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Review Paper

Kigelia africana (Lam.) Benth. — An overview

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Abstract

Our world harbours a rich source of medicinal plants which are used in treatment of wide range of diseases. The present review highlights the traditional uses, chemical constituents and pharmacological properties of ***Kigelia africana* (Lam.) Benth.** syn. *K. pinnata* (Jacq.) DC. This plant has great potential to be developed as drug by pharmaceutical industries but before recommending its use in modern system of medicine, clinical trials are to be done.

Keywords: Kigelia, *Kigelia africana*, *Kigelia pinnata*, Cucumber tree, Sausage tree, *Balmkheera*, Isopinnatal, Kigelin, Chemical constituents, Medicinal properties.

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Introduction

Nature has been a source of medicinal agents for thousands of years and an impressive number of modern drugs have been isolated from natural sources, many of these isolations were based on the uses of the agents in traditional medicines[1]. This plant-based traditional medicine system continues to play an essential role in health care with about 80% of the world's inhabitants relying mainly on traditional medicines for their primary health care[2]. ***Kigelia africana* (Lam.) Benth.** syn. *K. pinnata* (Jacq.) DC. of Bignoniaceae family is widely distributed in the South, Central and West Africa. It is known as the cucumber or sausage tree because of the huge fruits (average 0.6 m in length and 4 kg in weight), which hangs from long fibrous stalks. It is also known as *Balmkheera* in Hindi and distributed all over India but found abundantly in West Bengal. It is found mostly in wetter areas and spread abundantly across wet Savannah and riverine area[3-6]. The plant grows approximately 10 m high with odd pinnately, composite opposite leaves, leaflets are ovate to oblong in shape and 4-18 cm long. The flowers are found in spring or summer season, hanging ancillary panicles up to 2 m long, corolla of fused petals, irregularly bell shaped, 9-13 cm long two lipped, yellowish on outside and purple on inside. Fruits are oblong, hard 30-50 cm long, hanging on stalk for several month but not split easily[7, 8]. The present review highlights the contribution of ***K. africana*** in modern system of herbal medicine for new drug development. There is correlation established between the active constituents and their uses in different fields. Some cosmetics preparations available in market are also mentioned.

Traditional Uses

The kigelia plant have medicinal properties not only because of its perceived characteristics such as bitterness, astringent taste or smell but also because of forces that it seems to emit in connection with its location, orientation and association with other plants. It has a long history of use by rural and African countries particularly for medicinal properties. Several parts of the plant are employed for medicinal purposes by certain aboriginal people[9]. In Malwi during famine the seeds are roasted to eat. Baked fruits are used to ferment beer and boiled ones yield a red dye. Most commonly traditional healers used it to treat a wide range of skin ailments like, fungal infections, boils, psorasis and eczema. It also has internal application including the treatment in dysentery, ringworm, tape-worm, post-partum haemorrhage, malaria, diabetes, pneumonia and toothache[10]. The tonga women of Zambezi valley regularly apply cosmetic preparation of Kigelia fruits to their faces to ensure a blemish free complexion[11]. In the folk medicine, the fruits of the plant are used as dressing for ulcers, purgative and to increase the flow of milk in lactating women[12]. Roots are said to yield a bright yellow dye. The Shona people tend to use the bark or root as powder or infusion for application to ulcers, drunk or applied in the treatment of pneumonia, as a gargle for toothache, and the leaves in a compound applied for backache[13]. In West Africa, the root and


Tree


Leaves


Flower


Fruits

Kigelia africana

unripe fruit is used as a vermifuge and as a treatment for haemorrhoids and rheumatism[14].

The bark is traditionally used as a remedy for syphilis and gonorrhea. The fruits and bark ground and boiled in water are also taken orally or used as an enema in treating children's stomach ailments–usually worms. Unripe fruit is used in Central Africa as a dressing for wounds, haemorrhoids and rheumatism. Venereal diseases are commonly treated with the tree extracts usually in palm wine as oral medication[15].

