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PII: S0378-8741(16)30330-0
DOI: http://dx.doi.org/10.1016/j.jep.2016.05.049
Reference: JEP10187

To appear in: *Journal of Ethnopharmacology*

Received date: 5 January 2016
Revised date: 17 May 2016
Accepted date: 20 May 2016

Cite this article as: Idris Bello, Mustapha W. Shehu, Mustapha Musa, Mohd Zaini Asmawi and Roziahanim Mahmud, *Kigelia africana* (Lam.) Benth (Sausage tree): Phytochemistry and pharmacological review of a quintessentia African traditional medicinal plant, *Journal of Ethnopharmacology* http://dx.doi.org/10.1016/j.jep.2016.05.049

Kigelia africana (Lam.) Benth. (Sausage tree): Phytochemistry and pharmacological review of a quintessential African traditional medicinal plant.

Idris Bello [1]*, Mustapha W. Shehu [3], Mustapha Musa [4], Mohd. Zaini Asmawi [1,] Roziahanim Mahmud [2]

1 Department of Pharmacology, School of Pharmaceutical Sciences, University Sains Malaysia, 11800 Pulau Pinang, Malaysia.

2 Department of Pharmaceutical Chemistry, School of Pharmaceutical Sciences, Universiti Sains Malaysia (USM), 11800 Pulau Pinang, Malaysia.

3 Department of Environmental Science, Faculty of Science, Islamic University, Uganda.

4 Shehu Shagari College of Education, Sokoto, Nigeria.

* Corresponding author: Idris Bello (idrisbello1@yahoo.com). TEL; +60165466963.

Abstract

Ethnopharmacological relevance: *Kigelia africana* is a quintessential African herbal medicinal plant with a pan-African distribution and immense indigenous medicinal and non-medicinal applications. The plant is use traditionally as a remedy for numerous disease such as use wounds healing, rheumatism, psiarosis, diarrhea and stomach ailments. It is also use as an aphrodisiac and for skin care.

Aim of the review: The present review aims to compile an up-to-date review of the progress made in the continuous pharmacological and phytochemistry investigation of *K. africana* and the corresponding commercial and pharmaceutical application of these findings with the ultimate objective of providing a guide for future research on this plant.

Method: The scholarly information needed for this paper were predominantly sourced from the electronic search engines such as Google, Google scholar; publishing sites such as Elsevier, scienceDirect, BMC, PubMed; other scientific database sites for chemicals such as ChemSpider, PubChem, and also from online books.

Results: pharmacological investigations conducted confirm the anti-inflammatory, analgesic, antioxidant and anticancer activity of the extract of different parts of the plant. Bioactive constituents are found to be present in all parts of the plant. So far, approximately 150 compounds have been characterized from different part of the plant. Iridoids, naphthoquinones, flavonoids, terpenes and phenylethanoglycosides are the major class of compounds isolated. Novel compounds with potent antioxidant, antimicrobial and anticancer effect such as verbascoside, verminoside and pinnatal among others, have been identified. Commercial trade of *K. africana* has boosted in the las few decades. Its effect in the maintenance of skin has been recognized resulting in a handful of skin formulations in the market.

Conclusions: The pharmaceutical potentials of *K. africana* has been recognized and have witness a surge in research interest. However, till date, many of its traditional medicinal uses has not been investigated scientifically. Further probing of the existential researches on its pharmacological activity is recommended with the end-goal of unravelling the pharmacodynamics, pharmacokinetics, clinical relevance and possible toxicity and side effects of both the extract and the active ingredients isolated.

Key words: *Kigelia africana*; herbal; traditional; phytochemistry; pharmacology

Abbreviations:

ABTS, 2,20-azino bis-(3-ethylbenzothiazoline-6-sulfonic acid; ALP, alkaline phosphatase; ALT, serum alanine aminotransferase; AST, aspartate aminotransferase; bw, body weight; DPPH, 2-diphenyl-1-picrylhydrazyl; FSH, follicle stimulating hormone; GLUT-4, glucose transporter-4; HDL, high density lipoprotein; IC_{50}, concentration that causes 50% inhibition; i.p., intraperitoneally; EC_{50}, concentration that kills 50% of the test organisms; LH, Luteinizing hormone; M. Z. D, Mean diameter of growth inhibition zones; MFC, minimum fungicidal concentration; SRB, sulforhodamine B; SOD, superoxide dismutase; MIC, minimum inhibitory concentration; MTT, 2-(4,5-dimethylthiazol-2 yl)-3, 5-diphenyl-2H-tetrazolium bromide; ST, Serum testosterone; STZ, Streptozotocin; SNP, sodium nitroprusside SOD, superoxide dismutase; CAT, catalase; GPx, glutathione peroxidase; d-ALA-D, d-aminolevulinate dehydratase.

1 Introduction

Among the African medicinal plants, *Kigelia africana* (Lam.) Benth. (syn. *K. pinnata* (Jacq.) DC.) happens to be one of the most recognized due to its pantropical distribution (Dale and Greenway, 1961; Neba, 2006; Oliver, 1960; Sofowora, 1980). *K. africana* is a native of the African continent where it is commonly found in the southern, central and western regions (Burkill, 1985; Dunham, 1991) and widely used for treatment of a wide range of diseases and also as an agroforestry tree. The plant has been introduced to some countries of South-East Asia like India, Pakistan, China, Philippines and Iraq where it is mainly cultivated as an ornamental tree, commonly found in gardens and parks, both for its beautiful deep red flowers and its strange fruit; also in Miami, Florida, where it grown as a flamboyant tree and provides shade from the scorching sun for the inhabitants (Ann et al., 2002; Bygott, 1986; Kaur et al., 2011; Sharma and Kaul, 1993). Traditional African healers used preparations from different parts of *K. africana* to treat a wide range of skin complications and also to treat dysentery, constipation, wounds, ulcers, gonorrhea, rheumatism and abscesses among many others (Palmer and Pitman, 1972; Watt and Breyer-Brandwijk, 1962). Although its local recognition as a multipurpose tree with several domestic uses dates back to centuries (Beidelman, 1964; Dale and Greenway, 1961; Dalziel and Hutchinson, 1937), until recently, very little had been documented about its therapeutic potentials.

A number of concise reviews have been reported on its phytochemical and pharmacological uses (Gabriel and Olubunmi, 2009; Jackson and Beckett, 2012; Saini et al., 2009b) and more recent investigations have been conducted to evaluate its medicinal uses with results that either corroborates the previous findings or contravenes it. Interestingly, the commercial exploit and industrial utilization of the plant's parts, especially by the pharmaceutical and cosmetic industry, have thrived with a proportional surge in research interest (Van Andel et al., 2012; Van Wyk, 2008; 2015). The present review attempts to provide a more comprehensive and up-to-date report not only

on the ethnobotany, pharmacology, phytochemistry and traditional uses but also to compare the different studies conducted on its medicinal potentials, highlight the novel phytochemicals isolated and their respective activity as well as the nutritional, economical and industrial application of *K. africana* using both reported and unreported indigenous data in order to serve as a guide for further researches and other exploits on the medicinal and industrial potentials of this plant.

2 Methodology

The selection of relevant data was made through systematically searching the scientific databases (PubMed, Scopus, SciFinder and the Web of Science), Google and Google Scholar. The search terms used were "Kigelia", "Kigelia africana", "Kigelia pinnata" and "Sausage tree". Additional information on traditional use and botany was obtained from published books, dissertations and also oral input from few reputed traditional medicinal plant sellers in Sokoto state of northwestern Nigeria. The taxonomy of *K. africana* was validated by the databases (http://www.theplantlist.org/tpl1.1/record/kew-317427).

3 Botanical description and geographical distribution

Kigelia is now generally considered to be a monospecie genus of the family Bignoniaceae. Recently, the taxonomical identity of this species has become clearer after being referred to by several distinctive names (FAO, 1986; Houghton and Jâger, 2002). *K. africana* is a medium to large semi-deciduous tree that can grow up to 25 m in height, with a dense rounded crown (Fig 1). The leaves form an opposite extension which are crowded near the ends of branches with 3-5 pairs of leaflets plus a terminal leaflet; the lower leaflets have short petiolate, while the terminal pair are without petioles (Jackson and Beckett, 2012). The flowers are conspicuously dark-red with a cup-like shape that blooms at night on long, ropelike stalks that hang down from the limbs of the tree and fall off before morning. The foul-smelling and nectar-rich blossoms are pollinated by bats, insects and sunbirds in their native habitat (Harris and Baker, 1958). Its fruits are long and woody,

sausage like in appearance, hanging from the tree on a long cord-like stalks. The fruit are incredibly large and can grow up to 1 m x 18 cm, weighing up to 12 kg; thus caution should be exercise to avoid bodily injuries and damage to properties which falling fruit can cause under the tree. When ripe, the fruits appear greyish-brown and contain a hard inedible pulp in which many seeds are embedded (Gabriel and Olubunmi, 2009).

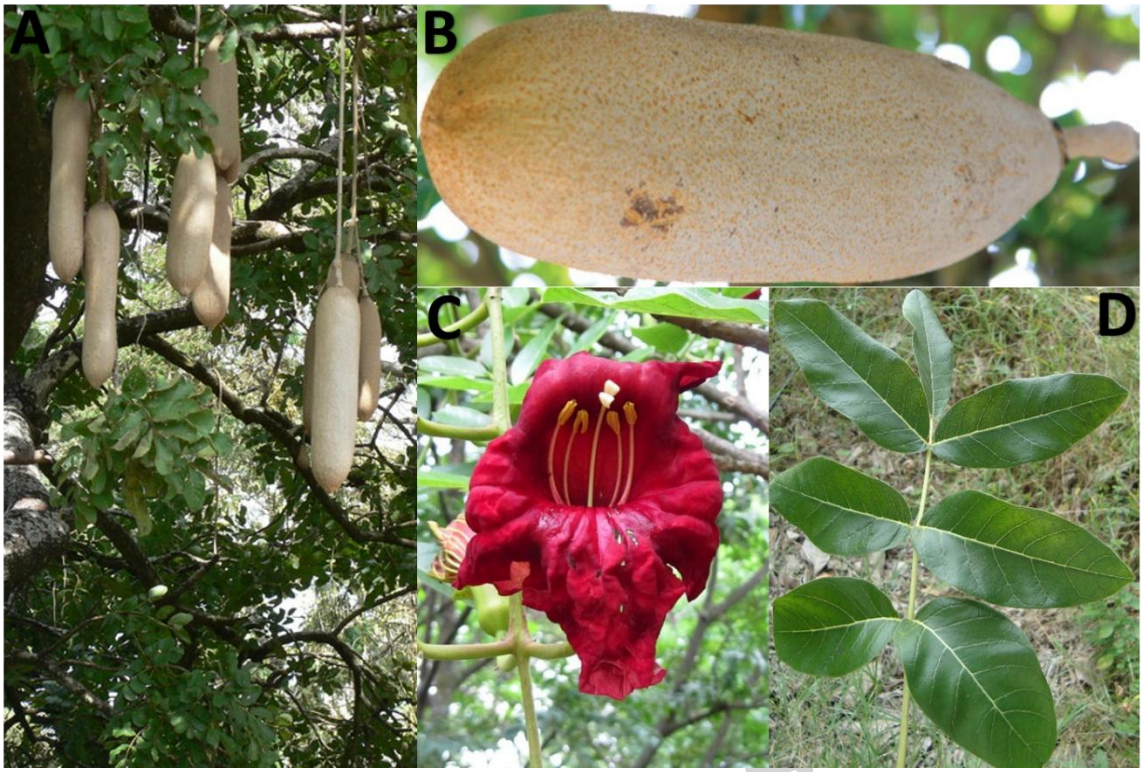

Figure 1: Pictures showing *Kigelia africana* tree with hanging fruits (A) fruit (B) flower (C) and leaves (D)

It is essentially a moisture–loving tree mostly found on riverbanks, along streams, in open woodlands and also on floodplains of Nigeria, Cameroon, Kenya, Guinea, and Senegal. It can also be found in open woodland from KwaZulu-Natal (South Africa) to Tanzania, Chad, and Namibia (Fig 2). In the Americas, sausage tree was one of the first tropical fruits and plants introduced by James L. Nugent (Henry, 1949) and since then has been an ornamental tree present in most gardens of south Florida (Austin, 1978) and other parts of South-east Asia (Ann et al., 2002; Lal and Yadav, 1983; Lim, 2012). In the open grassland, its expansive canopies makes it a useful shade tree. The common name 'sausage tree' is derived from the cylindrical shape of the fruit. In the African continent, it has several local names; *worsboom* (Afrikaans); *pandoro* (Yoruba, Nigeria) *muratina* (Kikuyu, Kenya); *mbungati*, *mwegea*, *mnyegea*, *mvongonya* (Swahili, South-east Africa): *balam kheera*, *hathi bailan* (Hindi, India); *yago* (Luo); (Malayalam) *shiva kundalam*; *yaanai pudukan* (Tamil, India) (Beidelman, 1964; Smith, 1966; Sofowora, 1980).

Figure 2: The map of Africa showing native geographic distributions of *Kigelia africana* (Lam.) Benth [adopted from FAO (1986) with modification].

4 Traditional uses

4.1 Medicinal uses

Traditionally, the tree is more widely known for its medicinal uses; commonly in the treatment of various skin related disease such as eczema, fungal infections, psoriasis and boils; to the more serious diseases, such as leprosy, impetigo, syphilis and skin cancer (Jackson and Beckett, 2012; Oyedeji and Bankole-Ojo, 2012). It also has internal applications, including the treatment of dysentery, malaria, diabetes, pneumonia, worm infestations, venereal diseases, convulsions,

toothache and as antidote for snakebite (Burkill, 1985; Houghton and Jâger, 2002; Maregesi et al., 2007). The fruit is believe to be a remedy for essentially all gynaecological complications (Awai and Igoli, 2015; Grace et al., 2003; Oyelami et al., 2012). Table 1 summarizes the traditional medicinal uses of different parts of the plant and the method of preparation and application.

4.2 Non-medicinal uses

The plant has a wide range of uses in the African communities. Besides it use as a traditional medicinal plant, it is also used as fodder for animals. While the fresh fruit is poisonous and technically inedible to humans due to its laxative effect on the bowel and the formation of blisters on the skin, the fruit seedling is eaten by monkeys, hippos, baboons, while the leaves are consumed by elephants and giraffes (Neuwinger, 1996; Watt and Breyer-Brandwijk, 1962). In Zimbabwe, *K. africana* have important spiritual values; it is believed that it can be used to hunt for witches and prevent witchcraft. The bark is used in preparing a witch-confession medicine to be drunk (Beidelman, 1963; Campbell et al., 1991). Among the Luo tribe in western Kenya, the fruit is used in funeral rites as a symbolic substitute for the body of a relative who has met a violent death in a distant place and whose remains could not be recovered (Raintree and Hoskins, 1988). It is particularly believed to be one of the only two plants with non-edible fruit that improve the fertility of soil for cultivation (McGregor, 1989). The fruit is a common ingredient in traditional alcoholic beverage called “dengelua" made by the Pare tribe (Wendelin et al., 1997). A Sausage Tree trunk makes good shelves, fruit boxes and dugout canoe used for fishing (Venter and Venter, 1996; Weiss, 1979).

5 Phytochemistry

Up to date, approximately 145 phytoconstituents have been isolated from different parts of the plant with iridoids, naphthoquinones and flavonoids as the major class of compounds. Coumarins,

terpenes, terpenoids and steroids were also detected and compounds from these class of phytoconstituents have been identified from *K. africana*.

