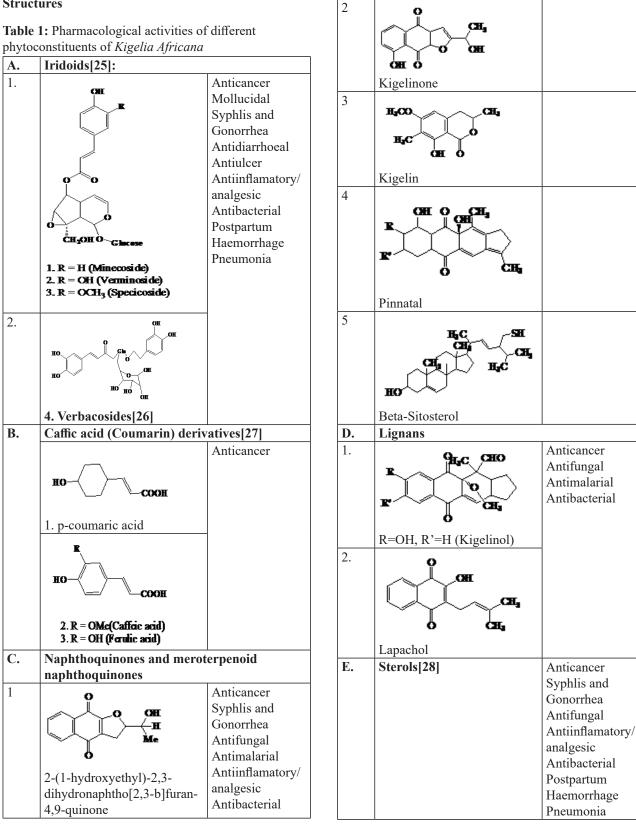
Various chemical investigations have been carried out on *K. africana* and many chemical compounds mainly iridoids, naphthaquinones, monoterpenoidnapht-haquinones, isocoumarins, lignans sterols, and flavonoids have been identified. An initial laboratory studies indicated the presence of two major naphthaquinones (kigelinone and isopinnatal) in the aqueous extract of the stem bark. These

show activities against *B. subtilis, E. coli, P. aeruginosa, S. aureus,* and yeast *C.albicans.*[10,11] Qualitative tests for the presence of plant secondary metabolites such as carbohydrates, alkaloids, tannins, flavonoids, saponins, and glycosides were carried out on the bark powdered.[12]

Chemical analysis of the polar extract of fruit indicated the presence of vermonosides.[13] Further investigation of the fruits yielded a new phenylpropanoid derivative identified as 6-p-coumaroyl-sucrose together with other known phenylpropanoid derivatives and flavonoid glycoside.[14] Four naphthaquinoids from K. pinnata rootbark were identified and assessed in vitro against chloroquine-sensitive (T9-96) and resistant (K1) plasmodium falciparium strains for cytotoxicity using KB cells. 2-(-hydroxyethyl)naphtho[2,3-b]furan-4,9dione posed good activity against two strains. Isopinnatal, kigelinol, and isokigelinol exhibited lower activity against the strains.[15] Naphthaquinones; 2-(1-hydroxyethyl)naphtho[2,3-b]furan-4,9-quinone, isopinnatal, kigelinol, and isokigelinol were isolated from the dichloromethane extracts of the root bark and stem bark. It shows antitrypanosomal activity.[16] 3b,19a -dihydroxyurs-12-ene-28oic acid, caffeic acid and chlorgenic were isolated from the fruits and 3b, 19a-dihydroxyurs-12ene-28-oic acid, ferulic acid and p-coumaric acid have been isolated from the root of K. pinnata. Three known iridoids: specioside, verminoside, and minecoside were isolated, characterized and identified using UV, IR, and H-NMR spectroscopic data. The verminoside was found to be more active than the standard drug, while specioside shows activities comparable to metronidazole.[18] Steriod, iridiods, and coumarins have been isolated from the root bark [10] and flavonoids and iridiods from the fruit and leaves.[14]

Dichloromethane extracts from the root and stembark of *K. pinnata* contains naphthaquinones,[19] which showed anti-trypanosomal.[16] Kiglin and 6-methoxymellein together with two known compounds, stigmasterol, and lapachol have been isolated from the root,[20] kigelin, β -sitosterol, 1,3-dimethylkigelin, and ferulic acid were isolated from the bark,[21] two non-quinonoid aldehydes, norviburtinal and pinnatal were obtained from the root bark.[22] 7-O-glucoside were isolated from the leaves and fruits, three isocoumarins 6-methoxymellein, kigelin, 6-demethylkigelin from the roots, lignan kigeliol from wood and neoligan balanophonin was isolated from the stem bark.[23] Sitosterol is isolated from *K. pinnata* fruit.[24]