Chemical Constituents

The ***K. africana*** plant has many medicinal properties due to the presence of numerous secondary metabolites. These compounds include irridoids, flavonoids, and naphthoquinones and volatile constituent, etc[16-18]. Pinnatal and isopinnatal were isolated from tropical trees that belongs to the plant family of Bignoniaceae. Pinnatal was found in a root bark extract of the plant. Thin layer chromatography (TLC) examination of the most active fractions of both stem bark and fruits showed the presence of the same major components which were found to be norviburtinal and β-sitosterol. Gouda *et al* isolated a furanone derivative, 3-(2'-hydroxyethyl)-5-(2″-hydroxypropyl)-dihydrofuran-2(3H)-one and four iridoids, 7-hydroxy viteoid II, 7-hydroxy eucommic acid, 7-hydroxy-10-deoxyeucommiol and 10-deoxyeucommiol together with seven known iridoids, jiofuran, jioglutolide, 1-dehydroxy-3,4-dihydroaucubigenin, des-*p*-hydroxybenzoyl kisasagenol B, ajugol, verminoside and 6-transcaffeoyl ajugol from the fruits[19]. They also isolated a phenylpropanoid derivative identified as 6-*p*-coumaroyl-sucrose together with ten known phenylpropanoid and phenylethanoid derivatives and a flavonoid glycoside from the fruits[20]. The structures of the isolated compounds were characterized by different spectroscopic methods. Govindchari *et al* isolated kigelin as the major constituent of the plant from the root heartwood[21]. The structure of kigelin was established by chemical methods and spectroscopic techniques as 8-hydroxy-6, 7-dimethoxy-3-methyl-3, 4-dihydroisocoumarin and it was concluded that the absolute configuration at C-3 was R on the basis of spectral analysis. They also isolated 6-methoxymellein together with two known compounds, stigmasterol and lapachol from the roots of this plant. Kigelin, β-sitosterol, 3-dimethyl kigelin and ferulic acid has also been isolated from its bark[22]. Five minor constituents isolated from root bark consisted of two known naphthaquinones and three new aromatic monoterpenes[23, 24]. Two non-quinonoid aldehydes, norviburtinal and pinnatal were obtained from the root bark by Joshi *et al*[25]. Biologically monitored fractionation of the butanol extract from stem bark led to the isolation of three known iridoids: specioside, verminoside and minecoside. All these irridoids were isolated earlier from root bark[26, 27] and further characterized. All the compounds were identified by comparing their UV, IR and NMR data with the literature values[28, 29]. Table 1 summarizes some of the pharmacological activities of different phytoconstituents of ***K. africana***.

Pharmacological Activities

Antibacterial and Antifungal

A biologically monitored fractionation of the methanolic extracts of the root and fruits led to the isolation of the naphthoquinones, kigelinone, iso-pinnatal, dehydro-α-lapachone, and

lapachol and the phenylpropanoids, *p*-coumaric acid and ferulic acid as the compounds responsible for the observed antibacterial and antifungal activity[30]. The compounds isolated were tested for their activity against *Staphylococcus aureus, Bacillus subtilis, Corynebacterium diphtheriae, Aspergillus niger, A. flavus, Candida albicans* and *Pullularia pullularis* (*Aureobasidium* sp.). The steroids and flavonoids are hygroscopic and have fungicidal properties.

Chemical investigation showed that the aqueous extracts of the stem bark of the plant contain iridoids as major components. In the light of the traditional uses of this plant, antimicrobial activities of the aqueous extracts and two major iridoids were tested against *Bacillus subtilis, Escherichia coli, Pseudomonas aeruginosa, Staphylococcus aureus* and *Candida albicans*. The crude aqueous extracts showed significant antimicrobial activity, which could be partially explained by the activity of the iridoids present[31]. The fruits are a popular source of traditional medicine throughout Africa. But the stem bark has been widely analysed for pharmacological activity, yet knowledge of the fruits is limited, despite more extensive use in traditional remedies. Crude extracts of stem bark and fruits were prepared with distilled water, ethanol or ethyl acetate. In the microtitre plate bioassay, stem bark and fruit extracts showed similar antibacterial activity against Gram negative and Gram positive bacteria. A mixture of three fatty acids exhibiting antibacterial effects was isolated from the ethyl acetate extract of the fruits using bioassay-guided fractionation. Palmitic acid, already known to possess antibacterial activity, was the major compound in this mixture. These results confirm antibacterial activity of ***K. africana*** fruits and stem bark, and support the traditional use of the plant in therapy of bacterial infections[32]. A disc diffusion susceptibility test was used to screen concentrated extracts from the bark of 3 medicinal plants (***Alstonia boonei* de Wild.**, ***Morinda lucida* Benth.** and ***K. africana***) for antimicrobial activity. Solvents with different polarity were used for the extraction (methylene chloride, ethyl acetate, 95% ethanol and acetonitrile), and the extracts were tested against *Candida albicans, Staphylococcus aureus, Enterococcus faecalis, Streptococcus faecalis, Escherichia coli* and *Pseudomonas aeruginosa*. The patterns of inhibition varied with the plant extract, the solvent used for extraction and the organism tested. The largest zones of inhibition were observed for ethanol extracts of ***K. africana*** against *S. aureus* and *P. aeruginosa*. *S. aureus* was the most inhibited microorganism. No inhibitory effects were observed against