5.1 Flavonoids and phenolics

Five flavonoids were isolated from the leaves and bark of *K. africana* (Fig. 3). These include the ubiquitous flavonol quercetin (**1**), and the flavones; luteolin (**2**), 6-hydroxy liteolin (**3**) together with their respective glycosides (**4** and **5**) (El-Sayyad, 1981). Other flavonoid glycosides isolated include isovitexin (**6**) from the leaves (Atolani et al., 2014a) and isoschaftoside (**7**) from the fruit (Gouda et al., 2006). Coumarins are among the first phytoconstituents identified from *K. africana.* In 1971, 6-methoxymellein (**8**), kigelin (**9**) and 3-demethylkigelin (**10**) were isolated from the root and bark (Govindachari et al., 1971) while 6-demethylkigelin (**11**) was identified from the fruit, bark and leaves (Dhindsa, 2005; Higgins et al., 2010). Of the phenolic class, five coumaric acids derivative were identified. These include 4-hydroxycinnamic acid (**12**), caffeic acid (**13**), caffeic acid methyl ester (**14**), ferulic acid (**15**) and 3, 4-dimethoxy cinnamic acids (**16**) (Dhindsa, 2005; Govindachari et al., 1971; Khan et al., 2012; Picerno et al., 2005). other phenolic acids identified are kojic acid (**17**) (Eyong et al., 2012; Sidjui and Zeuko'o, 2014), melitolic acid (**19**) (El-Sayyad, 1981), ethylgallic acid (**18**) and chlorogenic acid (**20**) (Arkhipov et al., 2014b).

5.2 Iridoids and limonoids

Iridoids are the major chemical compounds present in *K. africana* (Fig. 4). The first iridoid to be isolated was norbiturnial (**24**) (Asekun et al., 2007; Joshi et al., 1982). Gouda et al. (2003) isolated the simple iridods 10-deoxyeucommiol (**21**), 7-hydroxy-10-deoxy-eucommiol (**22**), 7-hydroxy eucommic acid (**23**), des-p-hydroxybenzoyl kisasaganol (**25**), jofuran (**26**) and jioglutolide (**27**), 7-hydroxy viteoid II (**29**) and 1-dehydroxy-3,4-dihydroaucubigenin (**30**); together with the iridoid glycosides ajugol (**32**) and caffeoyl ajugol (**33**) . Other iridoid glycosides characterize so far are

rehmaglutin C (**28**), catalpol (**31**), specioside (**34**), verminoside (**35**), minecoside (**36**) (Akunyili et al., 1991; Arkhipov et al., 2014b; Houghton and Akunyili, 1993; Khan et al., 2012).

Limonoids were also isolated and these include kigelianolide (**37**), khayanolide B (**38**), diacetylkhayanolide E (**39**), 1-O-deacetyl-2α-hydroxykhayanolide E (**40**) and 1-O-deacetyl-2α-methoxykhayanolide (**41**) (Jabeen and Riaz, 2013). Fig. 4 presents the structure of these class of compounds.

5.3 Phenyl ethanoglycosides and naphthoquinones

Phenyl ethanoglycoside from *K. africana* play a major part in its medicinal properties. From the fruit of *K. africana,* Gouda et al. (2006) isolated the phenyl ethanoglycosides decaffeoylacteoside (**42**), darensdoside A (**43**), verbascoside (**44**), isoacteoside (**45**), echinacoside (**46**), 2-(3-hydroxy-4-methoxyphenyl) ethyl O-α-L-rhamnopyranosyl-(1→3)-[β-D-gluco-pyranosyl-(1→6)]-(4-O-feruloyl)-β-D-glucopyranoside (**47**) and jionoside (**48**) (Fig. 3), together with the phenyl propanoids 6-p-coumaroylsucrose (**49**), 6-O-caffeoyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**50**) and 6-O-furolyl-β-D-fructofuranosyl-(2→1)-α-D-glucopyranoside (**51**) (Gouda et al., 2006; Picerno et al., 2005). The phenyl propanoids atranorin (**52**) was obtained from the bark, shereaphenol (**53**) from the twig and vanillin (**54**) from the wood (Inoue et al., 1981; Khan et al., 2012; Zofou et al., 2011).

Another class of major phytoconstituents present in *K. africana* are the naphthoquinones (Fig. 5). Lapachol (**55**) and its derivative dehydro-α- lapachone (**56**), kigelinone (**57**) and pinnal (**60**) were the first isolated from the root, wood and fruit respectively (Govindachari et al., 1971; Inoue et al., 1981; Joshi et al., 1981; Joshi et al., 1982). 2-(1-hydroxyethyl)-naphtho[2,3-b]furan-4,9-dione (**58**), 2-acethylnaphtho [2,3-b]furan-4,9-quinone (**59**), isopinnatal (**61**), kigelinol (**62**), isokigelinol (**63**) and 3-(2′-hydroxy-ethyl)-5-(2-hydroxypropyl) dihydro-furan-2(3H)-one (**64**) were obtained from its fruits (Arkhipov et al., 2014b; Higgins et al., 2010; Moideen et al., 1999). Tecomaquinone-1 (**65**)

was obtained from the chloroform partition of the stem heartwood methanolic extract (Sharma et al., 2014; Singh et al., 2010b). The lignans sesamin (**66**), paulownin (**67**) and kigeliol (**68**) were also isolated from the leaves, fruits and wood of *K. africana* (Inoue et al., 1981; Sidjui et al., 2015).

5.4 Terpenes, terpenoids and steroids

Asekun et al. (2007) isolated the monoterpenes limonene (**69**), terpinolene (**70**), α-pinene (**71**), β-pinene (**72**), α-terpineol (**73**) β- terpineol (**74**), β-phillandrene (**75**), α-ionone (**76**), β-damascenone (**77**), β-cyclocitral (**78**), trans geraniol (**79**) and geranyl acetone (**80**); the triterpenes squalene (**81**) and linalool (**82**). The diterpene phytol (**83**) and two cytotoxic diterpenes; 3-hydro-4, 8-phytene (**84**) and trans-phytol (**85**) were isolated from the leaves (Atolani et al., 2013b; Dhindsa, 2005). Sidjui et al. (2015) isolated the triterpenoids fibrarecisin (**85**), canophyllol (**86**), pomolic acid (**87**), hydroxy-pomolic acid (**88**), lupeol (**89**) and β-friedelinol (**90**) from the leaves and fruits (Fig. 6). The triterpene 2β-hydroxyoleanolic acid (**91**) and triterpenoid 2β, 3β, 19α-trihydroxy-urs-12-en-28-oic acid (**92**) were identified from the bark (Zofou et al., 2011). The steroids present in *K. africana* are β-sitosterol (**93**) and its glycoside (**94**), γ-sitosterol (**95**) and Stigmasterol (**96**) (Khan et al., 2012; Sidjui et al., 2015).

5.5 Miscellaneous

X-ray crystallographic analysis of the heartwood extract of *K. africana* revealed the presence a chemical compound rhodamine B (**97**) known to be used as a dye (Joshi et al., 1981). Of the polyphenols, a chromone glycoside known as tolaside (**98**) was characterized from the leaves (Atolani et al., 2014b). Naphthalene (**99**) and its derivative Di-n-octyl phthalate (**100**) were detected in the leaves and flowers (Asekun et al., 2007; Atolani et al., 2011), are among the miscellaneous phytoconstituents (Fig. 7).

6 Pharmacological activities

6.1 Antioxidant activity

The *in vitro* antioxidant capacity of *K. africana* was assessed on the n-hexane root extract (Atolani et al., 2011; Atolani et al., 2009), methanolic extract of the leaves (Agyare et al., 2013; Sikder et al., 2011b), water extract of the fruit (Akanni et al., 2014) and the ethanolic extract of the stem bark, fruit and leaves on reducing power, DPPH (2,2-diphenyl-2-picrylhydrazyl hydrate) radical scavenging, inhibition of Fe^{2+}/ascorbate-induced lipid peroxidation, scavenging of hydrogen peroxide & hydroxyl radical or nitric oxide activities. The results obtained from *in vitro* antioxidant studies on *K. africana* extracts are presented in Table 2.

In evaluating the wound healing activity of *K. africana* root extracts, Hassan et al. (2015) also studied the *in vivo* antioxidant activity on granulated tissue formed on the wound and liver tissue from rats orally treated with three doses (200, 400 and 600 mg/kg b.w). The extract was found to significantly and dose-dependently increased the granulated tissue glutathione (from 104.55 ± 3.52 in control rats to 246.40 ± 9.64 mg/100 mL in rats treated with 120 mg/kg b.w) and catalase concentration (0.76 ± 0.04 in control and 3.04 ± 0.09 µ/mg tissue); similarly, lipid peroxidation was reduced [0.52±0.09 in control and 0.06 ± 0.01 (nmole/g tissue) × 10^{-5} at 120 mg/mL]. This trend was also observed in the liver tissue homogenate of the treated rats, with the catalase and glutathione levels significantly improved and a reduction in lipid peroxidation. The boiled water extract of *K. africana* showed a significant protective effect against the formation of thiobarbituric acid reactive substances (TBARS) induced by different pro-oxidants (10 mM FeSO4, 5 mM sodium nitroprusside SNP and 2 mM 3-nitropropionic acid) (Olalye and Rocha, 2007). Moreover, *K. africana* also attenuate the lipid peroxidation effect and improve the activity of antioxidant enzymes such as superoxide dismutase (SOD), catalase (CAT), gluthathione peroxidase (GPx), and d-aminolevulinate dehydratase (d-ALA-D) activities, in paracetamol-induced liver damage in mice

(Azu et al., 2010a; Olaleye and Rocha, 2008). It is evident that the antioxidant potential of *K. africana* harmonizes its protective effect against liver damage and also facilitate its anti-inflammatory and wound healing effects. Although the antioxidant activity was more evaluated on the leaves (Table 2), the folkloric evidence shows that the stem bark and fruits are more recognized for their medicinal uses than the leaves. In cases where antioxidant evaluation of different parts of the plant was conducted simultaneously (Agyare et al., 2013; Solomon et al., 2014), the bark was reported to be more effective.

The plant's antioxidant potential is attributed to the presence of good number of phenolic and flavonoid compounds (Akanni et al., 2014; Sikder et al., 2011b). Isolated compounds from the leaves of the methanol extract of *K. africana* also showed antioxidant activity. Verbascoside (**47**) from *K. africana* possessed remarkable antioxidant properties in the *in vitro* experiments (Alipieva et al., 2014). Its metabolites were shown to significantly enhance the activities of major antioxidant enzymes (catalase, glutathione peroxidase and glutathione reductase) while suppressing pro-oxidant myeloperoxidase in the circulating lymphocytes, erythrocytes and neutrophils of rats (Quirantes-Piné et al., 2013).

6.2 Antimicrobial activity

One of the most common uses of *K. africana* in local medicine is the treatment of wide range of infectious diseases caused by microorganisms. Several investigations have been conducted on solvent extracts from different parts of the plant for antimicrobial activity; particularly the antibacterial and antifungal effect, with few studies on its antiviral activity. These studies have reported mixed-results as highlighted in the sub-section and summarized in Table 3.

6.2.1 Antibacterial

The antibacterial effect of *K. africana* against different strains of bacteria has been reported with highly variable results (Chenia, 2013; Fomogne-Fodjo et al., 2014; Kone et al., 2004; Naidoo et al., 2013). A preliminary antimicrobial assay of the methanolic extracts of the fruit and root gave significant inhibitory effect against gram-positive organisms tested (inhibitory zone range of 14-18 mm and 12-14 mm) but not significantly against the gram-negative. The streptomycin sulphate standard gave inhibitory zone of 18-26 mm at concentration of 1 mg/mL against these same gram-positive organisms (Binutu et al., 1996). The crude aqueous extracts of *K. africana* stembark showed significant antimicrobial activity, although less pronounced compare to the methanolic extract (Akunyili et al., 1991).

Idris et al. (2013) isolated seven distinct species of endophytic fungi cultured from different tissues of *K. African* of which four species were successfully identified as *Aspergillus flavus, Aspergillus* sp., *Curvularia lunata* and *Cladosporium* sp. Antibacterial screening was conducted on the fungi species crude extracts against *Bacillus subtilis, staphylococcus aureus* and *Escherichia coli.* The growth inhibition zones diameter (I. Z. D) values varied, ranging between 14-37 mm. The extracts from *Cladosporium* sp., *Aspergillus* sp. and two of the unknown species were effective with I. Z. D > 20 mm against all the bacterial strains. Meanwhile, the n-hexane extract of *K. africana* showed strong antibacterial effect against *Bacillus cereus* with a minimum inhibitory concentration (MIC) of 250 mg/mL and also against *S. aureus* (MIC 500 mg/mL) (Maregesi et al., 2008)

The aqueous, methanolic and chloroform extracts of *K. africana* bark were tested against *E. coli, Enterobacter aerogens, Klebsiella pneumoniae, Salmonella typhi, Proteus vulgaris, Pseudomonas aeruginosa* (Gram-negatives), *S. aureus* and *Bacillus cereus* (Gram-positives) by disc diffusion method (Jeyachandran and Mahesh, 2007). The methanolic extract presented a higher activity than the aqueous and chloroform extracts. The highest activity was exhibited against *S. typhi* and *P.*

vulgaris and moderate against *E. coli*, *S. aureus* and *B. cereus*. Less activity was observed against the remaining strains viz., *E. aerogens, K. pneumoniae* and *P. aeruginosa*. According to Ankur et al. (2011), the ethanolic and aqueous extracts of *K. africana* shows antibacterial activity at 20 mm and 17 mm zone which is similar to the result obtained by of Jeyachandran and Mahesh (2007). The dichloromethane, ethyl acetate and ethanolic extracts *K. africana* (bark) inhibited growth of *M. aurum* A+ with MIC values ranging between 0.19 and 1.56 mg/mL (Eldeen and Van Staden, 2008). Inhibition of *M. aurum* A+ growth is highly predictive of activity against *M. tuberculosis* (Chung et al., 1995).

Contrary to the positive antibacterial activity of *K. africana* as cited above, McGaw et al. (2000) reported a negative antibacterial results on this plant. According to this study, the methanolic, ethanolic and aqueous extract of *K. africana* leaves (100 mg/mL) did not exhibit activity against *B. subtilis*, *E. coli*, *K. pneumoniae* and *S. aureus*, (McGaw et al., 2000); though, in the same article, it also did not exhibit anti-amoebic activity but was active against nematodes (2-h and 7-day anthelmintic assays; at 2 mg/mL). However, *K. africana* was one of twenty five plants that was reported inactive among several species that were investigated. The inactivity maybe relative to the activity of the other 20 plant species that were reported.

It is interesting to know that the antibacterial effect of a number of bioactives isolated from various extract and parts of *K. africana* has been investigated. The aqueous extracts of the stem bark of *K. africana* contain iridoids as major components. In light of the traditional uses of this plant, antibacterial activities of the aqueous extracts and two major iridoids were tested against *B. subtilis*, *E. coli*, *P. aeruginosa*, *S. aureus* and *Candida albicans*. The crude aqueous extracts showed significant antimicrobial activity which could be partially explained by the activity of the iridoids present (Akunyili et al., 1991). Fractionation of the methanolic extracts of the root and fruits of *K. africana* led to the isolation of naphthoquinones. These class of compounds and their derivatives have been documented as potent antimicrobials (Brandelli et al., 2004; Riffel et al., 2002). From

this class, compounds **66** (which is the most active with MIC = 100 µg/mL) **64**, **59**, **58**, **12** and **15** isolated from the root were observed to be responsible for the antibacterial and antifungal effects (Binutu et al., 1996).

6.2.2 Antifungal

Most studies on the antifungal effect of *K. africana* were conducted in conjunction with the antibacterial activity. Against *C. albicans*, n-hexane extract of *K. africana* stem bark exhibited a weak minimum fungicidal concentration (MFC), which is above 1000 mg/mL (Maregesi et al., 2008; Shai et al., 2008). However, Owolabi et al. (2007) reported a better activity of the ethanolic extract against *C. albicans* with zones of inhibition measuring 20.75 ± 4.6 mm and an MIC of 7.92 ± 1.52 mg/mL.

The methanolic, water and ethyl acetate extracts of *K. africana* fruit powder also displayed broad spectrum of antifungal activity, each inhibiting the growth of 3 out of the 4 fungal species tested (*Aspergillus niger*, *C. albicans* and *Penicillium chrysogenum*; 75% MIC < 200 µg/mL) with much more lower efficacy compared to the bacterial species (MIC> 200 µg/mL). The extracts were effective in the order methanolic, ethyl acetate with the aqueous extract being the least active. Only *P. crysogenum* was resistant to these extracts. the zones of inhibition were relatively small, indicating that growth inhibition was not particularly strong for any extract against any of the fungi specie tested (Arkhipov et al., 2014a).