Structures



Review Article

F.	Flavonoids[29]	Anticancer
		Mollucidal
		Syphlis and
		Gonorrhea
		Antidiarrhoeal
		Antiulcer
		Antifungal
		Antiinflamatory/
		analgesic
		Pneumonia

PHARMACOLOGICAL STUDIES

Various pharmacological examinations such as antibacterial, antiviral and antioxidant activities have been carried out. The success story of chemotherapy lies in the continuous search for new drugs to counter the challenges posed by resistant strains of microorganism.[30] There are increasing interest in plants as a source of agent to fight microbial diseases and treatment of several infections (Table 1).[31,32]

Antidiarrhoeal Activity

The aqueous leaves extract of *K. africana* has been confirmed to possess antidiarrhoeal activity. In experimental animal models the extract shows reduced fecal output and protection against castor oil induced diarrhea. The extract remarkably decreased the propulsive movement of the gastrointestinal contents. On the isolated guinea pig ileum tissue preparation, the extract did not considerably affect acetylcholine and histamine induced contractions, but significantly reduced the nicotine evoked contractions.[33,60]

Antiprotozoal Activity

The chemical constituents from root and stem bark have shown significant anti-protozoal activity, the serial dilutions of butanol extract of stem bark were tested for their growth inhibitory effects against *Entamoeba histolytica* and exhibited antiamoebic activity. The three isolated iridoids specioside, verminoside and minacoside were purified and identified by testing against HK-9 strain of *Entamoeba histolytica* for their *in vitro* antiamoebic evalution by using metronidazole as reference drug in all experiments and it was found that verminoside has twice antiamoebic activity as compared to the reference drug and specicoside should comparable activity with reference drug.[34]

The isolated compounds, one furanonaphthoquinone; 2-(1-hydroxyethyl)-naphtho-[2,3-b] furan-4,9-quinone and three naphthoquinoids; isopinnatal, kigelinol and isokigelinol from stem bark extracts were comparatively evaluated, the compounds 2-(1-hydroxyethyl)-naphtho-[2,3-b] furan-4,9-quinone and isopinnatal possessed a good activity against both *Trypanosoma brucei brucei* and *T.B. rhodesiense* (IC₅₀; 0.12 and 0.045 μ M, respectively, for naphthoquinones and isopinnatal IC₅₀ 0.37 and 0.73 μ M) with a certain selectivity compared to KB cells (IC₅₀ 3.9 and 14.8 μ M for naphthoquinone and isopinnatal respectively). The kigelinol and isokigelinol shows less activity.[35,36]

Antimalarial Activity

The plant has been reported for its antimalaria activities[37]. Wood extract contains compound quinone possesses antimalarial activity against drug resistant strains of *Plasmodium falciparum* superior to chloroquine and quinine. Four naphthoquinoids isolated from root bark of the plant were assessed *in vitro* against chloroquine sensitive (T9-96) and chloroquine-resistant (K1) *P. falciparum* strains and for cytotoxicity using KB cells. The most active antiplasmodial agent against both strains was 2-(hydroxyethyl) naphtha [2,3-b] furan-4, 9-dione, its IC50 values were 718 nm for T9-96 and 627 nm for K1 strains.[38]

Molluscicidal Activity

The crude extract, the evaporated water extract and the methanolic extract of *K. africana* were screened for mollusicidal activity in the laboratory reared *Lymnaea natalensis* (adult snails). All three were containing lapachol and 2-hydroxy,3-alkyl naphthaquinones.[39,40] The lapachol and isolapachol showed strong molusicidal activity and LC 50 values were determined.[41]

Anti-Oxidant Activity

The ABTS assay-The plant shows the potent antioxidant effects due to caffeic acid derivatives and compounds unique to *Kigelia*. FRAPP assay-An ethanolic extract of *Kigelia* has been shown comparable activity to grape juice.[42] The antioxidant effect of *K. africana* fruit extract (KAFE) on normal rats. KAFE showed a non-dose dependent elevation in testicular catalase (p < 0.05), significant decline in malondialdehyde (p < 0.001) and an up-regulation of glutathone (p < 0.001) levels. Seminal parameters were also enhanced by KAFE with the lower dose producing better effects. Male infertility is frequently accompanied by increased testicular or seminal fluid oxidative stress. This result provides further scientific basis for the use of KAFE in the treatment of male infertility.[42]