Table 1: Pharmacological activities of different phytoconstituents of *Kigelia africana*

Activity	Irridoids	Naphthoquinone	Meroterpenoid naphthoquinones	Coumarin derivatives	Lignans	Sterols	Flavonoids
Anticancer	+	+	+	+	+	+	+
Mollusicidal	+	-	-	-	-	-	+
Syphilis and Gonorrhea	+	+	-	-	-	+	+
Antidiarrhoeal	+	-	-	-	-	-	+
Antiulcer	+	-	-	-	-	-	+
Antifungal	-	-	+	-	+	+	+
Antimalarial	-	-	+	-	+	-	-
Antiinflammatory/analgesic	+	+	+	-	-	+	+
Antibacterial	+	+	+	-	+	+	-
Postpartum Haemorrhage	+	-	-	+	-	+	-
Pneumonia	+	-	-	-	-	+	+

C. albicans. The extent of the inhibition of the bacteria was related to the concentration of the plant extract[33].

Antineoplastic

The crude dichloromethane extracts of stem bark and fruit showed cytotoxic activity *in vitro* against cultured melanoma and other cancer cell lines using the Sulphorhodamine B assay, which was used for bioassay-guided fractionation. TLC examination of the most active fractions of both stem bark and fruits showed the presence of the some major components which were found to be norviburtinal and β-sitosterol. Norviburtinal was found to be the most active compound but had little selectivity for melanoma cell lines while isopinnatal also showed some cytotoxic activity. β-Sitosterol was found to be comparatively inactive. HPLC analysis of the crude extract showed that the amount of norviburtinal present in the plant material did not account for all of the activity of the total extracts[34]. Investigation into the biological activity of ***K. africana*** has focussed on its antibacterial activity and its cytotoxic effects against cancer cell lines. These are related to the traditional uses of bark and fruit extracts for treating diseases caused by microorganisms and as a remedy for skin cancer. Considerable *in vitro* cytotoxicity has been demonstrated by extracts of the fruits and barks and the iridoid-related compound norviburtinal and the naphthoquinone isopinnatal have been shown to be two of the compounds responsible. The compounds also show cytotoxicity against mammalian cell lines. Kigelinone,5-or 8-hydroxy-2-(1-hydroxyethyl) naphtha [2, 3-*b*] furan-4, 9 dione, a phytochemical analog of naphtha [2, 3-*b*] furan-4,9 dione (furanonaphthoquinone [FNQ]) compounds, was isolated from the inner bark of the South American trumpet tree, ***Tecoma ipe*** **Mart** [syn. *T. avellanedae* Speg., *Tabebuia impetiginosa* (Mart. ex DC.) Standl., *T. cassinoides* (Lam.) DC.], or ***K. africana***, which is known to have antitumour activity[35]. Kigelia contains the constituent lapachol that is effective in the treatment of solar keratosis, skin cancer and kaposi sarcoma (an HIV-related skin ailment)[36]. Serial dilutions of standardised water, ethanol, and dichloromethane extracts of the stem bark and fruits of ***K. africana*** were tested for their growth inhibitory effects against four melanoma cell lines and a renal cell carcinoma line (Caki-2) using two different (MTT and SRB) assays. Lapachol, a possible constituent of these extracts, together with known therapeutic antineoplastic agents, was also tested in the same way. The IC_{50} of each extract was measured after extracts were diluted to 100 µg/ml in 1% ethanol or water. Significant inhibitory activity was shown by the dichloromethane extract of the stem bark and lapachol (continuous exposure). Moreover, activity was dose-dependent, the extract being less active after one hour exposure. Chemosensitivity of the melanoma cell lines to the stem bark was greater than that seen for the renal adenocarcinoma line. In marked contrast, sensitivity to lapachol was similar amongst the five cell lines[37]. The antitumour activity of Bignoniaceae is probably due mainly to its naphthaquinoids which among them, for example lapachol, have been considered as candidates for clinical use[38]. *In vitro* cytotoxic activity found in root bark extract of ***K. africana*** is attributed to γ-sitosterol which is comparable to standard, lapachol[39].