Serial extract of *K. africana* stembark were also investigated for their antifungal effect. The chloroform extract was observed to show the highest activity (MIC = 0.625- 1.25 µg/mL) than the petroleum ether and methanolic extract against the fungal strains *Cryptococcus neoformans*, *Candida tropicalis*, *Trychophyton rubrum*, *Microsporum furfure* and *Epidermophyton floccosum* (Jain and Belsare, 2009). The fruit methanolic extract of the plant was found to be active only

against *C. neoformans* out of six strains of fungi tested, albeit, with an MFC > 1 g/mL (Hamza et al., 2006).

6.2.3 Anti-viral

The growing endemic nature of HIV infections coupled with the appearance of drug-resistant strains has stimulate an urgency to identify new antiviral therapeutics against HIV-1. Moreover, the contemporary antiviral therapies offered at hospital institutions are too expensive for most Africans. This has created the urge to proffer alternative and cost effective means to manage the AIDS epidemic in Africa. One of the approaches is by utilizing plants based on their ethnomedicinal potentials. *K. africana* is one the medicinal plants used for the treatment of HIV-opportunistic infections and other viral diseases in some regions of Africa (Chinsembu et al., 2015; Lamorde et al., 2010; Oladunmoye and Kehinde, 2011).

Rukunga et al. (2004) studied the antiretroviral effect of some medicinal plants. *K. africana* leaves extract showed a weak inhibitory effect (33.07% at 100 µg/mL and 11.13% at 50 µg/mL) against HIV-1 reverse transcriptase. Even weaker is the fruit extract (13.20 % at 100 µg/mL and 0% at 50 µg/mL). The methanolic extract of the fruit tested against various viral strains showed a weak activity against one strain (Vesicular Stomatitis Virus T2; 1000 ug/mL: RF = 102), with no effect against Herpes Simplex Virus type 1 (HSV1), Coxsackie B2 (Cox B2) and Semliki Forest Virus A7 (SF A7) (Maregesi et al., 2008).

6.2.4 Antimalarial effect

Amongst several of its folklore medicinal uses is its traditional application as a remedy for malaria which has been documented in literatures (Azokou et al., 2013; Chinsembu, 2015; Moo-Key Kim, 2002; Oladele and Adewunmi, 2008). Others have conducted experiments to validate this anecdotal use. Oketch-Rabah et al. (1999) investigated the antimalarial activity of Kenyan medicinal plants

and reported low antimalarial activity of both the aqueous and organic extract of *K. africana* leaves against *Plasmodium falciparum* parasite strains (K39 and V1/S with an IC_{50} 53.2 ± 9.8 and 42.2 ± 12.2 µg/mL respectively).

In vitro antiplasmodial activity of ethyl acetate extracts of the stem bark showed a significant plasmodial growth inhibition (IC_{50} of 11.15 µg/mL, 4.74 µg/mL and 3.91 µg/mL for W-2, CAM10 and SHF4 strains respectively), whereas the n-hexane fraction showed a weak activity (IC_{50} = 73.78 µg/mL on W-2 and 21.85 µg/mL on SHF4). Four compounds were isolated from the plant out of which three showed good activity against all the three different parasite strains (IC_{50} < 5 µM). The highest activity was exhibited by Specicoside (**34**) on W-2 (IC_{50} = 1.54 µM) followed by 2β, 3β, 19α-trihydroxy-urs-12-en-28-oic acid (**82**) (IC_{50} = 1.60 µM) and atranorin (**55**) (IC_{50} = 4.41 µM), while p-hydroxycinnamic acid (**12**) was the least active (IC_{50}=53.84 µM) (Zofou et al., 2011).

Pinnatal (**63**), a naphthaquinone amply present in *K. africana*, investigated against *Plasmodium falciparum* and ECV-304 cell line displayed high inhibitory activity (IC_{50} = 2.2 ± 0.3) (Onegi et al., 2002). Naphthaquinones have been ascribed with the plants antimalarial activity. This has been further corroborated by the assessment of Weiss et al. (2000) on the rootbark against chloroquine-sensitive (T9-96) and resistant (K1) *Plasmodium falciparum* strains *in vitro*. Kigelinol (**65**), isopinnatal (**64**) and isokigelinol (**66**) showed poor activity against both strains, while 2-(1-hydroxyethyl)naphtho[2,3-b]furan-4,9-dione (**61**) possessed good activity against both strains [IC_{50} values 627 nM (K1) and 718 nM (T9-96)].

6.3 Anti-inflammatory activity

The anti-inflammatory activity of several parts of the plant have been evaluated. The ethanolic stem bark extract have been reported for its activity against inflammation induced on the hind-paw of rats by carrageenan injection (Amali et al., 2012; Owolabi and Omogbai, 2007; Vikrant and Arya, 2011) whereas, in another study, the leaves were used (Kumari et al., 2012 ; Namita et al., 2012). Studies

have also been conducted on the fruit part of the plant extracted with methanol (Carey et al., 2008) as well as the flower part extracted by maceration with methanol (Carey et al., 2010). The callus of the plant have also been investigated (Wilkinson, 2009). Overall, the plant have shown efficacy against experimentally induced inflammations as reported. This activity was further supported by its inhibitory effect against prostaglandin synthesis enzyme, Cycloxygenase-1 (COX-1) and Cycloxygenase-2 (COX-2). The leaf and bark extracts from *K. africana* showed significant activity against COX-1 while only the leaf ethanolic and bark dichloromethane extracts showed significant activity against COX-2 (Eldeen and Van Staden, 2008).

Compounds isolated from the fruit have been identified as responsible for the observed anti-inflammatory activity. Verbascoside (**47**) and Verminoside (**35**) isolated from the methanolic extract of the fruit of *K. africana* are attributed with the anti-inflammatory activity of *K. africana* (Alipieva et al., 2014; Santoro et al., 2008). The anti-inflammatory activity of **35** has been credited to the inhibition of inducible nitric oxide synthase (iNOS) and NO release from macrophages as stimulated by bacterial lipopolysaccharides (Picerno et al., 2005) while **47** inhibit NF-κβ activation, TNFα release, iNOS activity and nuclear translocation (Carrillo-Ocampo et al., 2013; Speranza et al., 2010). The endophyte, *Botryosphaeria dothidea*, isolated from *K. africana* and screened for its immunosuppressive potential was found to inhibit the release of pro-inflammatory mediators, particularly TNFα (Katoch et al., 2015). Its immunopressive activity underscores its folklore use for treating rheumatism (Fouche et al., 2008).

6.4 Wound healing effect

Wound healing involves various phases which include granulation, collagenation, collagen maturation and scar maturation. There is a long history surrounding the use of *K. africana* in wound healing, particularly in relation to burns and bacterial infections (Carey et al., 2010; FAO, 1986; Irvine, 1961). It has also been recognized in India as one of the medical plants active in wound

healing (Alam et al., 2011). The wound healing activity of *K. africana* bark aqueous extract was studied on three different wound models, at two different dose levels of 250 and 500 mg/kg (Sharma et al., 2010). In incision wound model and dead space wound model, the aqueous extract significantly increased the skin tensile strength on the tenth post-wounding day, at both dose levels. A significant increase in dry granuloma weight and granuloma breaking strength was also observed in the extract treated groups in the dead-space wound model with an elevation in the hydroxyproline content, while the excision wound model showed a significant decrease in the epithelization period, as evidenced by the diminished eschar shedding period compared to control.

Agyare et al. (2013) also reported a positive result for the leaves and bark methanolic extract in excision wound model with the leaves extract being more potent; showing a significant influences ($p < 0.05$) on the rate of wound closure from 7^{th} to 15^{th} day after treatment while the bark extract exhibited similar effects on wound healing from 10^{th} to 18^{th} day after treatment. Histological studies revealed profuse angiogenesis, profuse proliferation of fibroblasts (extract-treated and positive control treated with the 1% w/w silver sulphadiazine ointment wound tissue specimens showed 70 to 80% and 60 to 70% thick, dense fibrosis respectively), enhanced collagenation and re-epithelialization amidst persistent inflammation with wound tissues treated with the extracts compared to the untreated wound tissues. On the same wound model, the hydromethanolic extract (doses of 30, 60, 90 and 120 mg/mL) of the root of *K. africana* dose-dependently reduced the wound healing time when compared to distilled water and procaine penicillin (Hassan et al., 2015). At 120mg/mL, complete healing of the wounds was observed on 16 to 19th day. Faster reddening, dryness, pigmentation and cicatrisation was observed in the groups treated with the root extract. Attributed with the wound healing activity of *K. africana* is the phytoconstituents verbascoside (**47**) which is known to possess a combined wound healing, anti-inflammatory and anti-nociceptive activity (Alipieva et al., 2014).

6.5 Hepato-protective Effect

K. africana has been identified as one of the tropical medicinal plants that exhibit hepatoprotective potential (Olalye and Rocha, 2007). Liver toxicity induced by paracetamol is attributed to increase in oxidative stress with concomitant alteration in the concentration or activity of intrinsic biological molecules that are essential for normal functionality of the liver. These include Lipid peroxidation, the liver function marker enzymes (AST and ALT) level, hepatic GPx, δ-ALA-D, superoxide dismutase (SOD) and catalase activity. Analysis of the liver homogenate from albino mice with paracetamol-induced liver damage revealed that the aqueous extract of *K. africana* leaves have significant hepatoprotective effect in juxtapose of its antioxidant activity and thus, act as an hepato-buffer against alteration in the aforementioned parameters (Olaleye and Rocha, 2008). The methanolic extract of the leaves was also studied, yielding positive result that corroborate the previous study (Hemamalini et al., 2012a).

The fruit part of the plant was also assessed for hepatotoxicity prevention on male wistar rats with CCL4-induced liver toxicity. Enzyme biomarkers and hematological parameters were found to be significantly altered in the extract treated groups compare to the control (Shama and Marwa, 2013). Apparently, none of the reported studies examine the histopathological impact of the treatment with *K. africana* on the liver cells, thus, leaving room for further comprehensive studies.

6.6 Analgesic Activity

The methanolic extract of the stem bark was evaluated on hot plate test and mouse writhing assay for analgesic activity. Significant dose-dependent decrease in writhing was recorded in the extract treated and aspirin treated mice (29.6 ± 7.31 and 36.8 ± 5.8/30min respectively) compare to the control mice (85.0 ± 1.34/30 min). However, the hot plate reaction time was not significantly increased in the hot plate test (Owolabi and Omogbai, 2007). In contrast to the above study, Namita et al. (2011) and Fredrick et al. (2014) reported a significantly ($P< 0.001$) prolonged reaction time

on hot plate at different time intervals in mice treated orally with the leaves methanolic extract which was dose dependent.

The flower was reported to show significant analgesic activity. The methanolic extract of *K. africana* flower decreased the number of acetic acid induced-writhing in mice treated orally with 100, 200 and 400 mg/kg when compared to control animals. The analgesic activity of the extract was dose-dependent with inhibition (of writhing) of 48.72%, 53.42% and 80.77% respectively for the designated doses of the extract, while the standard reference drug (diclofenac sodium, 20 mg/kg) showed writhing inhibition of 76.50%. Reaction time at different time intervals was significantly and dose-dependently prolonged in hot plate test. The extract also decreased the number of times licking the hindpaw in both the first and second phases in formalin-induced nociception in mice (Carey et al., 2010).

Pressure test using analgesy-meter, hot water tail immersion test and acetic acid writhing response test were conducted on Wister albino rats treated with cold ethanolic extract of the bark. The threshold of pain tolerance in animals after applying pressure on the tail of rats pre-injected intraperitoneally with 25 and 100 mg/kg of *K. africana* significantly increased by 277.6% ($p<0.001$) and 290.9% ($p<0.001$) respectively. Tramadol hydrochloride 5 mg/kg also produced an increase in pain tolerance threshold of 349.7% ($p<0.001$) in this same time period. The hot water tail immersion test also showed increased the percentage pain inhibition threshold of 46.15% and 71.67% at 50 mg/kg and 100mg/kg by respectively. The percentage inhibition of acetic acid-induced abdominal constrictions in mice at a dose of 50 mg/kg, was 49.20% ($p<0.01$) while 100 mg/kg of the extract produced 71.12% inhibition ($P<0.01$) (Amali et al., 2012). The root extract also showed a dose-dependent inhibition of writhing by 11.55% and 47.29% at a dose of 250 and 500 mg/kg respectively (Khan and Islam, 2012); which is less effective compare to other parts of the plant studied. There is no traditional description from literature or any report on anecdotal use

of this plant for analgesia. However, it is known to be used in wound healing (Carey et al., 2010; Fouche et al., 2008), an aspect to which its analgesic activity may be a contributing factor.

6.7 Antidiabetic activity

In streptozotocin induced diabetic rats, daily administration of the defatted methanolic extract of *K. africana* flower for 21 days led to a significant ($P < 0.001$) dose dependent drop in blood glucose levels (from 288.45 ± 2.30 mg/dL to 152.48 ± 2.7 mg/dL) and (298.29 ± 3.50 mg/dL to 138.43 ± 3.5 mg/dL) at the doses of 250 and 500 mg/kg of the extract respectively (Kumar et al., 2012b). There was also a reduction in total cholesterol and triglycerides which showed the hypolipidemic effect of this plant. Similarly, methanolic extract of *K. africana* leaves was found to decreased serum glucose levels in alloxan-induced diabetic rats at a dose range of 100–400 mg/kg. The significant ($P<0.01$) effect on serum glucose level was found at a dose of 400 mg/kg body weight, observed on 15th and 21st day of oral treatment. Moreover, the most pronounced decrease in serum glucose was observed on 21st day at a dose of 400 mg/ kg. However, at a dose of 100 mg/kg, the extract failed to lower the blood glucose to a significance level as compared with diabetic control rats (Priya et al., 2014).

Increase translocation and redistribution of the glucose transporter-4 (GLUT4), which is required for the uptake of glucose inside the cell, leads to increase in glucose absorption by the skeletal muscle. The ethanolic extract, together with compounds **31**, **34** and **36 (**10 μM) isolated from the n-butanol fraction and tested for their GLUT4 modulatory effect exhibited significant stimulation of GLUT4 translocation to cell surface from intracellular compartments with respective percent of 50.0 % ($p < 0.01$), 41.8% ($p < 0.01$) and 45.6% ($p < 0.01$) over control (Khan et al., 2012). In another study on the α-amylase inhibitory effect of various solvent extract of the leaves (acetone, ethanol, chloroform, and water), a significant reduction in the activity of the enzyme was observed.

At 500 µg/mL, the ethanolic extract gave the highest activity (0.151 µmol /mL/min) compare to the acarbose as standard (0.278 µmol /mL/min) (Dhriti et al., 2014).

6.8 Anti-ulcerogenic activity

Hemamalini et al. (2012b) reported the antiulcer activity of the methanolic extract of *K. africana* leaves in pylorus ligation-induced ulcer model. At 200 mg/kg, the extracts significantly reduced the ulcer index (7.41 ± 0.24 opposed to the control 11.29 ± 0.03) and the ulcer formation was also significantly reduced by 34.36%. Similar to the above, a significant reduction in gastric volume (4.65 + 0.07 mL), free fatty acid (56 ±1.6 mEq/L) and total acid (89.17 ± 1.42 mEq/L) was noted. A follow up study on aspirin-induced ulcer in rats showed that *K. africana* significantly ($P < 0.05$) reduced the ulcer index from 4.33 ± 0.27 to 0.67 ± 0.16 at a dose of 450 mg/kg. The free acidity, pH, total acidity content also decreased in all three tested concentrations of the three extracts. Also, a mild inhibition of the ulcer index and a significant reduction in the pH of the gastric acid of the extract-treated rats was reported compare to the control rats. The sialic acid content of the gastric juice was highest on aspirin administered rats (30 ± 1.15 µg/mL) and lowest for *K. africana* administered albino rats at concentration of 450 mg/kg (6.0 ± 1 µg/mL) (Orole et al., 2013).

