

2 **Pharmacological and Therapeutic Activities of**
3 ***Kigelia africana* (Lam.) Benth**

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ABSTRACT

Occurring widely in Africa and beyond is *Kigelia africana* (Lam.) Benth, a medicinal plant with several attributes and considerable potentials. Various parts of the plant are used locally to treat cancer, ulcer, gynecological disorders, genital infections, skin diseases, diabetes, epilepsy, bacterial and fungal infections as well as being used as cosmetics. The antioxidant and anti-inflammatory properties of some parts of the plant have been explored for therapeutic purposes. Phytochemical analyses revealed the presence of a wide range of secondary metabolites. Toxicological evaluation of different extracts of the fruit, stem bark and leaf have also been reported. In this review up-to-date listing of established pharmacological and toxicological properties of *Kigelia africana* as well as its phytochemicals that are responsible for listed activities have been discussed.

Keywords: *Kigelia africana*; sausage tree; Bioactive compounds; Biological activity; Toxicological effects

1. INTRODUCTION

Kigelia africana (syn. *Kigelia pinnata*, *Kigelia aethiopica*) is commonly referred to as sausage or cucumber tree because of its huge sausage or cucumber-like fruit. It belongs to the Bignoniaceae family. Due to its wide occurrence, it has vernacular names in many African languages: Rawuya (Hausa, Nigeria); Uturubein (Igbo, Nigeria); Pandoro, Iyan (Yoruba, Nigeria); Bechi (Nupe, Nigeria); Mwegea (Swahili, Kenya, Tanzania); Umfongothi (Zulu, South Africa) [1, 2] and Ebie in Igala, Nigeria. In Hindi (India) it is known as Balmkheera [3].

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Kigelia africana occurs throughout tropical Africa. It grows particularly well in wetter areas, spreading across the wet savannah and riverine areas [3].

The tree can grow up to 20 m tall. It is evergreen where rainfall occurs throughout the year, but deciduous where there is a long dry season. The flowers (and later the fruit) hang down from branches on long flexible stems. Flowers are produced in panicles; they are bell-shaped, orange to reddish or purplish green and about 10 cm wide. Their scent is most notable at night indicating their reliance on pollination by bats, which visit them for pollen and nectar [4]. *Kigelia africana* is characterized by its huge fruits which can weigh between 5 to 10 kg [5]. The fruit is indehiscent, with woody wall and heavily marked with lenticels at the surface. It is grey-brown and many seeded when matured. The fruit is eaten by several species of wild animals that also disperse the seeds in their dung [4]. Parts of the plant are used for treating a wide range of ailments traditionally based mainly on cultural practices. The fruit is used to treat skin ailments like fungal infections, boils, psoriasis and eczema. Dysentery, ringworm, tapeworm, post-partum haemorrhage, malaria, diabetes and pneumonia are also treated with the fruit [3]. The fruit is also applied for the treatment of solar keratosis and malignant melanoma [6]. The bark is used to treat venereal diseases while the root is applied to treat ulcer [3].

This review on *Kigelia africana* is divided into biological activities such as antiprotozoal, antibacterial, antifungal activities; pharmacological properties such as anti-inflammatory and analgesic, anticancer, antidiarrheal, anti-ulcer effects as well as toxicological effects with the responsible phytochemicals.

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2. 0 USES OF *KIGELIA AFRICANA* IN TRADITIONAL MEDICINE AND THEIR PHARMACOLOGICAL EVALUATION

2.1 Anti-protozoal activity

One of the several uses of *Kigelia africana* is for treating malaria [7]. *In-vitro* studies [8,9] revealed the efficacy of hexane, dichloromethane, ethyl acetate and ethanol extracts of the root bark against *Plasmodium falciparum* [8], ~~and~~ *Trypanosoma brucei brucei* and *T.b. rhodesiense* [9], the causative organisms for malaria and sleeping sickness respectively [10]. The growth of *Entamoeba histolytica* was also inhibited by the stem bark butanol extract [11]. Four compounds that exhibited significant anti-plasmodial activity were isolated from the ethyl acetate extract of *Kigelia africana*. Three of the four compounds showed good activity against all the different parasite strains, the chloroquine-resistant W-2 and two field isolates of *Plasmodium falciparum*, with $IC_{50} < 5 \mu M$. Specicoside exhibited the highest activity on W-2 ($IC_{50} = 1.5 \mu M$) followed by 2β , 3β , 19α -trihydroxy-urs-12-en-28-oic acid ($IC_{50} = 1.60 \mu M$) and atranorin ($IC_{50} = 4.41 \mu M$) while p-hydroxycinnamic acid was the least active ($IC_{50} = 53.84 \mu M$) [12]. Lapachol in the methanol extract of the root and another compound (a quinone) obtained from the wood show anti-malarial activity. Three iridoids-specioside, verminiside and minecoside isolated from the butanol extract of the stem bark possess anti-amoebic activity [7]. The anti-trypanosome activity of the stem bark and root bark extracts are attributed to 2-(1-hydroxyethyl)-naphtho-[2,3-b]-furan-4,9-quinone and three naphthoquinoids: isopinnatal, kigelinol and isokigelinol [9].

2.2 Antibacterial and antifungal activities

Various parts of *Kigelia africana* are employed to treat bacterial and fungal infections. In a study to verify these properties [13], crude extracts of stem bark and fruits were prepared with distilled water, ethanol or ethyl acetate. In the microtitre plate bioassay, the stem bark and fruit extracts showed similar antibacterial effects against Gram-negative and Gram-positive bacteria [13]. A mixture of three fatty acids exhibiting antibacterial effects was

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isolated from the ethyl acetate extract of the fruits using bioassay-guided fractionation [13]. Palmitic acid was the major antibacterial compound in this mixture thus supporting the traditional use of the plant in therapy of bacterial infections [13]. 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 contributing to the observed antibacterial and antifungal activities [12].