Anti-Inflammatory Activities

The ethanolic extract of the stem bark was examined to show strong analgesic and anti-inflammatory activities. The extract components inhibited the synthesis of

prostaglandins and other inflammatory mediators which probably accounted for the analgesic and anti-inflammatory properties.[12] The dried fruit and bark extract is established to be a strong painreliever when administered on painful joints, back and rheumatism.[43] The pharmacological basis for the use of K. pinnata ethanolic fruit extract in medicine for the treatment of pain and inflammations was further investigated and evaluated on formaldehyde induced paw edema, acetic acid-induced vascular peritonitis models. The result obtained is well comparable to the respective standard drugs, the K. pinnata fruit extracts and indomethacin exhibits COX-2 inhibition activity and their respective IC₅₀.[44] The anti-inflammatory activity of verminoside, from K. africana was also carried out. It shows significant anti-inflammatory effects inhibiting both iNOS expression and NO release in the LPS-induced J774.A1 macrophage cell line [13].

Anticancer Activities

The root bark is recommended for the treatment of cancer of the uterus.[45] The extract has been tested against melanoma cells (a tumour of pigmented skin cells, which can develop into malignant melanoma-the potentially fatal form of skin cancer). The extract inhibited the growth of cultured melanoma cells to a significant degree.[46] The extract of stem bark and fruit are reported for their cytotoxic activities and showed promising results in treating melanoma and renal carcinoma.[46] The extracts of the plant have been shown to possess various potential anticancer agents.[12, 30,44,45,47] A significant antileukaemic activity however appears to be highest in stem bark, and least in the leaf. A study revealed the potential of ethanollic extracts of K. africana stem bark, fruit and leaf to reverse leukaemic effects in benzene-induced leukaemia bearing wistar rats and this suggest that the extracts might be promising natural, non-toxic and anticancer agents[48].

Treatment of Gynecological Disorders and Anti-Implantation Activities

K. africana is widely used to treat gynecological disorders. Study on the antioxidant effect of KA fruit extract on normal rats showed a non-dose dependent elevation in testicular catalase, a significant decline in malondialdehyde and an up-regulation of glutathione. Results offer scientific basis for the use of *K. africana* fruit extract in the treat of male infertility.[49] Aqueous preparation of the roots, fruits and flowers are administered orally or as a virginal pessary while the fruits and bark are used to promote breast development in young women or in contrast to reduce swelling and mastitis of the breasts.[5] The plant

has also been reported for its anti-implantation activities as well.[50]

Central Nervous System (CNS) Stimulant

The ethanolic stem bark extract was studied in mice using barbiturate induced sleeping time and Rota rod bar to check the extract effect on muscle coordination. The result indicates that the extract has stimulant effect on the CNS.[51]

Anti-Microbial and Antifungal Activities

The plant has also been screened to show anti-molluscidal activity.[41] In a research, the dried and powdered plant material was extracted successively with water, methanol and chloroform using the soxhlet extractor for 48 hours at a temperature not exceeding the boiling point of the solvents. The extract was tested against E.coli, Enterobacter aerogens, Klebsiella (gram negative), Staphylococcus aureus, and Bacillus Cereus (gram positive) by disc diffusion method. The methanol extract presented a higher activity than the aqueous extracts and chloroform extracts against all except E. aerogens, Klebsiella Pneumoniae and Psedomonas aeruginosa which presented less activity.[52] The dichlomethane extracts of the root bark and stem bark exhibited antitrypanosomal activity against Trypanosoma brucei in vitro.[16] The extract of the tree stem bark was also established to inhibit a number of harmful microorganisms which include E. coli (responsible for abscesses), P. aeruginosa (which causes skin sepsis and infections), S. aureus (which causes impetigo and skin abscesses), and albican (a fungal organism that causes thrust) in another experiment.[11] The antibacterial and antifungal test carried out on the crude ethanolic stem bark extract revealed exhibited antibacterial and antifungal activities against S. aureus and C. albicans. The aqueous extract exhibited no antibacterial and antifungal.

Activity whereas the activity of crude ethanolic extracts (20 mg/mL) is comparable to amoxicillin drug.[12] Butanol extract of the stem bark exhibited *in-vitro* antiamoebic activity when tested against HK-9 strain of *Entamoeba histolytica* (micro dilution method) using metronidazole as reference drug. It was found that verminoside (in the extract) has two fold antiamoebic activity as compare to the standard drug while specioside showed comparable activity with metronidazo.[18] The ethanolic bark extract of the plant have been shown to possess antimycobacterial against the growth of *M. aurum* A+ with mic values ranging between 0.19 and 1.5 mg/mL.[38] Other antibacterial activity of the fruit has been reported as well.[52]

Management of Polycystic Ovary Syndrome (PCOS)