Analgesic and Anti-inflammatory

The analgesic effect of the stem bark of ***K. africana*** has not been previously reported and the mechanism by which it occurs is mostly likely via the inhibition of prostaglandin synthesis as indicated by its inhibition of acetic acid-induced mouse writhing. Also, it is known that centrally acting analgesic drugs elevate the pain threshold of mice towards heat and pressure[40, 41]. The ethanolic extract was evaluated for analgesic property using acetic acid induced mouse writhing and hot plate reaction time and anti-inflammatory property using the carrageenan induced paw edema and its probable mechanism evaluated in mice and guinea pigs. The extract showed a dose dependent significant reduction of the number of writhes ($P<0.001$) with 500 mg/kg body weight dose giving the highest reduction. The extract showed an insignificant elongation of the hot plate reaction time ($P>0.05$). In the carrageenan induced paw edema, a dose dependent significant inhibition was observed ($P<0.001$) between the second and fifth hour. It is clear that the ethanolic stem bark extract has significant analgesic and anti-inflammatory activity. Inhibition of the synthesis of prostaglandins and other inflammatory mediators probably accounts for the analgesic and anti-inflammatory properties[42]. Chemical analysis of a polar extract of ***K. africana*** fruit indicated the presence of verminoside, an iridoid, as a major constituent, and of a series of polyphenols such as verbascoside. *In vitro* assays showed that it had significant

anti-inflammatory effects. Cytotoxicity and cutaneous irritation of the extract and of compounds verminoside and verbacoside were investigated. The crude extract did not affect cell viability *in vitro* either in cells grown in monolayers (ML) or in the reconstituted human epidermis (RHE, 3D) model; neither caused release of pro-inflammatory mediators or histomorphological modification of RHE[43, 44].

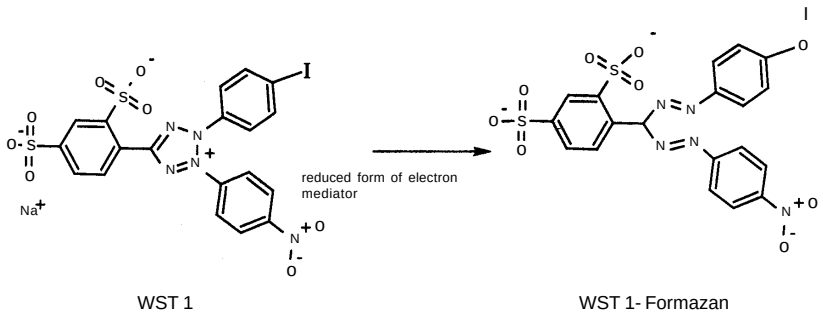
Supercritical CO_2 extracts of Kigelia have been shown to be more effective than Indomethacin a potent synthetic anti-inflammatory (Table 2). Two different anti-inflammatory assays: inhibition of "oxidative burst" on human neutrophils and inhibition of cyclooxygenase (COX-2) were done. ***K. africana*** extracts were tested against a control (buffer, neutrophils and WST-1) and against indomethacin[45]. Absorbance is measured at 450nm.

Anti-malarial

Four naphthoquinoids isolated from root bark of the plant were assessed *in vitro* against chloroquine-sensitive (T9-96) and chloroquine-resistant (K1) *Plasmodium falciparum* strains and for cytotoxicity using KB cells. The most active 2-(1-hydroxyethyl) naphtha [2, 3-*b*] furan-4, 9-dione showed good antiplasmodial activity against both strains; IC_{50} values were 627 nM for the K1 and 718 nM for the T9-96 strains. The IC_{50} values were comparable to those of related naphthoquinones isolated from ***K. africana*** and these compounds also exhibited marked toxicity against endothelial ECV-304 cells due to their antiplasmodial effect. An antimalarial compound known as lapachol has been extracted from the root. Another compound (quinone) obtained from the wood shows anti-malarial activity against drug resistant strains of *P. falciparum* and is superior to chloroquine and quinine[30, 46-49].

CNS stimulant

The ethanolic stem bark extract of ***K. africana*** has a potential central nervous system (CNS) stimulant effect that can be explored for therapeutic advantage as an alternative treatment in medical conditions associated with dizziness, drowsiness and sedation. CNS stimulant effect of the ethanolic stem bark extract was studied in mice using the barbiturate induced sleeping time and the Rota rod bar to check the extract's effect on muscle coordination. The results showed that the extract at all doses tested reduced the duration of sleeping time when compared to the control group that received distilled water. This difference in sleeping time was significant ($P<0.0001$ at all doses tested) and this was also found to be dose dependent. Its effect was also compared with caffeine (a known stimulant) and the extract gave a shorter duration of sleeping time compared to caffeine, ($P<0.05$ at 400 mg/kg dose) indicating better stimulant properties. In comparison with diazepam the extract at all doses tested, also gave a shorter duration of sleep ($P<0.0001$). On the Rota rod, the extract had no sedative effect as the animals maintained their balance on the rod through the entire period of the experiment[50].