In another antibacterial and antifungal study, Owolabi and co-workers[14] using the agar diffusion technique, reported that like amoxillin standard antibiotics, crude ethanolic extract exhibited antibacterial and antifungal activities against *Staphylococcus aureus* and *Candida albicans* with zones of inhibition measuring 15.0 \pm 0.95 and 20.75 \pm 4.6 mm respectively but the aqueous extract exhibited no antibacterial or antifungal activity. The minimum inhibitory concentration for the ethanol extract was found to be 6.25 \pm 1.07mg/ml for *S. aureus* and 7.92 \pm 1.52 mg/ml for *C. albicans*. In another study by Akunyili *et al.*, [15], it was also established that the stem bark extract inhibited a number of harmful micro-organisms, including *Escherichia coli*, *Pseudomonas aeruginosa*, *Staphylococcus aureus* and *Candida albicans* [15]. Similarly, evaluation of the antibacterial activities of ethanolic and aqueous extracts of *Kigelia africana* fruit against multi drug resistant *Pseudomonas aeruginosa* showed that the ethanolic extract was more potent than the aqueous extract [16].

2.3 Anti-inflammatory and analgesic activities

The use of the bark, stem, twigs, leaves and fruits of *Kigelia africana* to relieve rheumatism, toothache and headache has been documented [17]. Picerno and co-workers [18] reported that the anti-inflammatory property of *Kigelia africana* fruit polar extract was due to the constituent verminoside. The compound is known to cause significant anti-inflammatory

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effects inhibiting both iNOS expression and NO release in the LPS-induced J774.A1 macrophage cell line [18].

The ethanolic extract of the stem bark has been evaluated for analgesic property using acetic acid induced mouse writhing and hot plate reaction time; and anti-inflammatory property using the carrageenan-induced paw oedema [19]. The extract showed a dose dependent significant reduction of the number of writhes with 500 mg/kg body weight dose giving the highest reduction [19]. In the carrageenan-induced paw oedema, a dose dependent significant inhibition was observed ($p < 0.001$) between the second and the fifth hour, confirming that the ethanolic stem bark extract has significant analgesic and anti-inflammatory properties. Inhibition of the synthesis of prostaglandins and other inflammatory mediators has been suggested to be responsible for the analgesic and anti-inflammatory properties [19].

2.4 Anti-diarrhoea activity

One important local use of *Kigelia africana* is the use of the leaf for treating diarrhoea [20]. An administration of a dose of 100 or 200 mg/Kg of aqueous leaf extract to experimental animals caused anti-diarrhoea activity [20]. It also reduced fecal output in castor oil – induced diarrhoea in animals and remarkably decreased the propulsive movement of the gastro-intestinal contents [2]. On the isolated guinea pig ileum, the extract did not appreciably affect acetylcholine and histamine induced contractions [20]. In an antidiarrhoeal activity studied using castor oil to induce diarrhoea in rats (*in vivo*) and using isolated jejunum, 500 and 1000 mg/Kg ethanol root extract (*in vitro*) significantly reduced the frequency of diarrhoeal stool and the spontaneous propulsive movement of isolated jejunum [2]. *Kigelia africana* root extract also produced reversible inhibition of acetylcholine induced mobility of isolated rabbit jejunum [2]. The observed spasmolytic effects of the extract may

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explain its continual use in the management of chronic abdominal pains associated with diarrhoea [2]

2.5 Anti-diabetic and antioxidant activities

Like many other African food [21] and medicinal plants [22 – 25], the use of *Kigelia africana* to manage diabetes is traditionally practiced and reported [2,3]. The anti-diabetic activity and the antioxidant effect were studied [26]. Also, in a polyherbal preparation, ADD-199, *Kigelia africana* is in combination with three other plants: *Maytenus senegalenses*, *Annona senegalenses* and *Lannea welwitschii*. The anti-diabetic and antioxidant effects were investigated in streptozotocin-induced diabetic C3H mice and results were compared with two allopathic hypoglycaemic drugs, glibenclamide and metformin. Plasma glucose, insulin and lipids as well as liver glycogen and lipid peroxidation were measured following treatment for eight weeks. The results indicated that plasma insulin levels in normal controls at termination were approximately 76µmol/L compared to trace levels in untreated diabetic mice. Like glibenclamide, ADD-199 increased insulin levels in diabetic mice up to 70% of levels in untreated non-diabetic mice whilst metformin had no effect. Also, basal plasma glucose levels in diabetic controls (18.8 mM) were reduced to 14.0 mM by 100 mg/kg ADD-199 in < 2 weeks compared to 4 to 6 weeks for glibenclamide and metformin, respectively. This hypoglycaemic effect of ADD-199 was associated with the alkaloidal content of the extract. Treatment with ADD-199 or the hypoglycaemic agents reversed the observed elevation in plasma lipids but increased hepatic glycogen, triacylglycerol and cholesterol levels. Treatment also increased hepatic glucose uptake by isolated diaphragms and attenuated hepatic lipid peroxidation. These antihyperglycaemic and antioxidant actions of ADD-199 were comparable to those of the maximum daily therapeutic doses of glibenclamide (0.25 mg/Kg) and metformin at 50 mg/kg [26].

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Olaleye and Rocha, [27] carried out an *ex-vivo* assessment of the antioxidant property of *Kigelia africana* extracts in rat liver homogenate. Administration of different pro-oxidants: 10 μ M iron (II) sulphate, (FeSO_4), 5 μ M sodium nitroprusside (SNP), and 2 mM 3-nitropropionic acid led to increased formation of thiobarbituric acid reactive substances (TBARS), which indicates lipid peroxidation in the liver. Administration of *Kigelia africana* statistically ($p < 0.05$) reduced the production of TBARS in a concentration-dependent manner in all the pro-oxidant-induced oxidative stress, suggesting that the use of the plant in the treatment of various diseases, especially liver diseases could be due to its ability to act as an antioxidant [27]. Saini and co-workers [3] attributed the antioxidant potential of *Kigelia africana* to caffeic acid derivatives and other compounds unique to the plant.