K. africana leaves successively extracted with chloroform, diethyl ether and ethanol were investigated on three *in-vivo* rat ulcer models (Rajasekaran, 2014). At a dose of 200 mg/kg, the ethanolic extract showed a remarkable ulcer preventive effect of 70.46% followed by chloroform (57.84%) and diethyl ether (46.46%) in indomethacin-induced gastric ulcer. A dose-dependent ulcer prevention was also witness in rats administered with the extracts compare to the control in alcohol-induced gastric ulcer. Pylorus- ligation induced gastric ulcer was also attenuated by pretreatment with *K. africana* extract (doses of 100 and 200 mg/kg) by reducing the ulcer index, gastric volume, free acidity, total acidity and gastric pH significantly in comparison with control group (Rajasekaran, 2014). Another study on ethanol-induced stomach ulcer in albino rats indicated

a significant reduction in ulcer index in post-treated rats (ulcer index: 3.25 ± 0.21 at 7 mg/kg) compare to the ulcer-induced control rats (ulcer index: 16.25 ± 0.52) (dos Santos et al., 2014) with restoration of the stomach vitamin C concentration.

6.9 Antidiarrheal activity

One of the local medicinal use of this plant is in the management of diarrhea. In south Africa, *K. africana* is locally use to treat diarrhea and dysentery (Würger et al., 2014) while in west Africa, the Fulani cattle-rearing nomads are known to use *K. africana*, among other herbal remedies, in managing cattle diarrhea (Offiah et al., 2012). In 1996 the antidiarrheal activity of *K. africana* was investigated. The study revealed a preventive effect against castor oil-induced diarrhea in the extract-treated animals with concomitant reduction in fecal output. A significant attenuation in nicotine-induced contraction and mild effect on acetylcholine and histamine induced contractions was observed on the isolated guinea pig ileum (Akah, 1996). This is further consolidated by subsequent study by So and Uzochukwu (2010), who reported that the ethanolic extract of the root exhibited a dose-dependent antidiarrheal effect mediated by delaying the onset of diarrhea, minimizing the incidence of stooling and prevention of loose stool production.

6.10 Cytotoxic and anticancer activity

Pharmacological research interest regarding the anticancer potential of the plant were propelled by anecdotal reports for the traditional use of the fruit and stem bark extracts by indigenous African herbalists and the populace amongst whom the plant has a reputation as one of the herbal remedies that can be effectively used for treatment of cancer related infections, particularly melanoma and other skin neoplasms (Houghton and Jâger, 2002), as well as for the management of endometrial cancer (Ashidi et al., 2010; Ochwang'i et al., 2014).

The seed oil obtained from n-hexane extract showed significant suppression of heterogeneous human epithelial colorectal adenocarcinoma (Caco-2) and Human Embryonic Kidney cell (HEK-293) growth at all oil concentrations compared to the control ($p<0.05$). A significantly greater cell growth suppression ($p<0.05$) of Caco-2 cells than HEK-293 cells was observed at concentrations higher than 20 mg/mL (Chivandi et al., 2012). Moderate *in vitro* anticancer activity was reported for the leaf (dichloromethane) and root (methanolic and dichloromethane) extracts against renal (TK10), ER positive breast cancer (MCF-7) and melanoma cancer (UACC62) cell lines with respective total growth inhibition (TGI) of 42.9 µg/mL, 15.0 µg/mL and 8.02 µg/mL for the leaf and 14.90 µg/mL, 8.82 µg/mL and 0.01 µg/mL for the root extracts (Fouche et al., 2008). Human Rhabdomyosarcoma (RD) cancer cell line was used to evaluate the cytotoxicity activity of hexane, ethyl acetate and methanolic extracts of the root using 3-[4,5-dimethylthiazol-2-yl]-2,5-diphenyltetrazolium bromide (MTT) cell viability assay. Ethyl acetate extract (IC_{50}, 142.2 ± 1.1 ng/mL) gave the highest activity compared to the reference drug, cyclophosphomide (IC_{50}, 165.6 ± 1.0 ng/mL) (Atolani et al., 2013a).

The methanolic bark extract and its chloroform fractions was evaluated for *in vitro* cytotoxic effect against several human cancer cell lines of some important tumor diseases namely: B-cell lymphoma (DOHH-2), acute lymphoid leukemia (SKW-3 and REH), MCF-7, acute myeloid leukemia (HL-60), Hodgkin lymphoma (HD-MY-Z) and chronic myeloid leukemia (K-562) using MTT-dye reduction assay. The activity (MTT assay) against the cell lines was in order of MCF-7 (IC_{50} = 11.8 ± 3.8 µg/mL), the murine Lewis lung cancer (10.2 ± 2.7 µg/mL) and the acute T-cell leukemia SKW-3 (15.1 ± 3.4 µg/mL) which were significantly different compare to other cell lines (Momekova et al., 2012). The *in vitro* anti-proliferative activity of the root oil and its extracts was reported by Atolani et al. (2014c). Using MTT assay on the breast cancer cell lines (MDA cells), the cytotoxic effect of the ethyl acetate extract was the most effective (with IC_{50} = 5.01 ± 0.01

µg/mL) which followed by the root oil (IC_{50} = 10.53 ± 1.60 µg/mL). Least effective is the methanolic extract with IC_{50} = 33.01 ± 9.20 µg/mL.

In the *in vivo* antineoplastic study of the methanolic extract (37.3, 75 and 100 mg/kg) against Lewis lung carcinoma-bearing BDF-1 mice, the middle dose (75 mg/kg) elicited a better result with an increase the median survival time (MST = 34.4 days) compare the control (MST = 20 days); life span also increased by 66.7% while TGI was in the range of ca. 80 and 90% (Momekova et al., 2012). Female swiss albino mice induced with Ehrlich ascites carcinoma (EAC) tumor were treated with leaves methanolic extract for antitumor activity. The tumor size was significantly less in treated (6.697 ± 0.17 mm at 200 mg/kg) and positive standard group (4. 8 ± 0.19 mm for 5-Fluorouracil 20mg/kg/day) compare to control (10.83 ± 0.20 mm). Median survival time (MST) and life span also improved (Sri Sainadh et al., 2013). In mice benzo (a) pyrene-induced forestomach tumorgenesis model, oral administration of the extract to resulted in a significant inhibition in the tumor incidence and burden by 67% and 76%, respectively (Azuine et al., 1997). The dichloromethane extract of the stem bark inhibit the growth of four melanoma cell lines and a renal cell carcinoma line (Caki-2) examined using MTT and sulforhodamine B (SRB) assays (Houghton et al., 1994).

Several cytotoxic agents have been isolated from the plant by bioactivity-guided bioassay. Antiproliferative activity of compounds isolated from *K. africana* was determined by MTT assay against the human melanoma cell lines (SK‐MEL‐28 and Malme-3M) and breast cancer cells (MCF-7 and MDA‐MB‐468). Hydroxyethyl)-naphtho [2,3-b]furan-4,9-dione (**61**) was highly active with an $IC_{50} \leq 1$ µg/mL for all cell lines. Ferulic acid (**15**) gave an IC_{50} of 88.3 ± 11.5 and 71.7 ± 33.3 µg/mL for SK‐MEL‐28 and MalME-3M cells respectively, but no activity against breast cancer cells. Other compounds have $IC_{50} > 150$ µg/mL or no activity (Higgins et al., 2010). The n-hexane stem bark extract of *K. africana* and two of its products, atranorin (**55**) and 2beta, 3beta, 19 alpha-trihydroxy-urs-12-en-28-oic acid (**82**) showed cytotoxicity at high concentrations,

with **82** being more cytotoxic (EC_{50} = 9.37 mug/mL) (Zofou et al., 2011). Lapachol (**58**) (regarded as a potential anti-cancer drugs) (Higgins et al., 2010), norviburtinal (**24**) and isopinnatal (**64**) were reported to be active against melanoma cell lines (Houghton and Jâger, 2002; Jackson et al., 2000). Nevertheless, the relative contribution of the different compounds to the observed activity of the extracts remains elusive, mainly because these active compounds (e.g. norviburtinal and lapachol) are present in the plant materials at very low concentration to be asserted as the main anti-cancer constituents, while the cytotoxicity of others, such as γ-sitosterol has remained an issue of debate (Jackson et al., 2000; Khana and Mlungwanab, 1999).

6.11 Effect on male and female reproductive organs

Recently, studies have been conducted to validate the folklore use of *K. africana* in the management of fertility-related dysfunctions in both men and women (Dada et al., 2010; Naidoo et al., 2013; Ogbeche et al., 2002; Telefo et al., 2011).

Azu et al. (2009) conducted a preliminary study on the androgenic activity of *K. africana* fruit extract on male Sprague-Dawley rats orally administered with 100 and 500 mg/kg methanolic extract. After 4 weeks of treatment, semen assay revealed a significant increase in sperm count by 41.22% and 25% in the 100 and 500 mg/kg treated groups respectively, with a motility above 70%. Testosterone level was observed to have markedly increased ($p< 0.001$) compare to control groups. Serum concentration of testosterone (ST), follicle stimulating hormone (FSH) and luteinizing hormone (LH) were elevated with a concomitant increase in testicular weight. Histological examination of rats treated with *K. africana* (100 and 500 mg/kg) at both short and long term durations did not show any adverse effect on the germinal epithelium. interestingly, the 100 mg/kg dose was more effective in enhancing the parameters recorded than the 500 mg/kg dose (Azu et al., 2009). In a more extensive study on the effect of *K. africana* on cisplatin-induced testicular histo-morphometric changes in Sprague–Dawley (SD) rats, and in line with their previous findings, the authors reported an increase in sperm count, protozoal motility and androgenic hormonal activity

with a corresponding increase in the weight of the testes. Furthermore, the authors observed a preventive effect of *K. africana* against lipid peroxidation in the extract-treated rats compare to the capsacin-induced untreated rats, an upregulation of the glutathione pathway and a significant increase in the level of catalase which substantiate its antioxidant capacity (Azu et al., 2011; Azu et al., 2010b). In another study on the fertility activities *K. africana* fruit, an enhanced sperm motility ($p< 0.01$, 95.14 ± 1.35%) was observed when compared to that of male rats treated with testosterone and the untreated control rats which had 89.34 ± 1.45% and 82.81 ± 2.51% respectively. The result also showed that 77.8% pregnancy of mated pro-estrus female rats, 66.7% pregnancy rate in females mated with testosterone induced male and 44.4% for the control were recorded after a four day circle (Ogbeche et al., 2002).

On the other hand, a study on rats with arsenic-induced gonado-tocixity reported an antithetical result from the aforementioned, where treatment with *K. africana* (250 and 500 mg/kg) did not attenuate the significant ($p<0.05$) decrease in the level of serum testosterone (ST) (1.0863 ± 0.01575 nmol/L), luteinizing hormone (LH) (70.22 ± 5.46 mIU/mL) and follicle stimulating hormone (FSH) (36.58 ± 1.03 mIU/mL) in rats simultaneously treated with arsenic compared to control (ST, 1.10 ± 0.0032 nmol/L; LH, 150.28 ± 35.04 mIU/mL; and FSH, 40.31 ± 8.25 mIU/mL). Histopathology of the testes showed varying degree of cellular degeneration and necrosis in rats treated with arsenic. However, the toxic damages were not reversed or mitigated by *K. africana* extract. Consequently, the authors suggested that *K. africana* is ineffective as an antidote against gonadotoxicity (Bakare et al., 2015).

Although *K. africana* is largely used by African women as a panacea for gynecology and obstetrics complaints and sexual enhancement, few studies have been conducted with the intent of providing a scientific evidence to corroborate the traditional claims. Oyelami et al. (2012) reported an interesting revelation on the possible use of *K. africana* in the management of Polycystic Ovary Syndrome (PCOS) conducted on two patients (Case 1 and Case 2). After about a year of therapy on

K. africana powder, a reversal of the pathognomonic features in the right ovary of the second case suggests the usefulness of the plant in the management of the ailment. However, a more in-depth clinical examination and further tests on related body substances was recommended by the authors to buttress this finding.

6.12 Dermatological and Cosmetic Uses

Over the past decade, there has been growing interest by cosmeceutical market on natural plant products that have been reported to be used in ameliorating skin problems because of their perceived safety (Stallings and Lupo, 2009). In traditional African medicine, the fruits of *K. africana* are apply topically as poultice, paste and emollients to treat various skin irritations such as eczema, psoriasis and also for general skin care; particularly among African women. In certain African populations, women grind the fruit poultice, which is then rubbed on the breast to improve its firmness (Grace et al., 2003; Houghton and Jâger, 2002; Neuwinger, 1996). With documented and asserted anecdotal evidences supporting its usefulness in skin management among the African populace, it is no surprising that these properties are getting fervent attention from the cosmetic industry with the intent of producing various dermatological and cosmetic products. A number of advertised skin products containing *K. africana* can be found online (Table 4).

Majoe (2001) reported two cases of improvement in patients suffering from skin problems after using products containing *K. africana*; A 45 year old man suffering from psoriasis (case 1) and a female patient with eczema since birth and in her late forties (case 2). The patient in case 2, who experience severe flare-ups on her face, was reported to be free of eczema after experimenting with *K. africana* cream for three months. Still, no empirical, statistical and quantitative inference can be drawn from just two random reported cases. The general and specific etiology of most skin diseases are not clear (Brandt, 1950; Burns, 2004). However, it is now accepted that most skin diseases are chronic, immune-mediated inflammatory diseases (Braae Olesen, 2012; WHO, 2005), which susceptibility to infective agents is further compounded by the direct access of otherwise harmless

skin flora microorganism (e.g *Diphteroids* and *Staphylococci*) to the intradermal musculature (Griffiths and Barker; Scott, 1989); it may lead to microbial colonization and subsequent cutaneous infection. Thus, the antimicrobial and anti-inflammatory effects of *K. africana* may enhance it dermatological effect.

In addition to studying the anti-inflammatory activity of the polar extract of *K. africana*, Picerno et al. (2005) also investigated the cytotoxicity and cutaneous irritation of the extract and its major constituent, verminoside (**35**) in reconstituted human epidermis (RHE) *in vitro*. The RHE model has been reported to mimic morphologically and biochemically living skin to a more significant degree than monolayer cultures. It has been used to investigate complementary parameters of the irritation mechanism by the application of products directly on the skin surface. The RHE tissue was exposed topically to the extract (1-3% solutions in PBS) and **35** (0.25-1%) for 24 and 72 h. The polar extract and **35** showed no cytotoxic effect and a low pro-inflammatory cytokine (IL-1 R) release comparable to the control with a histopathological observation of a regular morphology of the epidermis layers at 24 and 72 h. Thus, the extract and compound appear to be safe for topical use.

Nonetheless, the RHE model pertains to the safety of the topical application of the polar extract and its constituent on skin. No tentative study (*in vitro* or *in vivo*) has yet been conducted targeting the skin firming or any of the dermatological effect of *K. africana*, thus, little to no information is available on the mechanism of its dermatological effect or the bioactive compounds responsible for the observed effect; and if it is a single bioactive constituent or a synergy of different agents present in the plant and their relative contribution in the overall effect (?). These are interesting perspective that should be further probed.

6.13 Other pharmacological activities

Recent studies have shown that *K. africana* can be use in the treatment of anemic conditions (Oyebanji et al., 2015; Peter et al., 2014). In ethylene glycol induced hyper-oxaluria model in rats, treatment with alcohol and aqueous extract of *K. africana* (100 and 250 mg/kg b.w) significantly

lowered the oxalate values ($p < 0.001$) compared to lithiatic control. Elevation in urine calcium and phosphorus level in rats taken calculi-producing diet was remarkably reduced by *K. africana* ($p < 0.001$). A supporting result from *in vitro* study on size and dissolution of calcium-oxalate crystal (CaOx) also indicate that the extract (5 mg/mL-5 mL) reduce the crystal size with the aqueous extract being more potent (2.98 µm; $p < 0.001$) than alcoholic extract (4.06 µm; $p < 0.001$) (Gupta et al., 2011; Kumar et al., 2012a). This suggest that *K. africana* is effective in the treatment of kidney calculi-stone formation (urolithiasis); hence may be effective in treatment of kidney related diseases. *K. africana* is also reported to exhibits a dose-dependent enhancement in the early hypersensitivity reaction and delayed type hypersensitivity reaction to the sheep red blood cells (SRBC) antigen, thus, increasing both humoral immunity and cell mediated immunity (Katoch et al., 2015; Nagarathna et al., 2014) . Beside its effect on the central nervous system (Shalini et al., 2014), which augments its use in the treatment of epilepsy (Singh et al., 2010a; Tettegah et al., 2011). *K. africana* also inhibit the oxytocin-induced contraction (Owolabi et al., 2008); hence, can be used to reduce peripheral resistance in the systemic circulation leading to reduction in blood pressure (antihypertensive effect).