WST 1 WST 1- Formazan

Table 2 : COX-2 activity of mixtures containing *Kigelia africana*

Plant parts used	Extract	Cox-2 activity(µg/ml)(IC50)
Fruit	Chloroform/ethanol/water	0.8
Fruit	Chloroform/methanol	0.8
Indomethacin	-	32

Antiprotozoal

A fractionation of stem bark and root bark extracts of the plant allowed the isolation of one furanonaphthoquinone, 2-(1-hydroxyethyl)-naphtho-[2, 3-*b*] furan-4, 9-quinone and three naphthoquinoids: isopinnatal, kigelinol,

and isokigelinol. Compounds 2-(1-hydroxyethyl)-naphtho-[2, 3-*b*] furan-4, 9-quinone and isopinnatal possessed a pronounced activity against both *Trypanosoma brucei brucei* and *T. b. rhodesiense* bloodstream forms (IC_{50}: 0.12 µM and 0.045 µM, respectively for naphthoquinones and isopinnatal 0.37 µM and 0.73 µM) with a certain selectivity compared to KB cells (IC_{50}:3.9 µM and 14.8 µM for naphthoquinones and isopinnatal, respectively)[51-53]. Compounds kigelinol and isokigelinol had a less potent antitrypanosomal activity with IC_{50} values. Although little ethnopharmacological evidence exists, the naphthoquinones are active against several protozoal species associated with disease. Serial dilutions of extracts from the stem bark were tested for their growth inhibitory effects against *Entamoeba histolytica*. Butanol extract of stem bark exhibited *in vitro* antiamoebic activity. Three known iridoids specioside, verminoside and minecoside were isolated, purified and identified by comparing their spectral data with the literature values. These compounds were tested against HK-9 strain of *E. histolytica* for their *in vitro* antiamoebic evaluation and Metronidazole was used as reference drug in all the biological experiments. It is found that verminoside has two fold antiamoebic activities as compared to the standard drug while specioside showed comparable activity with metronidazole[54].

Antidiarrhoeal

Aqueous leaf extract of ***K. africana*** was screened for antidiarrhoeal activity using experimental animal models. Evidence for antidiarrhoeal activity was provided by the reduced fecal output and protection from castor oil-induced diarrhoea in the extract-treated animals. The extract remarkably decreased the propulsive movement of the gastrointestinal contents. On the isolated guinea pig ileum, the extract did not appreciably affect acetylcholine and histamine induced contractions, but significantly reduced nicotine evoked contractions. The i.p. (intra peritoneal) LD_{50} of the extract in mice was estimated to be 785.65 ± 24 mg/kg[55].

Other activities

De Santos *et al*[56] and Sant'ana *et al*[57] tested the activity of lapachol and 2-hydroxy 3-alkyl naphthoquinones possessing nitrogenated alkyl chains against the snail *Biomphalaria glabrata* lapachol and isolapachol showed strong mollusicidal activity against adult snail[58, 59]. The plant shows the potent antioxidant effects due to caffeic acid derivatives and compounds unique to *Kigelia*. An ethanol extract of kigelia has been shown to possess some antioxidant activity[60, 61]. The plant shows antidiabetic activity also[62].

Cosmeceutical Preparations

The kigelia plant contains steroidal saponins and two flavonoids (luteolin and quercitin). Its fruit extract is useful to develop the bust and reinforce the strength and stability of Breast collagen fibers. A cream made from fruit extract is used to remove sunspots known as 'Solar Keratosis' particularly on the face and hands. A number of skin creams, scalp application and shampoos are derived from the fruit. Some common cosmetics made from kigelia as one of the active ingredients reduces wrinkle depth and fine lines leaves skin smooth, promotes tone elastic naturally lightens pigmentation, reduces skin blemishes, deep cleanses and eliminates impurities. Tightens the delicate skin around the eyes. Refines the skin and stimulates circulation. Its fruit pulp and extracts can be exploited in the nutraceutical, dietary/ herbal supplement, pharmaceutical, cosmeceutical and other products[63-65]. Specific products could include: (i) anti-melanoma and after-sun applications, anti-inflammatory agent, antioxidant agent and Cosmetic skin tightening active ingredient.