2.6 Anti-ulcer effect of *Kigelia africana*

The use of *Kigelia africana* fruit, bark and root to treat ulcer has been reported [3]. Owolabi and Nworgu [28] investigated the anti-ulcer activity of the ethanol extract of *Kigelia africana* stem bark in Wistar albino rats. In both preventive and curative models of ulcer, respectively induced by absolute ethanol and indometacin, the extract caused marked inhibition of ulceration, suggesting a dose-dependent gastro-protective effect by the plant in the two models of ulcer [28].

2.7 Toxicity of *Kigelia africana*

2.7.1 Acute toxicity

In a study on the diuretic activity of aqueous extract of the bark in experimental rats, Sharma and colleagues [29] reported that it was safe up to 5g/Kg. A determination of acute toxicity of the methanol fruit extract using male Sprague Dawley rats showed that the extract was well tolerated by the animals as there were no observable signs of acute toxicity effects like restiveness, seizure or dizziness after the administration of 400 mg/kg. However, at 6400 mg/kg, the animals showed signs of toxicity like jerks and writhes with 60% death. At 12,800

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mg/kg there was 80% death of the animals. The LD₅₀ was estimated from a log-dose curve to be 3,981.07 mg/Kg [30-32].

In another study by Olaleye and Rocha [27], 100 mg/Kg aqueous extract was administered to rats induced with acetaminophen liver toxicity. The extract countered the effect of acetaminophen on the activities of aspartate transaminase (AST), alanine transaminase (ALT), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and δ-aminolevulinic acid dehydrogenase (δ-ALA-D). This suggests that the extract can act as hepatoprotective agent against toxicity possibly through its antioxidant action [27].

2.7.2 Sub-chronic and chronic toxicity

The administration of the aqueous anti-diabetic polyherbal extract ADD-199 containing *Kigelia africana* and three other plants at a daily dose of 100 or 500 mg/Kg body weight over 30 days, to male Wistar albino rats appeared to show no effect on many haematological, urinary and plasma biochemical parameters [26]. It also had no effect on some modulators of some hepatic cytochrome P450 (CYP) isozymes normally measured as indices of organ specific toxicity or potential for drug interactions [26]. Specifically ADD-199 containing *Kigelia africana* did not affect plasma AST, ALT, alkaline phosphatase (ALP) and albumin or creatinine kinase (CK) levels [26]. It also did not affect plasma creatinine and urea levels. Furthermore, ADD-199 neither affected packed cell volume (PCV), nor the levels of red blood cells (RBC), reticulocytes, platelets, lymphocytes and granulocyte. It however, caused significant dose-dependent reductions in white blood cell counts at day 15 with varying degrees of recovery by day 30 [26]. ADD-199 also reduced the rate of body weight increases after week 3. However, no changes were observed in organ weight at termination. The ADD-199 did not significantly affect zoxazolamine-induced paralysis and pentobarbital-induced sleeping times as well as certain CYP isozyme activities in rats, suggesting that ADD-199

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had no overt organ specific toxicity and did not demonstrate a potential for drug interactions via CYP-mediated metabolism in rats following sub-chronic administration [26].

The protective effect of methanol extract of *Kigelia africana* fruit extract against cisplatin-induced renal toxicity in male rats has been studied [30]. The rats treated with cisplatin for 28 days, suffered loss in body weight, elevation in blood urea nitrogen and serum creatinine levels as well as tubular necrosis [30]. Pre-treatment with *Kigelia africana* fruit methanol extract as a prophylaxis significantly prevented these changes [30]. Though post-treatment of animals with the extract after cisplatin treatment did not completely restore serum catalase activity, it caused some alleviating effects [30], suggesting that *Kigelia africana* fruit extract may protect against cisplatin-induced renal toxicity, and hence might serve as a novel agent to limit renal injury [30].

2.7.3 Cytotoxic activity

The cytotoxicity of hexane, chloroform, ethyl acetate, ethanol and methanol extracts of different parts of *Kigelia africana* has been studied [32] on *Artemia salina* using the brine shrimp lethality test (BSLT). Some workers [32] have reported moderate toxicity of the ethanol extract of the root and fruit at a dosage of 593 and 124 µg/ml respectively while the ethyl acetate extract of the fruit was also moderately toxic at 495 µg/ml. Other workers [33] reported a moderate cytotoxicity of ethanol extract of the fruit to *Artemia salina* at a dosage of 1000 µg/ml. In an *in vitro* study, Zofue and colleagues [31] reported that the n-hexane extract and its isolated compounds speciciside and p-hydrocinnamic acid were non-cytotoxic ($CC_{50} > 30$ µg/ml) on LLC/MK2 monkey kidney cells. However, the ethylacetate extract and its isolated compound atranorin and 2β,3β,19α-trihydroxy-urs-12-en-28-oic acid showed cytotoxicity at high concentration, with the later being the more toxic ($CC_{50} = 9.37$ µg/ml). [31]

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2.8 Molluscidal and piscicidal effects

The molluscidal and piscicidal effects of the aqueous extract of *Kigelia africana* bark has been reported by Ashraf and colleagues [34]. In a study to evaluate the piscicidal effect of *Kigelia africana* aqueous bark extract against *Clarias gariepinus* fingerlings, graded concentrations of the extract, 40,80,120ppm were prepared into which twenty fingerlings were added in replicates [33]. The toxicity test lasted 24 hours during which observations were made at 1, 2, 4, 8, 12, 16, 20 and 24 hours. Varying degrees of mortality was recorded, with 100% death after 4 hours in the tank of 120ppm concentration and the causative agent identified as coumarins [33]. Table 1 summarizes the toxic effects of *Kigelia africana* extracts on different species of animals.