Parasitic nematodes account for most annual crop damage and several other crops such as yam, maize, cassava and vegetables. The nematicidal activity of Isovitexin (**6**), isolated from *K. africana*, was assessed against the root-knot nematode, *Meloidogyne incognita*. Isovitexin (**6**) produced a significant nematocidal mortality rate (39.76%) compared against the control (2.18%) (Atolani et al., 2014a). Similarly, the isochrome glycoside tolaside (**141**) was reported to exhibit a mortality of 29.43% against *Meloidogyne incognita* juveniles (Atolani et al., 2014b). The aqueous extract of *K. africana* was also reported to be active against *Proteus mirabilis* (MIC = 285 µg/mL) (Cock and van Vuuren, 2014). In the treatment of helminthiasis, both hexane and ethanolic extract of *K. africana* displayed antilarvicidal activity against *Caenorhabditis elegans* (McGaw et al., 2000).

Naphthoquinones, especially **63** analogous exhibit a promising antileishmanial drug potential when tested against *L. (Viannia) braziliensis* and *L. infantum* (Malerich et al., 2013).

6.14 Toxicity

Few toxicity study on different extracts obtained from *K. africana* were reported and these studies are mostly on the acute toxicity. Overall, the median lethal dose (LD_{50}) for acute toxicity studies on *K. africana* was found to be low. Akah (1996) estimated the LD_{50} of the aqueous leaf extract administered intraperitoneally (i.p) in mice to be 785.65 ± 24 mg/kg. In another study, a rather higher LD_{50} (i.p) of the stem bark methanol extract in mice was reported to be at 3000 mg/kg (Amali et al., 2012). The acute oral toxicity study of the leaves methanolic extract conducted on mice showed no behavioral alterations, toxic reaction or mortality up to 2500 mg/kg b.w. On the contrary, a dose of 5000 mg/kg caused mortality and the manifestation of toxic symptoms (Hemamalini et al., 2012b). Fredrick et al. (2014) used six different doses to evaluate the oral acute LD_{50} of the methanolic stem bark. The first three lower doses (10 mg/kg, 100 mg/kg and 1000 mg/kg) did not caused animal death (n = 3), while each of the other three higher doses (1600 mg/kg, 2900 mg/kg and 5000 mg/kg) caused the death of the treated animals. The LD_{50} was calculated as the square root of the product of the lowest lethal dose (1600 mg/kg) and the highest non-lethal dose (1000 mg/kg); thus was derived as 1264.9 mg/kg b.w. A similar result was reported for oral administration of ethanolic bark extract with an LD_{50} of 955 mg/kg b.w. (Khan and Islam, 2012). Unfortunately, the authors did not report the observed toxicological symptoms in the treated mice and rats neither did they conduct any form of histopathological examination on the organs of the dead animals.

At molecular level, investigations on *K. africana* toxicity reported the activity of the ethanolic root extract on lethality assay on brine shrimp larvae (nauplii). The percent mortality increased dose dependently. The mean ± SD was found to be 52.50 ± 24.37 ($P < 0.0001$) and the LC_{50} and LC_{90}

values were found to be 100 and 350 µg/mL, respectively (Khan and Islam, 2012). *K. africana* (aqueous and organic extracts) displayed some degree of toxic or inhibitory properties at 100 mg/ml against the human kidney epithelial cell line. When comparing the activity of *K. africana* to the positive control (100% cell growth), the aqueous and organic extracts of *K. africana* inhibited 22% and 16% cell growth, respectively; which is considered to have some significance (Naidoo et al., 2013). The bioactive compound verminoside, an iridoid derivative, and verbascoside, a phenylethanoid compound are present in *K. africana* and have been studied for their genotoxic tendencies. A concentration ranging from 0.01 mM to 0.1 mM of these active ingredients was found to induce structural chromosome aberrations in verbascoside- or verminoside-treated lymphocytes (Santoro et al., 2008).

Considering the numerous therapeutic potentials of *K. africana* as an alternative medicine effective for a wide range of diseases and infections, as reported in a number of scientific papers, it is only pertinent that a safety profile of the plant be established as a guide for the management of its applications and usage in herbal preparations. At present, there is not enough systemic data about the pharmacokinetics and toxicity of this plant, especially target organ toxicity (e.g dermatotoxicity) and the safety of long term oral intake; therefore, more investigations should be done in the future. It is important to clinically investigate the dosage range that is safe for humans in treating various diseases.

6.15 Commercial value, potentials and sustainability

Commercially, it is one of the medicinal plant sold in its powdered form in many African herbal markets, particularly in South Africa, Ghana, Nigeria and Zimbabwe (Van Andel et al., 2012; Van Wyk, 2008; 2015). A nonprofit trade organization known as PhytoTrade Africa (www.phytotradeafrica.com) has expand the commercial outreach of African herbal and natural products into the international food, beverages, herbal medicine, pharmaceuticals and cosmetics

market, which is estimated to be currently valued at $65 billion USD per annum and is booming with a 15-20% annual growth rate in the last few years; while that of southern Africa region is estimated (as of October 2010) at $12 million USD per annum (Smartt and Haq, 2008). Under the supply chain for natural products developed by PhytoTrade, two member organizations, Blue Sky Botanics (www.blueskybotanics.com) and Afriplex (Pty) Ltd (www.afriplex.co.za), supply extracts of *Kigelia* to cosmetic lines.

In terms of the market potentials of African medicinal plants, *K. africana* is considered as one of the "big five" along with *Adansonia digitata* L. (Baobab), *Sclerocarya birrea* (A.Rich.) Hochst. (Marula), *Moringa oleifera* Lam. (Moringa) and *Schinziophyton rautanenii* (Schinz) Radcl.-Sm. (Mongongo). In a 2006 report on the potential scale of the emerging opportunity in natural products exported from Southern Africa region, *K. africana* has the third trade value per year at $375,563 behind the Baobab tree ($11,203,928 per annum) and Marula ($425,000,563 per annum). Interestingly, the trade opportunity prospect for *K. africana* was projected to skyrocket to $1.6 billion per annum; a figure which outstrip the projections for both Baobab tree (1 billion per annum) and Marula ($263,001,008 per annum) (Bennett, 2006). In Central and West Africa regions, the estimated annual market value of *K. africana* was in the range of $18-81 (Oluwalana and Momoh, 2015; Williams, 2008); an indication that the commercial propensity of *K. africana* in Central and West Africa regions has not been fully utilized. The regional disparity in the commercial growth of *K. africana* between the Southern and Western regions of Africa can be linked to the market evolution, favorable market policy enacted by the government and the development of industries that utilizes natural products. Considering these factors, South Africa, with a growing cosmeceutical industry, has a substantive edge which has triggered a regional cognizance of the economic value of traditional medicinal plants. Moreover, with an established whole sale outlet such as PhytoTrade, Blue Sky Botanics and Afriplex in South Africa, the international demand has also increased. This has reflected in the overall annual turnover which is

exceedingly higher in the Southern region compare to other regions of Africa. For availability and sustainability of supply, a survey in 2004 has suggested the prioritization and domestication of several medicinal plant species, among which is *K. africana*, to meet the burgeoning commercial demand (Katumba et al., 2004).

6.16 Conclusion

The relevance of *K. africana* in the scheme of traditional medicinal plants in Africa has spanned decades with ever growing interest by both traditional medical practitioners (herbalist) and also academic scientific researchers. In recent time, *K. africana* has witness a surge in popularity which has prompt a number of scientific researches in order to provide methodical and experimental base evidence to many of its traditional therapeutic uses in treatment of diseases. Investigations and evaluations for pharmacological activity has confirmed it anticancer, anti-inflammatory, antimicrobial, antioxidant and also as a remedy for skin diseases and complications of the sexual organs. The pharmacological activity of the plant has been attributed to a number of phytoconstituents isolated. Naphthoquinones, iridoids, flavonoids and other polyphenol class of compounds have been identified and isolated. While preliminary phytochemical analysis has detect the presence of tannins and alkaloids (Abdulkadir et al., 2015; Solomon et al., 2014), compounds from these class are yet to be isolated.

Despite the current recognition of *K. africana* as a quintessential African medicinal plant with growing interest of research and a boost in its commerce and industrial application for formulation of therapeutic products, it can be safely postulated that its therapeutic potentials has not been fully explored. At present, researches and commercial interest on *K. africana* is skewed towards its cosmeceutical application which has dwarfed research interest in its potential as a remedy for other diseases. Thus, further researches on its pharmacological activity is recommended with the end-goal of unravelling the pharmacodynamics, pharmacokinetics and clinical relevance. In addition, toxicity

risk assessment studies of both the bioactive extracts and isolated constituents needs to be given more attention.

Acknowledgement.

We extend our appreciation to Universiti Sains Malaysia (USM) for the award of USM-Fellowship

TABLES

Table 1: Uses of different plant parts of Kigelia africana in folk and traditional medicine.

Plant part	Region/Country	Disease	Method of preparation (s)/ route of administration	Reference
bark	Cameroon	Abortifacient, filariasis and cataract	Decoction taken orally.	(Focho et al., 2009; Neuwinger, 1996)
bark	Ivory coast	Articular rheumatism	Affected body part bathed with bark macerate or bark powder eaten.	(Neuwinger, 1996)
bark	Nigeria and Ghana	Dysentery	The bark is pounded and added to pap made from corn powder.	(FAO, 1986)
bark	Kenya	Epilepsy	An infusion from the bark is used to wash the head as a way of treating epilepsy.	(FAO, 1986; Grace et al., 2003; Maregesi et al., 2007; Neuwinger, 1996)
bark	Kenya	Fungal infestations	Athlete's foot are washed with the water in which bark has been macerated.	(Maheswari and Rajagopal, 2013)
bark	Tanzania, Nigeria	Galactogogue	Hot decoction of powdered bark taken orally after parturition.	(de Wet and Ngubane, 2014)
Bark	South African, Cameroon	Infertility	Administration mostly decoctions of powdered bark mixed in porridge and infusions taken orally.	(de Wet and Ngubane, 2014; Van Wyk et al., 1997)
bark	Nigeria	Leucorrhea	A concoction of *K. africana* bark, *Terminalia glauscens* root and *Diodia scandens* leaves taken orally.	(Neuwinger, 1996)
bark	Tanzania	Malaria, gonorrhea, syphilis, febrile and convulsions	– Infusion taken orally to lower body temperature and reduce headache. – *Kigelia africana, Zehneria scabra, Acanthus pubescens, Emilia javanica* and *Oxygonum sinuatum* are mixed & boiled and the decoction taken daily for the treatment of malaria. – Stem bark is boiled in water and sipped.	(Gessler et al., 1995; Maregesi et al., 2007; Moshi et al., 2009)

bark	Tanzania	Gonorrhea	A concoction of the stem bark of *K. africana* with leaves of *Cassia occidentalis* taken orally for gonorrhea.	(Maregesi et al., 2007)
bark	Togo, Kenya and west Africa	Anticancer	100 g of Kigelia africana stem bark and 25 g fruits of *Xylopia aethiopica* cooked in 1 L of water. Three tablespoons of this mixture are drunk three times daily during two months.	(Grace et al., 2003; Houghton and Jâger, 2002)
bark	Africa	Pneumonia and toothache	– Decoction of bark taken orally. – Powdered bark flecked around the inflamed teeth.	(Houghton and Jâger, 2002)
Bark	Sudan, Senegal, Tanzania, Benin and Kenya	Rheumatism, Cough, dysentery	– Decoction of the bark taken orally – The bark is pounded and added to pap made from corn powder. – Decoction of the bark mixed with cow milk. – Decoction of stem bark cooked with soda and flour.	(Cunningham, 1993; Eldeen and Van Staden, 2007; MaClean, 1969)
bark	Uganda	Spleen infection	– A decoction of the stem bark of *K. africana* and the leaves of *Irvingia gabonensis* is used to cure spleen infection. – Cold water extract also drank over a long period.	(FAO, 1986)
Bark	West and Central Africa	Venereal diseases	– Mostly use on children. Treated simultaneously with a drink and wash prepared from decocted bark. – Palm wine, in which dried and ground bark is macerated for 2-3 days. About 100 ml is taken daily for 8 days or more.	(Neuwinger, 1996)
Bark + fruit	Congo	Asthma	Hot water concoction is taken orally after straining.	(Neuwinger, 1996)
bark + fruit	South Africa	Gynecological and obstetric conditions	– Chopped bark and fruit boiled in 2 L of water for 1 h, cool before straining and taken orally, half a cup thrice a day for blood cleansing and pelvic pains during pregnancy, or alternatively, an enema with three Size-6 syringes once a day.	(de Wet and Ngubane, 2014; Van Wyk, 2011)

			– The bark is peeled on the east and west side of the tree and chopped with *Acalypha vilacaulus* root. A handful of plant material is boiled with water just covering the plant material until water drops to the same level of plant material, cool before straining. Half a cup is taken three times a day to induce lactation by a new mother just after delivery. – Equal amounts of dry or fresh bark of *K. africana* and *Searsia nebulosa* are pounded together and three handfuls are boiled in 2 L of water for 30 min, cool before straining. Half a cup of the decoction is taken twice a day to treat dysmenorrhea.	
bark + fruit	Nigeria and Ghana	Rheumatism, wounds and malignant tumors	Oily paste made from the mixture are used to rub on rheumatic parts and on malignant tumors.	(FAO, 1986; Irvine, 1961)
Bark + leaves	Namibia and South Africa	Boils, eczema, psoriasis, leprosy, skin cancer, herpes Syphilis	Stem bark and leaves are crushed together, boiled in water and decoction is concentrated and used to wash or rub onto infected skin parts.	(Chinsembu et al., 2015; Chinsembu et al., 2011; Van Wyk, 2011)
Bark + Leaves	Zimbabwe	Malaria fever	A decoction of leaves and stem bark for drinking use for bathing to serves as cure for malaria fever.	(FAO, 1986)
flower	Cameroon	sore eyes	Sap expressed from the buds is used as drips.	(Solomon et al., 2014)
Fruit	South Africa	Penile enlargement	Fruit juice dripped or rubbed on the penis.	(Moll et al., 1994; Neuwinger, 1996)
Fruit	Tanzania	anemia especially with pregnant women	The fruit is boiled and taken orally.	(Maregesi et al., 2007)