Conclusion

K. africana is an interesting example of a plant, used in traditional medicine for many years, but which is now attracting interest and use far beyond its original geographical range. Experiments into the effect of Kigelia extracts and some of the pure compounds contained therein, on microorganisms and cancer cells have shown that the traditional use of this plant is given considerable justification. The chemical constituents of the plant provide molecules, which could be of immense medicinal applications. Considering the many medicinal purposes for which it is used, there is enormous scope for future research on ***K. africana***, and further pharmacological investigation is warranted.

References

1. Cordell GA, Biodiversity and drug discovery: a symbiotic relationship, *Phytochemistry*, 2000, **56**, 463-480.

2. Farnsworth NR, Akerele O and Bingel AS, Medicinal plants in therapy, *Bull WHO*, 1985, **63**, 965-981.

3. Cragg GM and Newman DJ, Medicinals for the millennia, *Ann NY Acad Sci*, 2001, **953**, 3-25.

4. Heine H, *In:* Flora of Tropical West Africa, by J Hutchinson and JM Dalziel (Eds), 2nd Edn, revised by FN Hepper, 1963, Vol. **2**, p. 385.

5. Sofowara A, The present status of knowledge of the plants used in traditional medicine in Western Africa: a medical approach and chemical evaluation, *J Ethnopharmacol*, 1980, **2**, 109-118.

6. Sofowora A, Medicinal Plants and Traditional medicine in Africa, Published by John Wiley and Sons Ltd, Ist Edn, 1982, **131**, 168 -171.

7. Roodt Veronica, *Kigelia africana* in the Shell Field Guide to the Common Trees of the Okavango Delta and Moremi Game Reserve. Gaborone, Botswana: Shell Oil Botswana, 1992, pp. 176-180.

8. Handbook of the Birds of the World, by J Hoyo, A Elliott and J Sargatal (Eds), Lynx Edicions, 1997, **4**, 415-420.

9. Burkill HM, The useful plants of Tropical West Africa, Royal Botanical Garden, 1985, Vol **2**, Families A-D, pp. 254-257.

10. Gill LS, Ethnomedical uses of plants in Nigeria, Uniben Press, Benin City, 1992, p. 143

11. Pooley E, The complete guide to trees of Natal, Zululand and Transkei, Natal Flora Publications Trust, 1993, pp. 22-24.

12. Oliver-Bever B, Medicinal Plants in Tropical West Africa, Cambridge University Press: Cambridge, London, New York, New Rochelle, Melbourne, Sydney, 1986, pp. 240-245.

13. Maisiri M and Gundidza M, The effects of crude extracts of *Kigelia africana* and *Aloe excelsa* on deep wound healing, University of Zimbabwe, Harare, Department of Pharmacy, 1999, pp. 91-94.

14. Irvine FR, Woody plants of Ghana, with special reference to their uses, Oxford University Press, London, United Kingdom, 1961, pp. 736-740.

15. Walt JM and Breyer-Bradwijk MG, The medicinal and poisonous plants of Southern and Eastern Africa, Livingstone, London, 1962, p. 52.

16. Houghton PJ, The sausage tree (*Kigelia pinnata*): ethnobotany and recent scientific work, *South Afr J Bot*, 2002, **68** (1), 14-20.

17. Asekun OT , Olusegun E and Adebola O, The volatile constituents of the leaves and flowers of *Kigelia africana* Benth, *Flav Fragr J*, 2006, **22**(1), 21-23.

18. Gormann R, Schreiber L and Kolodziej H, Cuticular wax profiles of leaves of some traditionally used African Bignoniaceae, *Z Naturforsch,* 2004, **59** (9-10), 631-635.

19. Gouda YG, Abdel-baky AM, Darwish FM, Mohamed KM, Kasai R and Yamasaki K, Iridoids from *Kigelia pinnata* DC. Fruits, *Phytochemistry,* 2003, **63** (8), 887-892.

20. Gouda YG, Abdel-Baky AM, Mohamed KM, Darwish FM, Kasai R and Yamasaki K, Phenylpropanoid and phenylethanoid derivatives from *Kigelia pinnata* DC. fruits, *Nat Prod Res*, 2006, **20** (10), 935-939.

21. Govondachari TR, Patankar SJ and Visananthan N, Isolation and structure of two new Dihydroisocoumarins from *Kigelia pinnata*, *Phytochemistry*, 1971, **10**, 1603-1606.

22. Desai HK, Gawad DH, Govindachari TR, Joshi BS, Kamat VN and Modi JD, Chemical investigation of some Indian plants, *Indian J Chem*, 1971, **9**, 611-613.

23. Akunyili DN and Houghton PJ, Meroterpinoids and naphthaquinones from *Kigelia pinnata* bark, *Phytochemistry*, 1993, **32**, 1015-1018.