2.9 Anticancer activity

There are many publications suggesting the use of *Kigelia africana* to either prevent or to treat cancer [4, 35, 36, 37, 38, 39]. In a study to determine the effect of *Kigelia africana* seed oil on cell proliferation in culture, human colon adenocarcinoma (Caco-2) and human embryonic kidney (HEK-293) cells were maintained and treated with various concentrations (0, 20, 40, 80, 100 and 120mg/l) of *Kigelia africana* seed oil. In this study trypan blue dye exclusion method was used to determine cell growth 48 hours after oil treatment. The seed oil was found to suppress both Caco-2 and HEK-293 cell growth in a dose dependent manner. The seed oil did not cause an increase in cell death as the number of dead cells remained unchanged under control and oil-treated conditions. The number of dead cells remained unchanged under conditions, implying that the oil did not increase cell death. The oil significantly suppressed Caco-2 cell growth compared to HEK-293 cell growth at all oil concentrations. The suppression of Caco-2 and HEK-293 cell proliferation by *Kigelia africana* seed oil suggest a potential antiproliferative effect of the oil on the two cell lines [36].

In another study [35], methanolic extract of the root of *Kigelia africana* contains the constituent lapachol [35] which is reported to be effective in the treatment of solar keratosis,

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skin cancer and Kaposi sarcoma, an HIV-related skin ailment [36]. In this study, serial dilutions of standardized aqueous, ethanol and dichloromethane extracts of the stem bark and fruits of *Kigelia africana* were tested for their growth inhibitory effects against four melanoma cell lines and a renal cell carcinoma line (Caki-2) using two different assays (3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyl tetrazolium bromide, MTT and Sulforhodamine B, SRB assays). Lapachol, a possible constituent of these extracts of *Kigelia africana*, together with known therapeutic anti-neoplastic agents were also subjected to the same evaluation. Results showed significant inhibitory activity of the dichloromethane extract of the stem bark and lapachol in a dose-dependent and time-dependent manner. Chemosensitivity of the melanoma cell lines to the stem bark was greater than that seen for the renal adenocarcinoma line, but in marked contrast sensitivity to lapachol which was separately evaluated was similar with the five cell lines. This suggests that lapachol is the active ingredient that exhibit anti-cancer property [39].

2.10 Effect on the Central Nervous System

Among the recorded uses of *Kigelia africana* is in the treatment of epilepsy, CNS (central nervous system) stimulating activity and as antidotes against snake poisons. Snake bite antidotes are made with an infusion of the fruits, stem, leaves, twig or bark taken orally or rubbed onto the bite [40]. The CNS stimulant activity of the ethanolic stem bark extract has been verified by Owolabi *et al.*, [41]. The barbiturate induced sleeping time and the Rota rod bar were used to study the effect of the extract on muscle coordination in mice. 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 was 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

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a statistically significant 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 [41].

2.11 Effects on reproductive system

For, sexual ailments such as infertility, poor libido, sexual asthenia and impotence are treated with herbal prescriptions containing the fruit, roots or leaves of *Kigelia africana* are administered by traditional healers [40]. 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 [5]. The fruits are also applied on the breast to improve flow of milk in lactating women [3].

Kigelia africana fruit aqueous extract has been successfully used as fertility enhancing agent in rats [42]. 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 [43]. A study by Adeparusi *et al.*, [43] to investigate the effects of varying dietary supplementation of *Kigelia africana* 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 [43].

2.12 Use as cosmetics

Traditionally, *Kigelia africana* is used as cosmetic to enhance beauty [5]. For this purpose preparations contain extracts of one or more parts, mainly the fruit, stem bark or the pendulum (where the fruit hangs from, or a product thereof) are used. The preparation contains 50% extract mixed with carrier, excipients and colorants. Aqueous or alcohol extracts are ideal for water based cosmetic products such as gels, lotion, water or oil

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emulsions and creams. The products are used to make anti-ageing and regenerating skin care products, skin tightening cosmetics such as bust firming products. Anti-inflammatory, antioxidant and antibacterial agents are some of the products products that are commercially made from *Kigelia Africa* (PhytoTrade Africa).

2.13 Diuretic activity

The diuretic activity of *Kigelia africana* aqueous bark extract was investigated Sharma *et al.* [29] through the determination of urine volume, electrolyte concentration and diuretic potency in male albino rats. Different concentrations of the extract, 250 and 500 mg/kg were orally administered to hydrated rats and their urine output was immediately measured after 5 hours of treatment. Furosemide (10 mg/kg) was used as reference drug while normal saline (0.9%) solution was used as control. The result showed that the bark extract exhibited dose dependent diuretic property. The onset of diuretic action was within 1 hour and lasted up to 5 hours, with 500 mg/kg displaying a potency of 0.8 and 250 mg/kg giving 0.32. The extract also caused a marked increase in Na⁺, K⁺ and Cl⁻ levels [28].

3.0 Nutritional value

Kigelia africana provides a nutritious source of food during times of famine [40] For this purpose the seeds are roasted to eat. In other instances fruit and bark are used in the brewing process to aid fermentation and enhance the flavor of traditional beer. The fruit pulp is not edible as it may cause blistering of the tongue and skin. However, fallen fruits along with leaves and flowers are browsed or foraged by livestock and wildlife [5].