Fruit	Africa, India	Breast development	Ointment made from fresh fruit rubbed on the breast before bedtime by young girls for breast enlargement and by women for breast firming.	(Burkill, 1985; Lal and Yadav, 1983)
Fruit	India	Kidney stone, diarrhea, abdominal pain	Fruit distillate prepared from 4 kg mass of crushed fresh fruits added to 1.5 L of water, 25 g of ammonium chloride and 25 g common salt in an earthenware pot. The close pot will be kept in sunlight for 2-3 months to ferment and then distilled in clay vessel. A 2-3 drops dosage for children and 4-5 drops for adults twice a day after meals for a week.	(Neuwinger, 1996; Sharma and Kaul, 1993)
fruit	India	leprosy	The fruit paste is used for leprosy by inhabitants of Kurukshetra district in Haryana, India.	(Carey et al., 2010; Kumawat et al., 2015)
fruit	Africa, India	Skin Cancer, reduce breast metastasis and Leprosy	Fruit paste or powdered fruit as a poultice is rubbed around infected area on the skin.	(Carey et al., 2010; Lal and Yadav, 1983)
fruit	Western and southern Africa	Sexual stimulant	– A small amount of unripe fruit is chewed, or an aqueous preparation is taken orally, and the intoxicating traditional beer to which they are added is drunk as an aphrodisiac. – The fruit is ground up and mixed with water to help young men improve their manhood.	(Dalziel and Hutchinson, 1937; Grace et al., 2003)
fruit	Togo Cameroons	anticancer, boils	Paste is made from the fruits and rubbed on infected skin.	(Grace et al., 2003; Houghton and Jâger, 2002)
fruit	Central Africa	Syphilis and rheumatism	– The green fruit is used to make a poultice for syphilis – The powdered mature fruit is used to treat rheumatism.	(Fouche et al., 2008)
fruit	Africa	Wounds, ulcers and	Dried fruit is extensively used in dressing infected body parts.	(Carey et al., 2010; Fouche et

		sores.		al., 2008)
Fruit	Botswana	Aphrodisiac, sexually transmitted diseases	Fruit boiled with milk, cooled and taken orally as remedy.	(Setshogo and Mbereki, 2011)
Fruit + root	Ghana	Infertility	– A mixture of grounded *K. africana* young fruit and snails rolled into balls and allowed to dry is eaten with a cup of tea daily. – The fruit and roots along with the male tassel of the plantain inflorescence are boiled together to make a	(Azu et al., 2010a; FAO, 1986; Neuwinger, 1996)
Fruit + roots	Central Africa	Parturition haemorrhage.	The fruits and roots of *K. africana* boiled along with the stem and tassel of a plantain are used medicinally as a cure for post parturition haemorrhage.	(FAO, 1986; Oyelami et al., 2012)
leaves	Uganda	High blood pressure	Ashes from roasted leaves combined with honey and taken a tea spoon once in the morning and evening.	(Gachati and Mabatanzi, 2014)
leaves	Benin, Ivory coast and South Africa	jaundice	A decoction of the leaves is drunk for jaundice.	(Eldeen and Van Staden, 2007; Neuwinger, 1996)
leaves	South Africa	Sexually transmitted infections	Boil a handful of chopped roots or leaves in 5 L of water with a handful of chopped *Hypoxis hemerocallidea* corm and a handful of crushed *Senecio serratuloides* and Kigelia africana leaves. Take half a cup three times a day to treat sores.	(De Wet et al., 2012)
leaves	Nigeria	stomach ulcer	Hot-infusion preparations from it leaves are popularly used to treat stomach ulcer.	(Solomon et al., 2014)
root	Nigeria	ante-natal and post-natal disorders, Fibroid, conception	– The root is cut into pieces and boiled in water. – Roots are boiled with the leaves of *Newbouldia laevis* for conception. 100 mL is taken twice daily.	(Chima et al., 2013; Solomon et al., 2014)

		and infertility in women		
Roots	South Africa, Ethiopia	Gynecological complaints, constipation and tapeworm	Roots hot macerate is taken orally.	(Fouche et al., 2008; Getahun, 1976)
Seeds	Kenya	Enlargement of sexual organs	The roasted seeds mixed with beer taken orally.	(Azu et al., 2010a)
Seeds	South Africa	Pneumonia, malaria, diabetes, antifungal, eczema, waist pain	Seeds are roasted and eaten or crushed; Use orally or as ointments.	(Fomogne-Fodjo et al., 2014; Saini et al., 2009a)

Table 2: *In vitro* antioxidant activities of *K. africana* plant extracts.

Extract/ Compound	Plant part	Model	Activity observed/ IC_{50} (µg/mL)	References
Methanol (MeOH)	Fruit and leaves	DPPH assay	The IC_{50} result for the fruit was 0.08 mg/mL while that of the leaves showed little activity, thus, the IC_{50} value of could not be determine.	(Solomon et al., 2014)
MeOH, pet ether	Leaves	DPPH assay	The MeOH extract (ME) and pet ether extracts exhibited an antioxidant property with the IC_{50} value of 21.68 µg/mL and 10.21 µg/mL.	(Sikder et al., 2011b)
70 % acetone	leaves	Inhibition of 15-lipoxygenase (15-LOX)	Gave a moderate activity with IC_{50} 42.3 µg/mL compare to the quercetin control (IC_{50} = 8.75 µg/mL)	(Adebayo et al., 2015)

MeOH	fruits	Hydrogen peroxide, hydroxyl radical scavenging, DPPH assay, Nitric oxide radical scavenging and Fe2+/ascorbate-induced lipid peroxidation.	At 100 µg/mL, it showed low peroxide scavenging activity of hydrogen peroxide with 22.4 ± 1.50% when compared to catechin, 19.5 ± 1.56%. The Activity decrease with increasing concentration (6.4% at 1000 µg/mL); A t 100 µg/mL, gave an inhibition of 39.5 ± 7.04% compare to catechin with 89.9 ± 3.62% against hydroxyl radical scavenging; A low concentration-dependent increase in scavenging activity of extracts was observed. At 100 µg/mL, the percentage scavenging activity of the extracts and catechin were 2.3% and 42.2% while at 750 µg/mL the scavenging activity were 28.1% and 67.8% respectively; At 500 ug/mL, gave a better NO radical scavenging activity of 43.3% compare to the standard, catechin with 20.9%; Exhibit no lipid peroxidation (LPO) inhibition potential.	(Akanni et al., 2014)
ClH_4, MeOH, H_2O and Pet ether	leaves	DPPH assay	A positive concentration-dependent activity was noted in all extracts. The highest free radical scavenging activity was recorded in the methanol extract, with an IC_{50} 0.32 mg/mL comparable to the standard (vitamin C) with an IC_{50} 0.27 mg/mL.	(Nasiru and Oluwasegun, 2014)
n-hexane	leaves	DPPH assay	Scavenging activity was observed for the extract at all concentrations assayed with 250 µg/mL having the lowest activity while the highest anti-oxidant capacity was observed at 1000 µg/mL.	(Atolani et al., 2009)
n-hexane, EtOAc and MeOH	Root	DPPH assay	EtOAc showed a higher antioxidant value and the total antioxidant activity peaked at 0.25 mg/mL as the activity declined toward 0.5 mg/mL	(Atolani et al., 2011)
MeOH	Leaves and stem bark	DPPH assay	The bark of showed a better antioxidant capacity with an IC_{50} 13.7 μg/mL compare to the leaves with an IC_{50} of 56.9 μg/mL. α-tocopherol was used as the standard with an IC_{50} of 1.5 μg/mL	(Agyare et al., 2013)

EtOH	leaves	reducing power, phosphormolybdenum and DPPH assay method	The reducing power EtOH extract % at 500 μg/mL Showed a concentration dependent activity with 61% compared to ascorbic acid with 85; Against phosphormolybdenum, EtOH and acetone gave a concentration-dependent antioxidant activity with 61% and 59% respectively, at 500 μg/mL compare to the standard (Ascorbic acid = 85%); EtOH and acetone gave better activity with 65% and 63%, followed by chloroform and water with 56% and 45% respectively.	(Dhriti et al., 2014)
Verbascoside		– DPPH assay, – superoxide anion (O^2-) – H_2O_2 Scavenging – ROS-induced hemolysis of red blood cells (RBC)	– IC_{50} = 7.18 Mm – 75% of inhibition at 100 μ M – IC50 = 13.4 μ M – 70% of hemolysis inhibition at 30 μ M	(Alipieva et al., 2014)

Table 3: Tabular summary of the antimicrobial activity of *K. africana*.

Plant part used	Extract	Test model	Organism tested	Result Summary	References
Antibacterial					
Bark	Ethanol extract	agar diffusion method	Sa, Ec, Pa	The activity of 20 mg/mL of the ethanolic extract gave MIC of 6.25 ± 1.07 mg/mL against S. aureus which was found to be similar to that of 25 µg disc of amoxicillin. The extract showed no activity against the strains of E. coli and P. aeruginosa tested.	(Owolabi et al., 2007)
	n-Hexane	liquid dilution method	Bc, Kp, Sa	The highest activity was against *B. cereus* with Mic of 250 µg/mL followed by Sa with MIC 500 µg/mL. least activity was against *K. pneumoniae* with MIC> 1000 µg/mL	(Maregesi et al., 2008)
Bark and leaves	methanol extracts	microplate dilution method	Ec, Pa, Sa, Bs, Ca	The methanolic extracts of both the bark and leaves (KAL, KASB) were found to be active against the test organisms with varying mean zones of inhibition. *P. aeruginosa* was found to be less susceptible to the extracts. The MIC ranges against the test organisms were from 2.25 to 7.5 mg/mL.	(Agyare et al., 2013)
Leaves	methanol extracts	agar diffusion method		The MICs of leaf extract against tested organisms in the range of 2.5-7.5 mg/mL and stem bark extract were 2.25-7.5 mg/mL.	(Binutu et al., 1996)
	Methanol extract and its fractions	Disc diffusion method	Bc, Bs, Sl, Sa, Ec, Sp, Sb, Sd, Pa, Vm, Vp	The chloroform fraction showed a greater antimicrobial activity (8-11 mm zone of inhibition) with better activity against *P. aeruginosa* and *Shigella boydii* (11.00 mm each). Other fractions gave a lower zone of inhibition.	(Sikder et al., 2011a)
	n-hexane, dichloro methane	microplate dilution	Sa, Ef, Pa Ec	The highest activity was obtained from dichloromethane fraction with MIC in the range of 0.08- 1.25 mg/mL against	(Shai et al., 2008)

	and acetone	method		the tested bacterial strains. The acetone and n-hexane extracts showed lower total activity (MIC range = 0.1-2.5 mg/mL).	
	n-hexane (Cuticular wax)	Disc diffusion method	Kp, St, Sa	Moderate antimicrobial activity compare to the standards Chloramphenicol and Tetracycline with MIC of 5 μg/mL for *S. typhi*, *S. aureus* and *T. mentagrophyte*.	(Atolani et al., 2009)
fruit and bark	water, ethanol and ethyl acetate	microtitre plate bioassay	Sa, Bs, Ec and Kp.	The bark aqueous extract gave an activity of MIC 2.5 mg/mL against *E. coli* and *S. aureus*; activity was not detected against *B. subtilis* and *K. pneumoniae*. Fruit aqueous extract did not show activity. The ethanolic bark extracts showed the greatest activity against *B. subtilis* (MLC = 0.63 mg/mL) while against E. coli, *K. pneumoniae* and *S. aureus* gave an MIC of 2.5 mg/mL. The ethyl acetate bark extract showed good inhibitory activity against *E. coli* and *K. pneumoniae* (MIC = 2.5 mg/mL). Ethyl acetate fruits extract was most active against *B. subtilis* (MIC = 0.313 mg/mL.	(Grace et al., 2002),
fruit	Methanol, dichloromethane, thyl acetate and hexane	Agar Diffusion Assay, Violacein Inhibition	biosensor system strains of Cv (ATCC 12472) , Atu (A136 and KYC6) and	At 4 mg/mL in Susceptibility Test, resistance of all four crude extracts was observed for *A. tumefaciens* strains. Resistance to the ethyl acetate and dichloromethane extract and moderate susceptibility to the methanol and hexane extracts was observed for *C. violaceum.* In Violacein Inhibition assay, ethyl acetate (90% at 1.97 mg/mL, IC_{50} of 1.89 mg/mL), dichloromethane (90% at 3.93 mg/mL, IC_{50} of 0.50 mg/mL) and n-hexane (97% at 1.31 mg/mL, IC_{50} of 0.58 mg/mL) crude extracts gave a concentration-dependent inhibition of violacein production by *C.*	(Chenia, 2013)

				violaceum ATCC 12472	
fruit	methanol, water, ethyl acetate, chloroform and hexane	Disc diffusion method	Tested against 18 bacterial species	The methanolic extract showed a broader spectrum of activity, inhibiting the growth of 12 of the 18 bacteria tested (lowest MIC is 176.3 µg/mL against *E. coli*) followed by water extract with inhibition of 11 of the 18 bacteria tested (61 %, lowest MIC is 84.7 µg/mL against *E. coli*). The ethyl acetate extract also displayed antibacterial activity, inhibiting the growth of 4 (22 %) of the 18 bacteria tested.	(Arkhipov et al., 2014a)
	Methanol	microtitre plate method	Sa, Kp, Mc, Ms and Ma	Moderate activity was observed with the highest against Mycobacterium aurum (MIC 250 µg/mL) least effective against *S. aureus* with MIC > 8000 µg/mL.	(Fomogne-Fodjo et al., 2014)
Root oil	Root oil (from hexane), Ethyl acetate & Methanol extract	disc agar diffusion method	Bc, St, Sa, Ec, Pa, Msp., Psp.	Methanolic extract showed Significant antibacterial activity against *Proteus sp.* With inhibition zone of 14.67 at 1 mg/mL (MIC = 125 µg/mL), *Salmonella typhi* With inhibition zone of 12.67 at 1 mg/mL (MIC = 250 µg/mL). The root oil showed significant activity against *Aspergillus sp.* but not on the other organisms.	(Atolani et al., 2014c)
Antifungal					
Fruit	methanol	broth	Ca, Cg,	The fruit extract. Showed moderate	(Hamza et

	extracts	microdilution method,	Ct, Cp, Ck and Cn	activity on only one strain, *C. neoformans*. With MIC of 1000 µg/mL. Other strains gave an MIC above 4000 µg/mL.	al., 2006)
	methanol, water, ethyl acetate, chloroform and hexane	Disc diffusion method	An, Ca and Pc	The methanolic, water and ethyl acetate extracts also had broad spectrum inhibitory activity against the fungal species, each inhibiting the growth of 3 of the 4 fungal species tested (75 %, albeit with MIC > 2000 µg/mL), including an ampicillin strain of *A. niger*.	(Arkhipov et al., 2014a)
root	Root oil (from hexane) and its Ethylacetate & Methanol extract	disc agar diffusion method	Ca, Rsp, Asp.	The methanolic extract also had the most significant MIC against the fungi *Rhizopus sp*. (250 µg mL–1). Other extracts had a MIC greater than 500 µg mL–1. Ethyl acetate extract showed moderate activity.	(Atolani et al., 2014c)
bark	crude ethanol extracts	agar diffusion method	Ca	The Mean zone of inhibition (mm) of the extract was 20.75 ± 4.60 while the MIC was 7.92 ± 1.520 mg/mL against *C. albican*	(Owolabi et al., 2007)
	petroleum ether, chloroform and methanol	Sabouraud's glucose broth as media for assay.	Cn, Ct, Tr, Mf, Ef	The choloroform extract showed the highest inhibitory activity against the tested fungi strains (MIC range = 0.625-1.25 µg/mL). Lower activity were observed with the pet ether and methanolic extract with MIC in the range of 0.625-2.5 µg/mL	(Jain and Belsare, 2009)
Leaves	acetone, n-hexane or dichloro methane	microplate dilution method	Ca, Cn, Af, Ss and Mc	The hexane extract showed highest activity with MIC 0.08 mg/mL against *M. canis* followed by hexane and dichloromethane with MIC 0.23 mg/mL against *C. albicans*. Total activity is in the range of 4-125 mL.	(Shai et al., 2008)

Bacterial species are Sa = Staphylococcus aureus, Kp = Klebsiella pneumonia, Mc = Morexella cattarhalis, Ms = Mycobacterium smegmatis, Ma = Mycobacterium aurum, Bc = Bacillus cereus, Bs = B. subtilis, Sl = Sarcina lutea, Sa = Staphylococcus aureus, Ec = Escherichia coli, Sp = Salmonella paratyphi, Sb = Shigella boydii, Sd = S. dysenteriae, Pa = Pseudomonas aeruginosa, Vm = Vibrio mimicus, Vp = V. parahemolyticus, Ef = E. faecalis, Pa = P. aeruginosa, St=Salmonella typhimurium; Fungal species include Af = Aspergillus fumigatus, Ss = Sporothrix schenckii, Mc = Microsporum canis, Ca = Candida albicans, Cg = Candida glabrata, Cp = Candida parapsilosis, Ct = Candida tropicalis, Ck= Candida krusei, Cn = Cryptococcus neoformans, Ab = Alternaria brassicae, Cp = Colletotrichum papaya, Hsp. = Helminthosporium sp., Tr = Trychophyton rubrum, Mf = Microsporum furfure, Ef = Epidermophyton floccosum, Cv = Chromobacterium violaceum and Atu = Agrobacterium tumefaciens. MIC= minimum inhibitory concentration.

Table 4: Cosmetic products with *K. africana* extract as the major ingredient.