24. Inove K, Inove H and Cheng C Cheng, A naphthoquinone and a lignan from the wood of *Kigelia pinnata*, *Phytochemistry*, 1982, **20**(9), 2271-2276.

25. Joshi KC, Singh P, Taneja S and Cox PJ, New terpenoid aldehydes from *Kigelia pinnata*: Crystal structure of Pinnatal, *Tetrahedron*, 1982, **38**, 2703-2708.

26. El-Sayyad SM, Flavonoids of the leaves and fruits of *Kigelia pinnata*, *Fitoterapia*, 1981, **4**, 189-91.

27. Houghton PJ and Akuniyli DN, Irridoids from *Kigelia Pinnata* bark, *Fitoterapia*, 1993, **64**, 183-186.

28. El- Naggar SF and Doskotch RW, Specioside: A New Iridoid Glycoside from Catalpa speciosa, *J Nat Prod*, 1980, **43**, 524-526.

29. El-Naggar LJ and Beal JL, Iridoids: A Review, *J Nat Prod*, 1980, **43**, 649-707.

30. Binutu OA, Adesogan KE and Okogun JI, Antibacterial and antifungal compounds from *Kigelia pinnata*, *Planta Med*, 1996, **62** (4), 352-353.

31. Akunyili DN, Houghton PJ and Raman A, Antimicrobial activities of the stem bark of *Kigelia pinnata*, *J Ethnopharmacol*, 1991, **35** (2), 173-177.

32. Grace OM, Light ME, Lindsey Kl, Mulholland DA, Van Staden J and Jäger AK, Antibacterial activity and isolation of active compounds from fruit of the traditional African medicinal tree *Kigelia africana, South Afr J Bot*, 2002, **68** (1), 220-222.

33. Kwo VT and Craker LE, Screening Cameroon medicinal plant extracts for antimicrobial activity, *Acta Hortic*, 1996, **426**, 147-155.

34. Jackson SJ, Houghton PJ, Retsas S and Photiou A, *In Vitro* Cytotoxicity of Norviburtinal and Isopinnatal from *Kigelia pinnata* Against Cancer Cell Lines, *Planta Med*, 2000, **66**, 758-761.

35. Inoue K, Inoue H and Chen C, Quinones and related compounds in higher plants, A naphthoquinone and a lignan from the wood of *Kigelia pinnata*, *Phytochemistry*, 1981, **20**, 2271-2276.

36. Hussain H, Krohn K, Ahmad UV, Miana GA and Green IR, Lapachol: an overview, *ARKIVOC*, 2007, **2**, 145-171.

37. Houghton PJ, Photiou A, Sala Uddin, Shah P, Browning M, Jackson SJ and Retsas S, Activity of Extracts of *Kigelia pinnata* against

Melanoma and Renal Carcinoma Cell Lines, *Planta Med*, 1994, **60**, 430-433

38. Rao MM and Kingston DGI, Plant anticancer agents: isolation and structure elucidation of new cytotoxic quinones from *Tabebuia cassinoides, J Nat Prod*, 1982, **45**, 600-604.

39. Khan MR and Mlungwana SM, γ-Sitosterol, a cytotoxic sterol from *Markhamia zanzibarica* and *Kigelia africana, Fitoterapia*, 1999, **70** (1), 96-97.

40. Adeyemi OO, Okpo SO and Ogunti OO, Analgesic and anti-inflammatory effect of the aqueous extract of leaves of *Persea americana* Mill (Lauraceae), *Fitoterapia*, 2002, **73**, 375-380.

41. Akah PA and Nwambie AI, Evaluation of Nigerian traditional medicines: plants used for rheumatic (inflammatory) disorders, *J Ethnopharmacol*, 1994, **42,** 179-182.

42. Owolabi OJ and Omogbai EKI, Analgesic and anti- inflammatory activities of the ethanolic stem bark extract of *Kigelia africana* (Bignoniaceae), *Afr J Biotechnol,* 2007, **6** (5), 582-585.

43. Picerno P, Autore G, Marzocco S, Meloni M, Sanogo R and Aquino RP, Anti-inflammatory activity of verminoside from *Kigelia africana* and evaluation of cutaneous irritation in cell cultures and reconstituted human epidermis, *J Nat Prod*, 2005, **68**, 1610-1616.

44. Kolodziej H, Protective role of *Kigelia africana* fruits against benzo(a)pyrene-induced fore-stomach tumourigenesis in mice and against albumen-induced inflammation in rats, *Pharm Pharmacol Lett*, 1997, **2**, 67-70.