The pro-fertility effect of dried fruit meal (KAFM) was investigated on reproductive performance of female *Clarias gariepinus* fed with increasing levels for 90 days in relation to egg production and quality (number, shape, structure, fecundity) and hatchability (percentile fertilization, percentile hatching, percentile survival). The decrease in percentile deformity in

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hatchlings of *Clarias gariepinus* fed dietary KAFM compared with the control diet suggest that KAFM improves the quality of larvae. The highest percentile survival of hatchlings was recorded in the fish fed with dietary KAFM (100 g KAFM /kg diet). Egg sizes for fish fed the control diet and dietary levels revealed no significant difference in egg size. The result showed that dried KAFM had pro-fertility effect on male and to some extent, female *Clarias gariepinus* [42].

4.0 PHYTOCHEMISTRY OF VARIOUS PARTS OF *KIGELIA AFRICANA*

The occurrence of secondary metabolites in different parts of *Kigelia africana* is responsible for its several medicinal applications [3]. These compounds include naphthaquinones, iridoids, sterols, coumarins, flavonoids and alkaloids among others [3, 45, 46]. Structures of isolated compounds have been characterized and identified using gas chromatography by Atolani and Olatunji [46], ultraviolet spectroscopy, infrared spectroscopy, nuclear magnetic resonance and other spectroscopic techniques like, mass spectrometry, or gas chromatography-mass spectrometry [12, 18, 47, 48]. The use of *Kigelia africana* in traditional African medicines has been verified by corresponding pharmacological properties thereby validating its numerous diverse phytoconstituents.

4.1 Chemical constituents of *Kigelia africana* fruit

Gouda and colleagues [47] reported that a new furanone derivative formulated as 3-(2'-hydroxyethyl)-5-(2''-hydroxypropyl) dihydrofuran-2-(3H)one and four new iridoids named: 7-hydroxyviteoid II, 7-hydroxyeucommic acid, 7-hydroxy-10-deoxyeucommiol and 10-deoxyeucommiol have been isolated from the fruits in addition to seven known iridoids namely, jiofuran, jioglutolide, 1-dehydroxy-3,4-dihydroaucubigenin, des-p-hydroxybenzoyl kisasagenol B, ajugol, verminoside and 6-transcaffeoyl ajugol. Further phytochemical investigation Gouda *et al.* [48] of the fruits of *Kigelia africana* yielded a new phenylpropanoid derivative identified as 6-p-coumaroylsucrose together with ten known phenylpropanoid and

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phenylethanoid derivatives and a flavonoid glycoside [48]. A biologically monitored fractionation of the fruit led to the isolation and identification of the naphthoquinones, kigelinone, isopinnatal, dehydro-alpha lapachol and the phenylpropanoids p-coumaric acid and ferulic acid[48].

4.2 Chemical constituents of *Kigelia africana* stem

A study by Binutu *et al* [12] of the antimicrobial properties of the aqueous stem bark extract of *Kigelia africana* revealed the presence of two naphthoquinones kigelinone and isopinnatal. Three known iridoids: specioside, verminoside and minecoside have also been isolated from the stem bark [49]. The dichloromethane extract of the stem bark contain naphthoquinones which possess anti trypanosomal properties [3,4] while kigelin, β -sitosterol, 1,3-dimethylkigelin and ferulic acid have been isolated from the bark, while the isolation of kigeliol from the wood and balaphonin from the stem bark have also been reported [17, 50].

4.3 Chemical constituents of *Kigelia africana* root

Earlier workers [8, 47, 49] reported the isolation and identification of the naphthoquinones, kigelinone, isopinnatal, dehydro-alpha-lapachol and the phenylpropanoids p-coumaric acid and ferulic acid from the root of *Kigelia africana*. Steroids, iridoids and coumarins have been isolated from the root bark [50] as well as three isocoumarins: 6-methoxymellein, kigelin and 6-demethylkigelin [51]. The isolation of kigelin and 6-methoxymellein together with two known compounds, stigmasterol and lapachol from the root has also been reported [39]. Naphthoquinones that possess anti-trypanosomal properties have been reported in the dichloromethane extract of the root [3,4] while two non-quinonoid aldehydes, norviburtinal and pinnatal have been obtained from the root bark [4, 39].

4.4 Chemical constituents of *Kigelia africana* leaf

The hexane extract of the leaf of *Kigelia africana* has been reported to be rich in hydrocarbons and some volatile compounds. In a study that qualitatively and quantitatively analyzed the hexane extract for various chemical compositions, it was revealed to contain twelve compounds with the major ones identified as n-hentriacontane, 1-tricosene, 11-(2,2-dimethylpropyl)heneicosane, 2,6,10-trimethyldodecane, pentafluoroheptadecyl ester, 2-ethylhexyloctadecyl sulfurous acid ester, heneicosane and hexyloctylsulfurous acid ester. Others are 4,4-dimethylundecane, methyl-12-methyltetradecanoate, 1-iodohexadecane and 1-iodododecane. Hentriacontane have been reported to have a possible anti-tumour activity while methyl-12-methyltetradecanoate has also been reported for its inhibition capacity on the development of coneal angiogenesis, which is responsible for blindness and other infections [46] Flavonoids and iridoids [47] and a 7-O-glucoside [9,39] have also been found in the leaves (Table 2). The structural formulae of some of the chemical constituents isolated from *Kigelia africana* are presented in Figure 1.

5.0 CONCLUSION

With the wide occurrence of *Kigelia africana* and its extensive folk medicinal applications, including in treating microbial infections, relieving pains and inflammation, cancer and in the management of diabetes, ulcer, anaemia, respiratory, cardiac and hepatic disorders, considerable interest has developed to scientifically prove the medicinal claims. The studies have led to the revelation that natural products from diverse groups such as naphthoquinones, monoterpenoids, coumarins, sterols and iridoids. Other natural products present are flavonoids, lignans acids and hydrocarbons. Like in other members of the Bignoniaceae family, *Kigelia africana* is known for iridoids which accumulate differentially in roots and flowers. Hence there is a need for quantification of these phytoconstituents in different parts of the plant for better medicinal applications. Furthermore, studies could still be performed on the therapeutic efficacy of bioassay-guided fractions of various extracts of the different parts which can ultimately lead to the discovery of new drugs.