The effect of twice daily ingestion (a table spoonful) of dried *K. africana* fruit powder in the management of polycystic ovary syndrome (PCOS) in two patients of 25 and 22 years. Both patients had the classical triad of amenorrhoea, acne, and hirsutism. The use of herbal preparation restored the menstrual flow in both of them as well as leading to significant reduction in the acne but there was no noticeable effect on the hirsutism. There was no observable side effect associated with the use of the powder. These preliminary data thus suggest that *K. africana* fruit powder may be beneficial for cases of PCOS especially in the developing countries where the new generation oral contraceptives, presently being used for the condition, may not be readily available.[53]

Antiurolithiatic Activity

Its fruit extracts can be sed in the treatment of kidney stone problems. KAFE inhibited CaO_x nucleation, aggregation and crystal formation in the synthetic urine *in vitro*. The lithogenic treatment caused polyurea, weight loss, hyperoxaluria and impairment of renal function which was prevented by KAFE. Hyperoxaluria and CaO_x crystal deposition in the renal tubules caused by EG intake was prevented by KAFE treatment. This study indicates that the antiurolithiatic activity of *K. africana* fruit extracts (KAFE) possibly mediated through inhibition of CaO_x crystallization, hypo-oxaluria and improvement of kidney function as well as the cytoprotective effect may justify its curative and prophylactic use in urolithiasis.[54]

Anti-Hyperlipidemic Activity

The aqueous and alcoholic extracts of the fruit tested for anti-hyperlipidemic potential, exhibited activity in albino rats when compared to standard drugs. The activity was assessed by studying the lipid profiles of serum and liver of the control and standard/extract treated animals. The aqueous and alcoholic extract significantly increased (p < 0.0001) plasma HDL and decreased plasma total cholesterol LDL and triglyceride (TG) levels as compared to hyperlipidemic control animals.[55]

Reproductive System Performance Improvement Activity

Poor libido, infertility, sexual asthenia, and impotence are treated with herbal prescriptions of the fruit, roots or leaves. A small amount of unripe fruit is chewed or an aqueous preparation of the fruit is taken orally as a sexual stimulant, and the intoxicating traditional beer to which they are added is drunk as an aphrodisiac. The fruits are also applied on the breast to improve flow of milk in lactating women. Fruit aqueous extract has been successfully used as fertility enhancing agent in rats.[56] The steroidal components are thought to enhance reproductive ability since steroids as androgen and estrogen have shown to contain fertility properties necessary for the improvement and production of reproductive organs. A study to investigate the effects of varying dietary supplementation of it on the sperm quality and fertility in African catfish, *Clarias gariepinus* showed that dietary inclusion of the plant positively affected some parameters of sperm quality in the fish, with increases in sperm counts, percentage motility, milt volume and motility duration.[57]

Antitrypanosomiasis and its Antileishmanial Effect

Isolated 9 different phytoconstituents form this plant from different geographical regions. The most striking bioactivity of *K. africana* was its anti-trypanosomiasis and anti-leishmanial effect against *L. donovani*.[58-62]

CONCLUSION

K. africana (Lam) Benth, a native of Africa is well known traditionally for varieties of medicinal purposes where it grows. This review confirms the therapeutic values of K. africana. It is well reported for the presence of naphthoquinones, fatty acids, courmarins, iridoids, caffeic acid, norviburtinal, sterols and flavonoids. The plants is used traditionally for treating cancer of the breast, uterus and skin, digestive disorder, genitor-urinary tract, veneral diseases, gynaecological disorder, bladder ailments, sicklecell anaemia, epilepsy, nutritional illness, leg oedemas, internal parasitic infestations (especially tapeworm), leprosy, rheumatism, boil, acne, cysts, whitlows, psoriasis, etc. There are inadequate reports on the phytochemical studies, phytoanalytical studies and pharmacological screening of the plant. Furthermore, explicit isolation of each chemical constituent using various methods including thin layer chromatography, column chromatography should be carried out. There is enormous scope for the future research of K. africana considering the many medicinal purposes it serves. It has a high potential for development into viable drugs as more facts emanates from its uses, especially as a strong anti-cancer agent. It is therefore recommended that more research work should focus on the anti-cancer properties. Studies should also be focused on its sustainability and its use as effective erosion control and riverbank stabilization in order to prevent its extinction. It has been reported that the plant extract is not toxic even at high concentration, but more work needed to be reported on its toxicity. Reports on the in vivo work done are scanty and require urgent attention. It is hoped that this report

will serve as a basis of information for future project to be embark on in order to evaluate the potentials of *K. pinnata* (Lam) Benth as a strong medicinal plant in improving human health status.

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