Product Name	Brief product description	Country	Price ($)	Online website outlet
Sausage Tree Cream (50ml)	Formulated for the natural treatment of Solar Keratoses (skin cancer). It is also helpful in the treatment of Psoriasis, Eczema and other skin irritations.	Zambia	9.304	http://www.faithful-to-nature.co.za/Sausage-Tree-Cream-Africana-Kigelia-p-92.html
Kigelia Cream (50ml)	Excellent for dabbing on sun spots and can help with Melanoma. Ideal for those spending a lot of time outdoors	South Africa	8.698	http://www.medicoherbs.co.za/
Sausage Tree Skin Cream (75ml)	This deeply hydrating blend is specially formulated to intensively heal and improve skin. Sausage Tree Cream will moisturize very dry or mature skin, soothe irritation and fight infection	USA	29.99	http://kigeliashop.com/product/kigelia-africana-sausage-tree-cream-75ml/
KIGELIA Africana balm ointment (50ml)	Smoothes wrinkles, protects the skin from oxidation and UV radiation. Africa used sunburned or extra dry skin, acne, mellfeszesítésre, stretch marks and scars on it. Paraffin, paraben-free, hypoallergenic.	Hungary	17.93	http://wellmed.hu/kigelia_gyogyir
Creme pour le buste (50ml)	Rich in firming ingredients, this repair treatment for the bust gives shapes the chest and strengthens the supporting tissues. The firming qualities of Kigelia africana, deemed develop breasts, are supported by the reshaping and tightening effect of Wheat Proteins and the virtues veinotonic oil Bellis.	France	19.36	https://experiment.com/u/Gem8kQ, http://www.amazon.fr/Melvita-cr%C3%A8me-buste-tonus-fermet%C3%A9/dp/B002VUAJBC
bioBotanica Kigelia Formulas (60ml)	An extra strong formula designed for use on aged, marked or sun damaged skin. A lush blend of Kigelia extract, sesame, jojoba and rosehip oil work in unison to hydrate and repair. The most aromatic of our range - rich earth and nuts, a taste of Africa.	South Africa	25.00	(http://www.biobotanica.com.au/products.htm),
Melvita Gel cream (50ml)	The well-known firming qualities of *Kigelia africana* reinforce the firming effect of the argan nut extract. The toning properties of bellis oil are combined with orange	United kingdom	20.72	http://www.mondebio.co.uk/organic-brand/melvita/gel-cream-for-the-bust-with-kigelia-bellis-et-argan-

	peel extract, rich in vitamin C and trace elements, and the stimulating qualities of geranium and orange essential oils to give the product maximum effect.			50ml/930.html
Scolpito (250 ml)	Firming, elasticizing body cream with Kigelia africana. A rich and smooth cream, for instantly soft skin , as well as preventing loss of tone and the formation of stretch marks	Italy	21.50	(http://www.bottegaverde.eu/body-care/toners)
Paul Penders Kigelia Lipo (40g)	A natural alternative to surgical procedures, Firmer Curves contains extract prepared from the Kigelia Africana tree.	United kingdom	54.62	http://www.bolocare.com/paul-penders-kigelia-lipo-phyto-tocotrienol-firmer-curves-40g.html
Kigelia Booster Serum (30ml)	Deepened wrinkles, age spots and uneven pigmentation, dry and dull-looking skin that has lost its youthful glow. Targets the visible signs of photo-aging and helps clarify, brighten and even skin tone for a more youthful, glowing appearance.	United States	54.99	http://www.katavibotanicals.com/product/kigelia-booster-serum/

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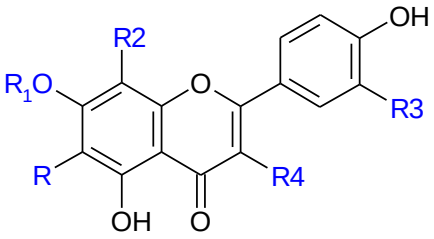
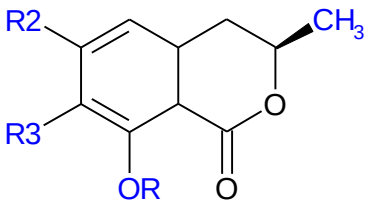
Flavonoids

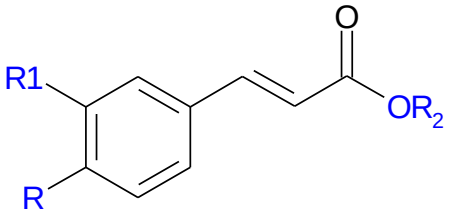


1	R = R1 = R2 = H, R3 = R4 = OH.	Quercetin
2	R = R1 = R2 = R4 = H, R3 = OH.	Luteolin
3	R = R1 = R2 = R4 = H, R = R3 = OH.	6-Hydroxyluteolin
4	R = R2 = R4 = H, R3 = OH, R1 = Glu.	Luteolin-7-O-glucoside
5	R2= R4 = H, R = R3 = OH, R1 = Glu.	6-Hydroxyluteolin-7-O-glucoside
6	R1 = OH, R2 = , R3 = H R = Glu.	Isovitexin
7	R1 = R3 = R4= H, R = Arab, R2 = Glu.	Isoschaftoside

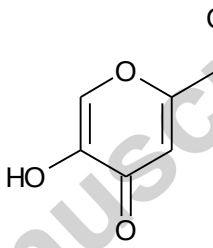
Courmarins, coumaric acids and derivatives



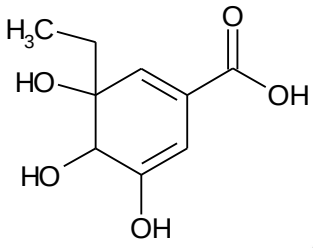
	R^1	R^2	R^3	
8	H	OCH_3	H	6-methoxymellein
9	H	OCH_3	OCH_3	kigelin
10	H	OCH_3	OH	3-demethylkigelin
11	H	OH	OCH3	6-demethylkigelin



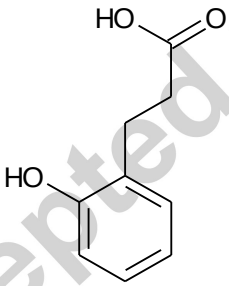
12 R1 = R2 = H, R = OH 4-hydroxy cinnamic acid
13 R2 = H, R = R1 = OH caffeic acid
14 R = R1 = OH, R2 = CH_3, caffeic acid methyl ester
15 R2 = H, R = OH, R1 = OCH_3 ferulic acid
16 R2 = H, R = R1 = OCH3 3,4-dimethoxy cinnamic acid



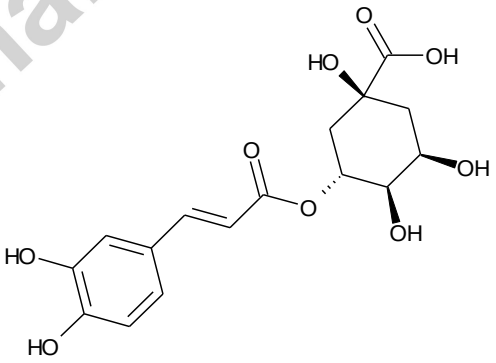
17 Kojic acid



18 3-ethylgallic acid



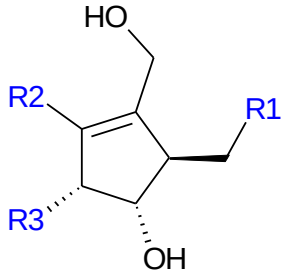
19 Melilotic acid



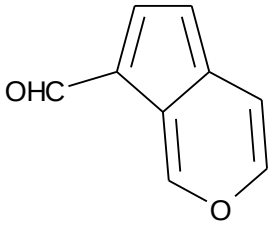
20 chlorogenic acid

Figure 3: Chemical structure of flavonoids and phenolic acids isolated from K. africana.

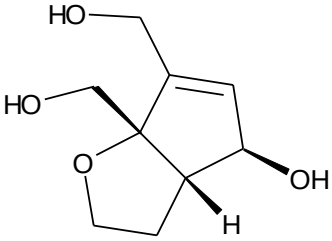
Iridoids



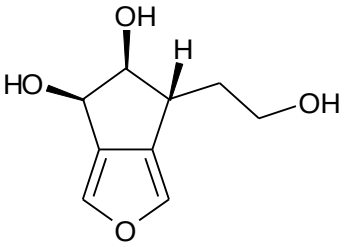
	R1	R2	R3	
21 =	CH_2OH	CH_3	H	10-deoxyeucommiol
22 =	COOH	CH_3	OH	7-Hydroxy-10-deoxyeucommiol
23 =	COOH	CH_2OH	OH	7-hydroxy eucommic acid



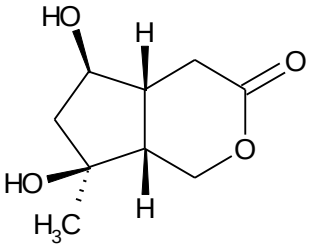
24 Norviburtinal



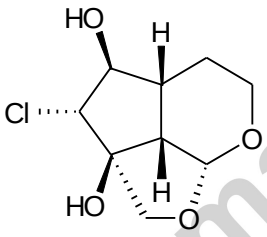
25 Des-p-hydroxybenzoyl kisasagenol B



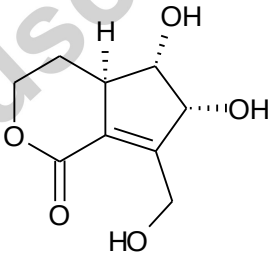
26 Jiofuran



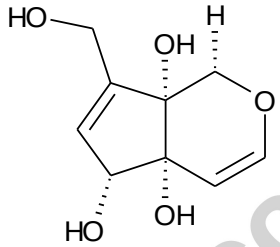
27 Jioglutolide



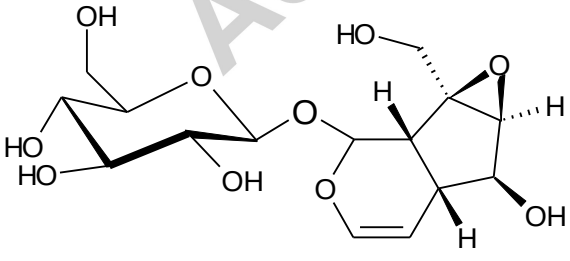
28 Rehmaglutin C_5



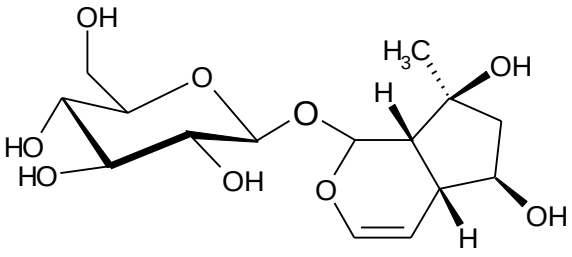
29 7-hydroxy viteoid II



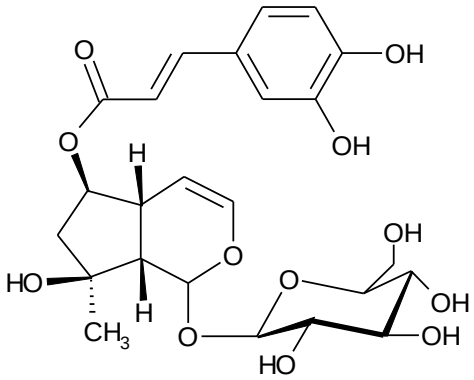
30 1-dehydroxy-3,4-dihydroaucubigenin



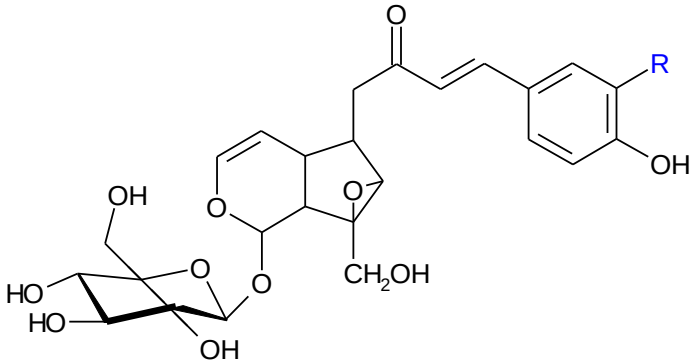
31 catalpol



32 Ajugol

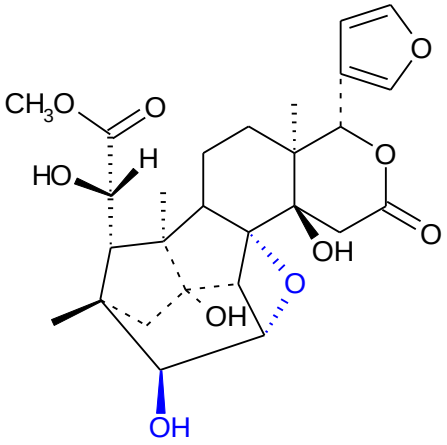


33 Caffeoyl ajugol

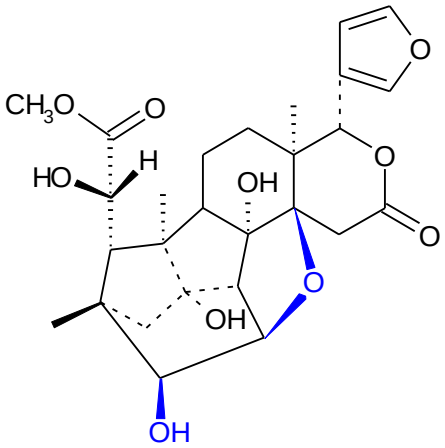


34 R = H specioside
35 R = OH verminoside
36 R = OCH3 minecoside

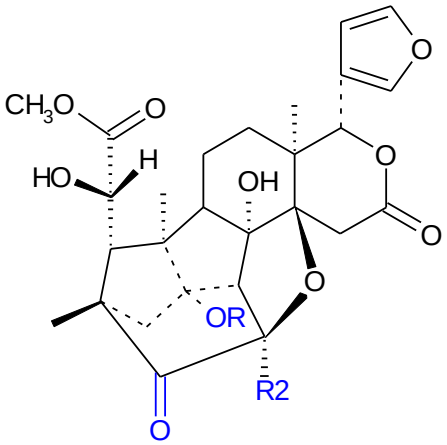
Limonoids



37 Kigelianolide



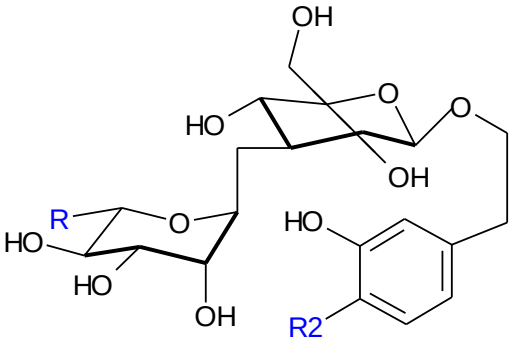
38 khayanolide B



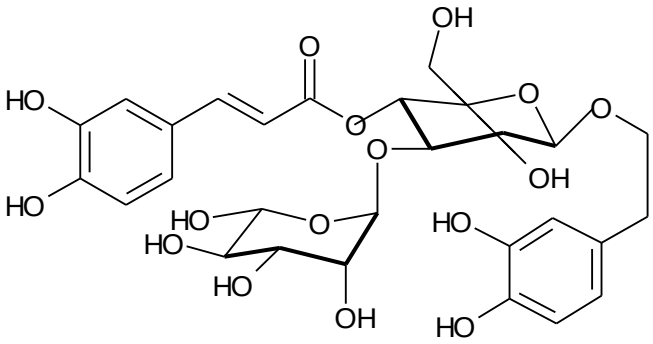
39 R = H; R2 = H; 1-O-deacetyl-khayanolide E
40 R = H, R2 = OH; 1-O-deacetyl-2a-hydroxykhayanolide E
41 R = H, R2 = OCH3; 1-O-deacetyl-2a-methoxykhayanolide

Figure 4: Chemical structures of iridoids and limonoids isolated from K. africana.