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COMPETING INTERESTS

We hereby declare no conflicting interest

AUTHORS' CONTRIBUTIONS

Author S.E. Atawodi conceived the review, provided the general guide and refined the final materials, while O.D. Olowoniyi performed most of the literature search and wrote the initial draft of the manuscript. All authors read and approved the final manuscript.

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Table 1 Toxic effects of *Kigelia africana* extracts on different species of animals

S/N	Animal Species	Observed effect	Plant part	Extract	Dose	Route	Reference:
1	<i>Artemia salina</i>	Moderate toxicity	Root	Ethanol	593 μ g/ml	Whole body	[32]
			Fruit	Ethanol	124 μ g/ml		
			Fruit	Ethyl acetate	495 μ g/ml		
2	<i>Artemia salina</i>	Moderate cytotoxicity	Fruit	Ethanol	7500 μ g/ml	Whole body	[52]
3	<i>Artemia salina</i>	Low toxicity	Leaves	Methanol	250 μ g/ml	Whole body	[53]
4	Fish	Increased opercular ventilation and tail fin	Bark	Aqueous		Oral/whole body	[54]

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5	Sprague-Dawley rats	beat leading to eventual fatigue and eventual death Protective effect against cisplatin-induced kidney oxidant injury	Fruit	Methanol	500mg/kg 100mg/kg	Oral	[30]
6	Wistar albino rats	No overt organ specific toxicity and did not demonstrate a potential for drug interaction via cytochrome P450-mediated metabolism	Fruit	Aqueous	100-500mg/kg	Oral	[26]
7	Mice	Reversed the effects of severe hepatic necrosis induced by a large dose of paracetamol	Leaves	Aqueous	100mg/kg	Oral	[27]

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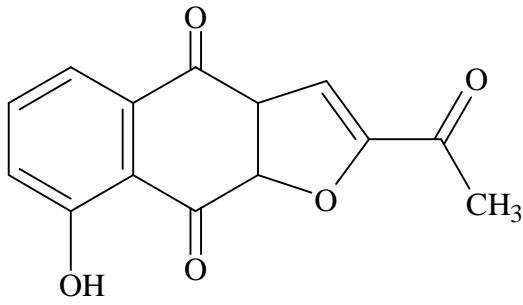
Table 2: Chemical Constituents of *Kigelia africana*

S/No	Compound	Plant Part	Bioactivity	Reference
	Kigelinone	Stem bark	Antibacterial, Antifungal	[50] [15, 12]
	Isopinnatal	Stem bark	Antibacterial, antifungal, anti- malaria	[15, 8, 36, 12]
	Kigelinol	Stem bark	Anti-malaria	[8]
	Isokigelinol	Stem bark	Anti-malaria	[9, 36]
	Lapachol		Anti-cancer	[12, 35]
	Dehydro-alpha-lapachone			
	2-(1-hydroxyethyl)naphtha[2,3-b]furan-4,9-quinine	Stem bark	Antitrypanosoma	[9, 12]
	Kigeliol	Wood		[55] [55]
	Balaphonin	Stem bark	Cytotoxicity	[56, 57]
	B-Sitosterol	Bark		[13]
	Caffeic acid	Bark		
	Specioside	Stem bark	Antibacterial, Antifungal	[49]
	Verminoside	Stem bark		[49, 47, 17]
	Minecoside	Stem bark		[49]
	Carbohydrates, alkaloids, tannins, saponins and glycosides	Bark		[45]
	7-Hydroxyviteoid II	Fruit		[47]
	7-Hydroxyeucommic acid	Fruit		[47]
	7-Hydroxy-10-deoxyeucomiol	Fruit		
	10-Deoxyeucommiol	Fruit		[47]
	Jiofuran	Fruit		[47]
	Jioglutolide	Fruit		[47]
	1-Dehydroxy-3,4-dihydroxy-3,4-dihydroaucubigenin	Fruit		[47]
	des-p-hydroxybenzoyl kisasagenol B	Fruit		[47]
	Ajugol	Fruit		[47]
	6-trans caffeoyl ajugol	Fruit		[47]
	6-p-Coumaroyl sucrose	Fruit		[47]
	β -Sitosterol	Fruit		[56, 57]
	Quercetin	Fruit		[13]
	Luteolin	Fruit		[13]
	3-(2'-hydroxyethyl)-5-(2''-hydroxypropyl) Dihydrofuran-2-(3H)one	Fruit		[47]
	Isocoumarins			
	6-Methoxymellein	Root		[58]

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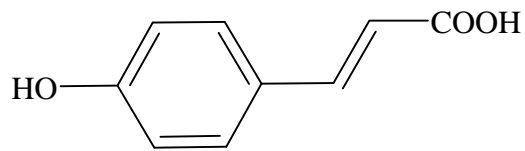
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Kigelin	Root		
6-Demethylkigelin	Root		
3-Dimethylkigelin	Root		
Phenylpropanoids			
p-Coumaric acid	Root bark	Antibacterial, Antifungal	[12, 13]
Ferulic acid	Root bark		[12, 13]
Stigmasterol	Root		[58]
Non-quinonoid aldehydes			
Norviburtinal	Root bark		[59]
Pinnatal	Root bark		[59]
Hydrocarbons			
n-Hentriacontane	Leaf	Antitumour	[46]
1-Tricosene	Leaf		[46]
11-(2,2-Dimethylpropyl)heneicosane	Leaf		[46]
2,6,10-Trimethyldodecane	Leaf		[46]
Heneicosane	Leaf		[46]
4,4-Dimethylundecane	Leaf		[46]
Pentafluoroheptadecyl ester	Leaf		[46]
2-ethylhexyloctadecyl sulphurous acid ester	Leaf		[46]
Hexyloctyl sulphurous acid ester	Leaf		[46]
Methyl-12-methyltetradecanoate	Leaf	Inhibition of corneal angiogenesis	[46, 13]
1-Iododecane	Leaf		[46]
11-Iodohexadecane	Leaf		[46]