45. Use of mixtures, which contain parts of the plant *Kigelia africana. Hans Knoll Institut f?r Naturstoff Forschung Patent number* DE10200490 (2003).

46. Weiss CR, Moideen SVK, Croft SL and Houghton PJ, Activity of extracts and isolated naphthoquinones from *Kigelia pinnata* against *Plasmodium falciparum, J Nat Prod*, 2000, **63**, 1306-1309.

47. Carvalho LH, Rocha EMM, Raslan DS, Oliveira AB and Krettli AU, *In vitro* activity of natural and synthetic naphthoquinones against erythrocytic stages of *Plasmodium falciparum, Braz J Med Biol Res*, 1988, **21**, 485-487.

48. Joshi KC and Singh LB, Quinonoid and other constituents from the heartwood of *Tecomella undulata, Phytochemistry*, 1974, **13**, 663-664.

49. Weenen H, Anti-malarial activity of Tanzanian medicinal plants, *Planta Med*, 1990, **56**, 368-370.

50. Owolabi OJ, Amaechina FC and Eledan AB, Central nervous system stimulant effect of the ethanolic extract of *Kigelia africana, J Med Plants Res,* 2008, **2**(2), 020-023.

51. Hoet S, Opperdoes F, Brun R and Quetin-Leclercq J, Natural products active against African trypanosomes: a step towards new drugs, *Nat Prod Rep*, 2004, **21**, 353-364.

52. Moideen SVK, Houghton PJ, Croft SL and Rock P, Activity of *Kigelia pinnata* root bark against *Trypanosoma brucei brucei* trypomastigotes, *J Pharm Pharmacol*, 1998, **50**, 224-228.

53. Moideen SVK, Houghton PJ, Rock P, Croft SL and Aboagye-Nyame F, Activity of extracts and naphthoquinones from *Kigelia pinnata* against *Trypanosoma brucei brucei* and *Trypanosoma brucei rhodiesiense, Planta Med*, 1999, **65**, 493-588.

54. Bharti N, Singh S, Fehmida N and Amir A, Isolation and *in vitro* antiamoebic activity of iridoids isolated from *Kigelia pinnata, ARKIVOC*, 2006, 69-76.

55. Akah PA, Antidiarrheal Activity of *Kigelia africana* in experimental animals, *J Herbs Spices Med Plants*, 1998, 31-38.

56. Santos AF, Ferraz PAL,Pinto AV, De abreu FC, Chiori EAV, Pinto MCFR, Goulart MOF and Sant'Ana AEG, Molluscicidal and Trypanocidal Activities of Lapachol Derivatives, *Planta Med*, 2001, **67**, 92-93.

57. Sant'Ana AEG, Santos AF, Ferraz PAL, Pinto AV, Pinto MCFR and Goulart MOF, Molluscidal activity of 2-hydroxy-3-alkyl-1,4-naphthoquinones and derivatives, *Int J Parasitol*, 2000, **30**, 1199-1202.

58. Kela SL, Ogunsusi RA, Ogbogu VC and Nwude N, Screening of some Nigerian plants for molluscicidal activity, *Rev Elev Med Vet Pays Trop*, 1989, **42**(2), 195-202.

59. Kela SL, Ogunsusi RA, Ogbogu VC and Nwude N, Susceptibility of two-week old *Lymnaea natalensis* to some plant extracts, *Rev Elev Med Vet Pays Trop*, 1989, **42** (2), 189-192.

60. Olaleye MT and Rocha BT, Acetaminophen-induced liver damage in mice: Effects of some medicinal plants on the oxidative defense system, *Exp Toxicol Pathol*, 2008, 17, **59** (5), 319-327.

61. Olalye MT and Rocha JB, Commonly used tropical medicinal plants exhibit distinct *in vitro* antioxidant activities against hepatotoxins in rat liver, *Exp Toxicol Pathol,* 2007, **58** (6), 433-438.

62. Nyarko AK, Okine LKN, Wedzi RK, Addo PA and Ofosuhene M, Subchronic toxicity studies of the antidiabetic herbal preparation ADD-199 in the rat: absence of organ toxicity and modulation of cytochrome P450, *J Ethnopharmacol*, 2005, **97** (2), 319-325.

63. Dampeirou C, Cosmetic compositions with high viscosity for female breast care containing *Kigelia* extract, 2002, US 2002/ 0176874

64. Cosmetic or dermo-pharmaceutical composition for firming the breast, reducing hair loss, and reducing the growth of bristles, contains an extract of *Kigelia africana,* 1997, FR 2 759 910.

65. Makado Isamu, Skin care preparation, 2003, Patent number: JP2003137763.