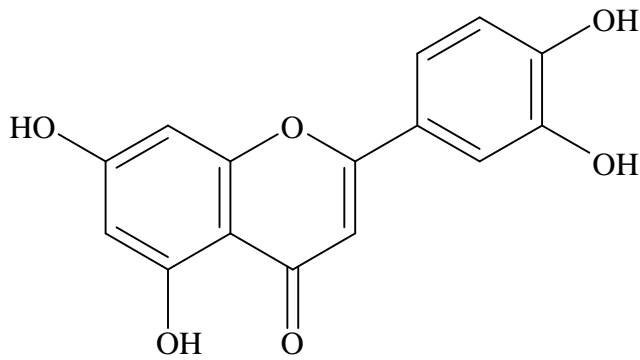
Kigelinone

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Coumaric acid

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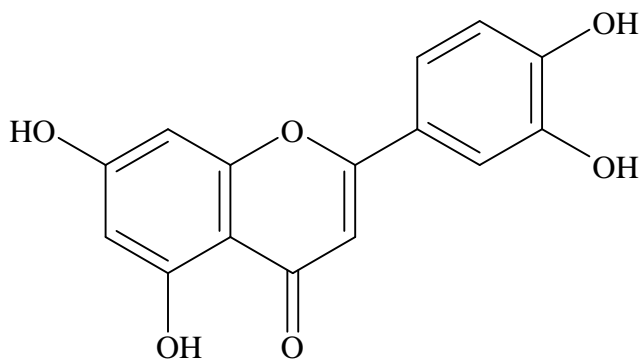


Luteolin

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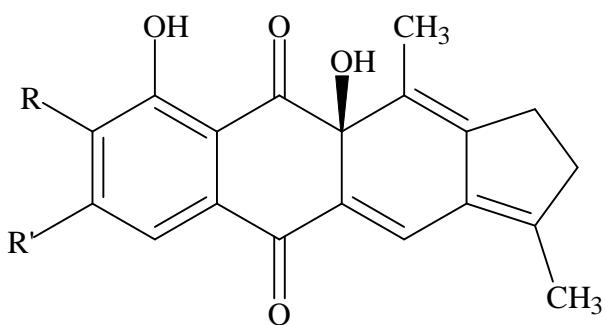
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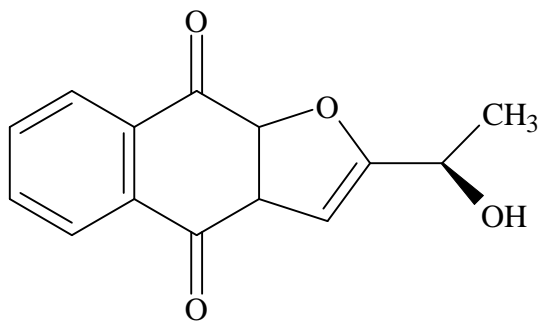
Luteolin

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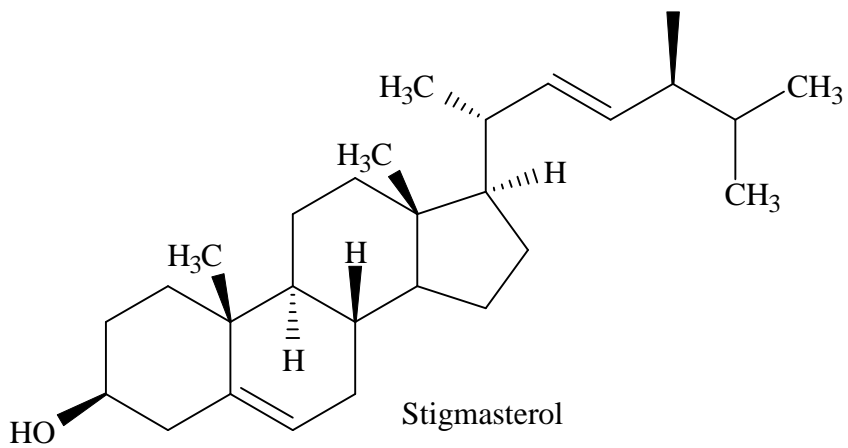
R=OH, R'=H Pinnatal
R=H, R'=OH Isopinnatal

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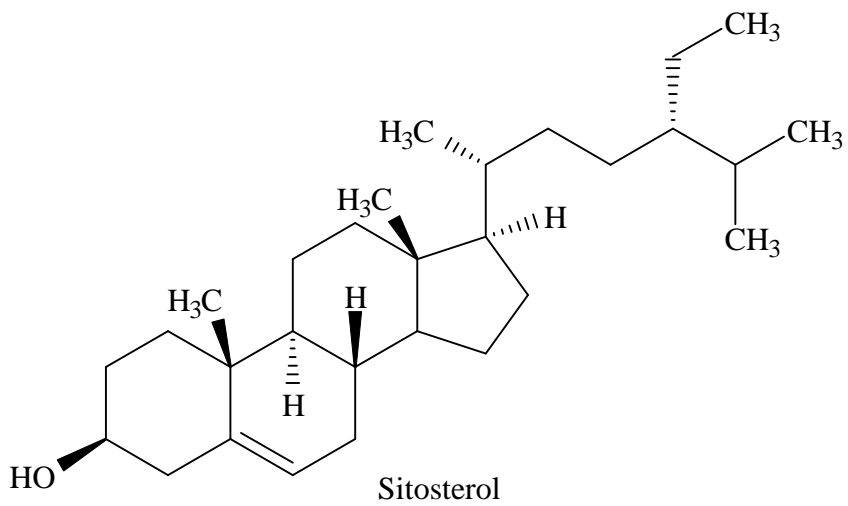


2-acetylnaphtho[2,3-b]furan-4,9-quinone

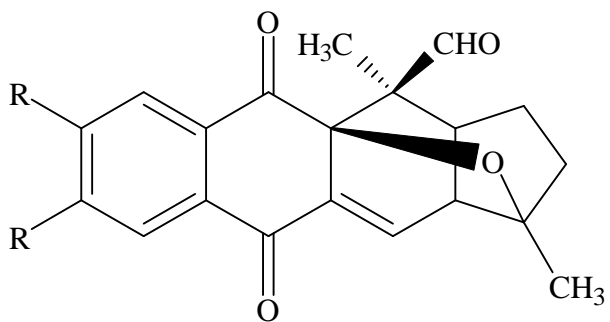
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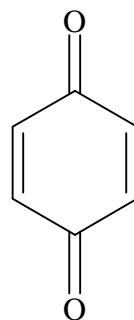
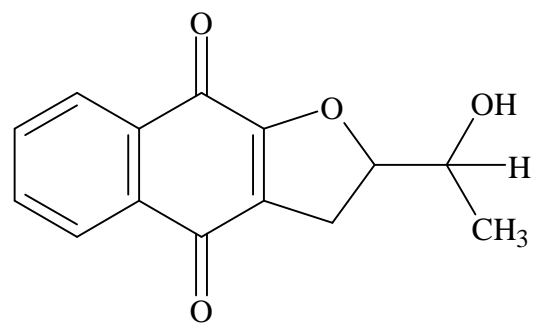
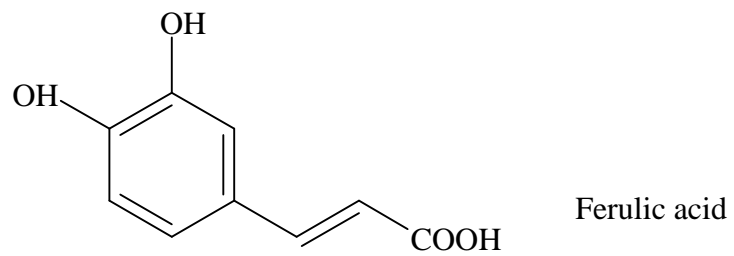
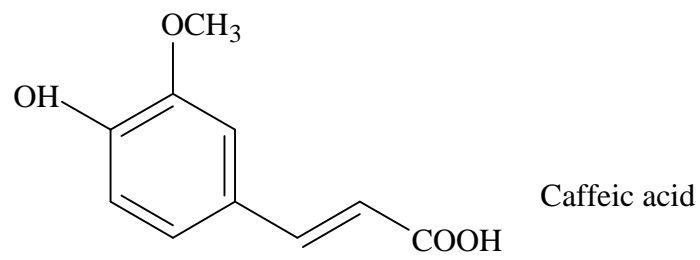


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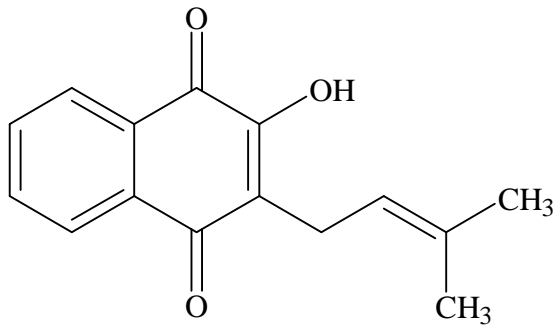
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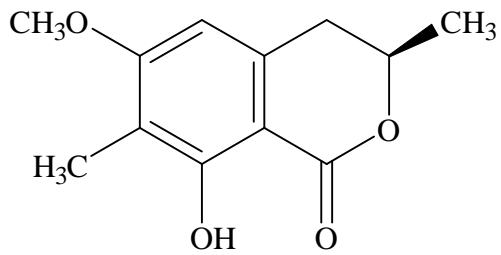
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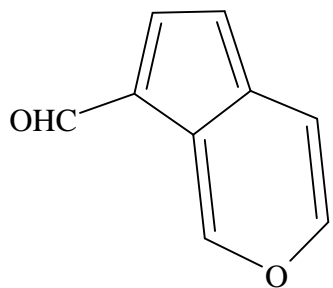
Lapachol

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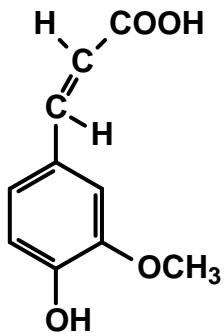
Kigelin

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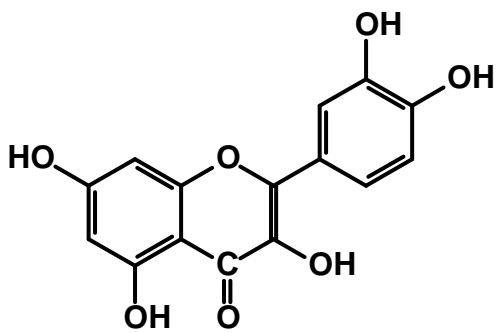
Norviburtinal

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Ferulic acid



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Quercetin

Figure1: Structural formulae of some compounds found in *Kigelia africana*

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