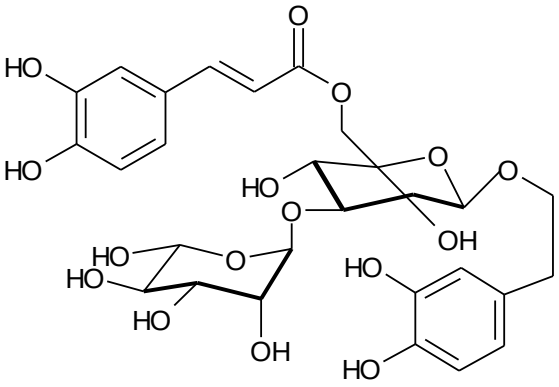
Phenyl ethanoid glycosides



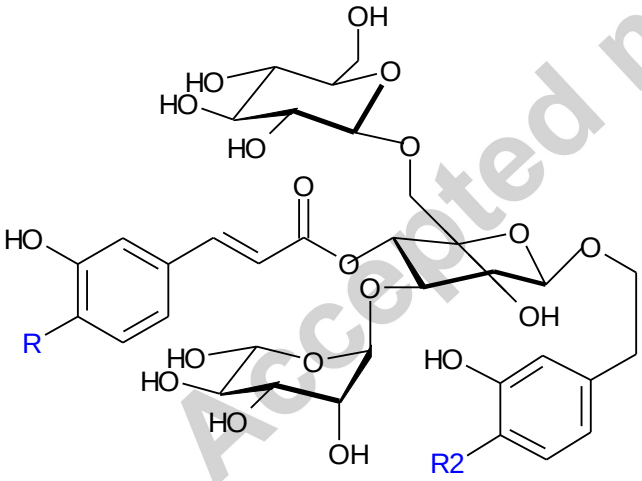
42 R = R2 = OH, Decaffeoylacteoside
43 R = CH_3 R2 = OCH_3 Darendoside A



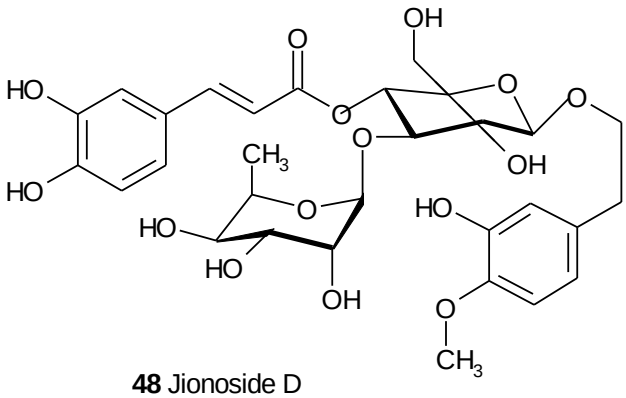
44 verbascoside (Acteoside)



45 Iso-Acteoside

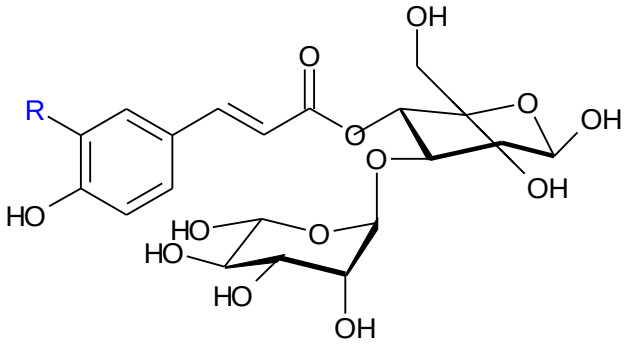


46 R = R2 =OH Echinacoside
47 R = R2 = OCH3 2-(3-hydroxy-4-methoxyphenyl) ethyl O-a-L-rhamnopyranosyl-(1-3)-[b-D-glucopyranosyl-(1-6)] -(4-O-feruloyl)-b-D-glucopyranoside

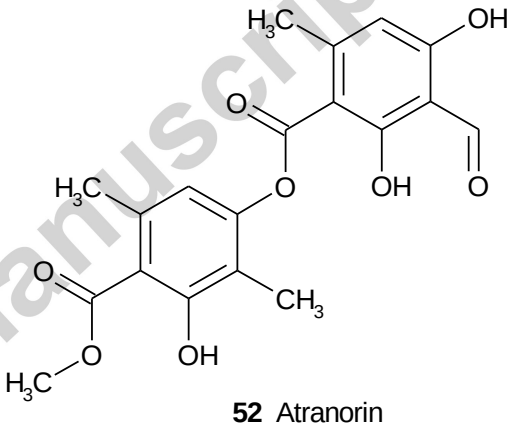


48 Jionoside D

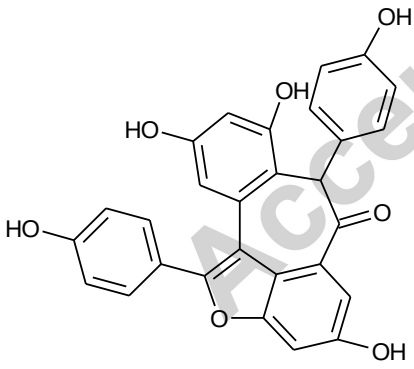
Phenylpropanoides



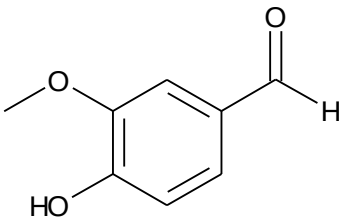
49 R = H 6-O-p-coumaroylsucrose
50 R = OH 6-O-caffeoylsucrose
51 R = OCH_3 6-O-feruloylsucrose



52 Atranorin

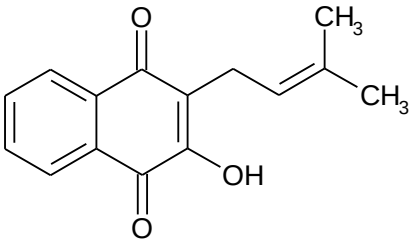


53 shoreaphenol

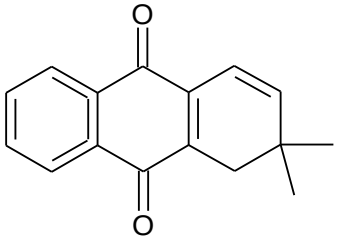


54 Vanillin

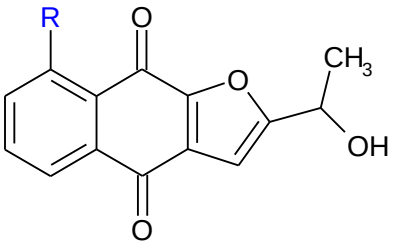
Naphthoquinones



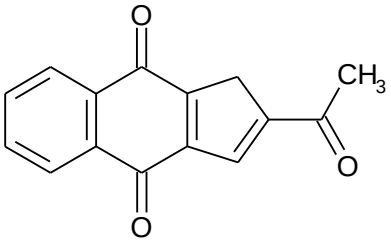
55 Lapachol



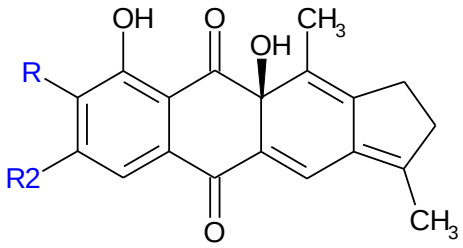
56 Dehydro-alpha- lapachone



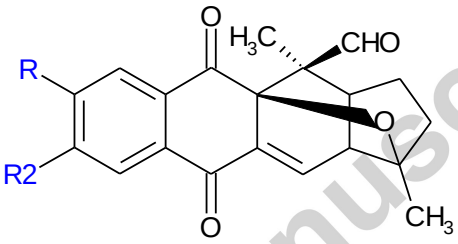
57 R = OH Kigelinone
58 R = H 2-(1-Hydroxyethyl)naphtho (2,3-b)furan-4,9-dione



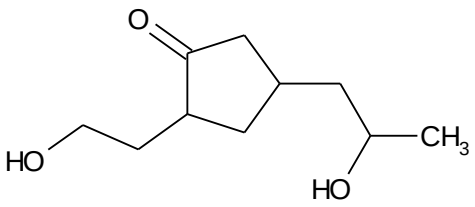
59 2-acetylnaphthao [2,3-b]furan-4,9-quinone



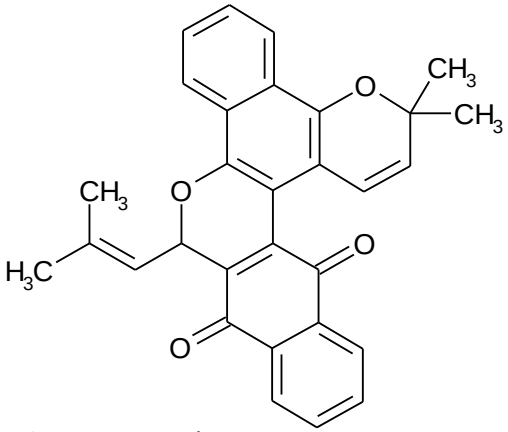
60 R = OH, R' = H Pinnatal
61 R = H, R' = OH Isopinnatal



62 R = OH, R' = H Kigelinol
63 R = H, R' = OH Isokigelinol

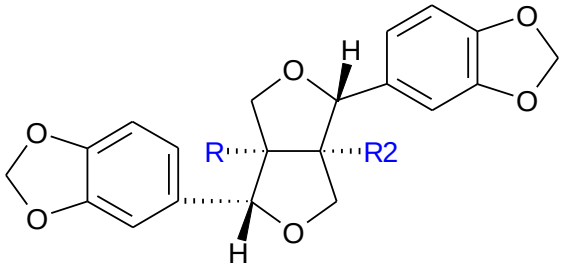


64 3-(2'-hydroxy-ethyl)-5-(2''-hydroxypropyl) dihydro-furan-2(3H)-one



65 Tecomaquinone-1

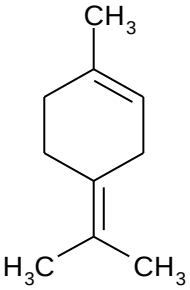
Lignans



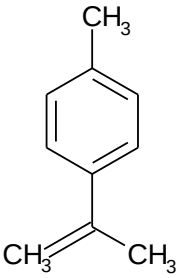
	R	R2	
66 =	H	H	Sesamin
67 =	H	OH	Paulownin
68 =	OH	OH	Kigeliol

Figure 5: Chemical structure of phenyl ethanoglycosides, phenyl propanoids, naphthoquinones and lignans isolated from K. africana.

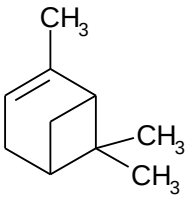
Terpenes and terpenoids



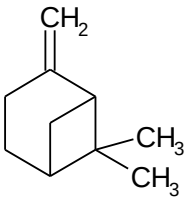
69 Limonene



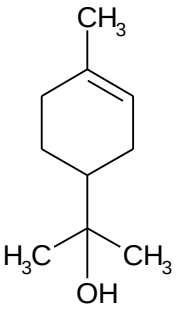
70 Terpinolene



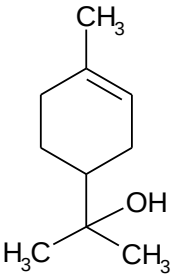
71 a-Pinene



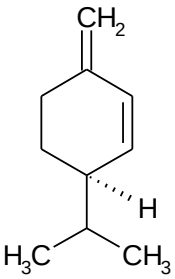
72 b-Pinene



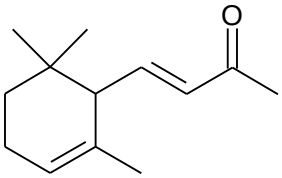
73 a-Terpineol



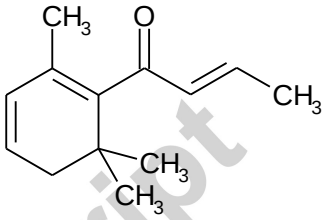
74 beta-Terpineol



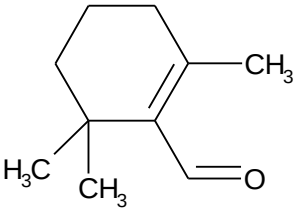
75 ß-Phellandrene



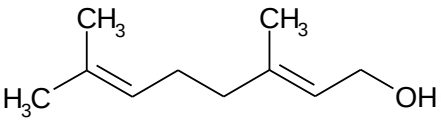
76 alpha-Ionone



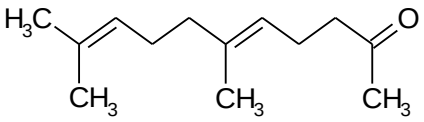
77 ß-Damascenone



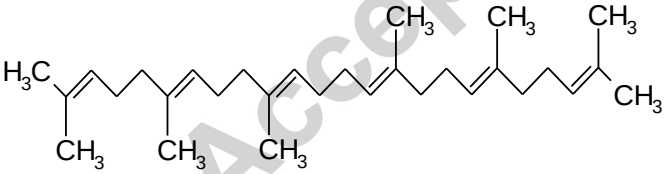
78 ß-Cyclocitral



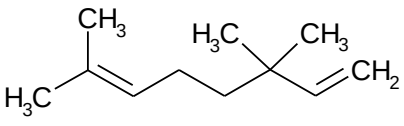
79 Trans geraniol



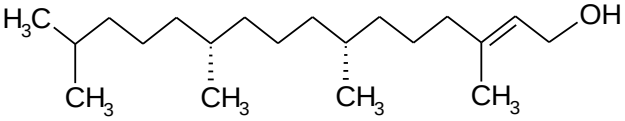
80 Geranyl acetone



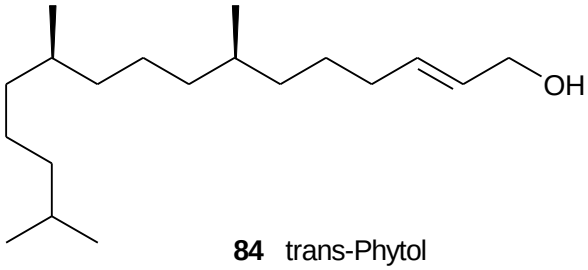
81 Squalene



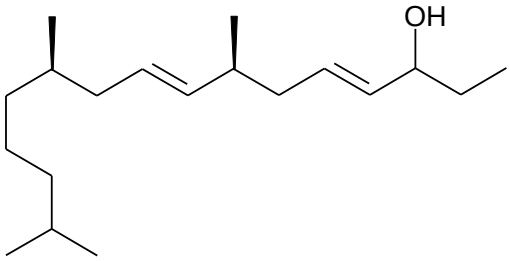
82 Linalool



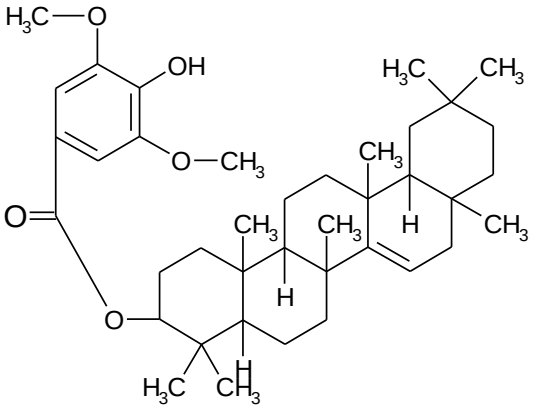
83 Phytol



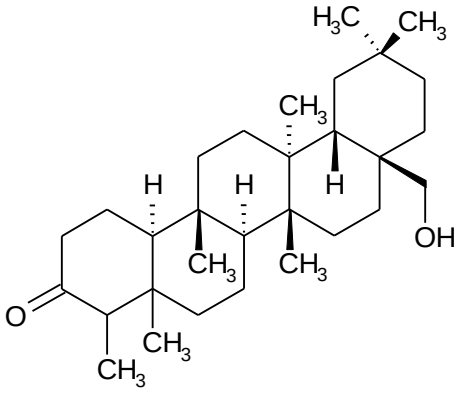
84 trans-Phytol



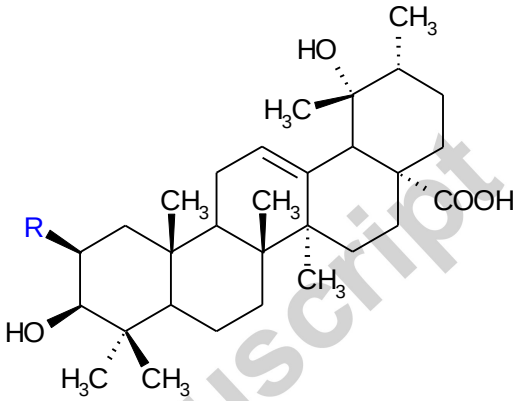
85 3-hydro-4,8-phytene



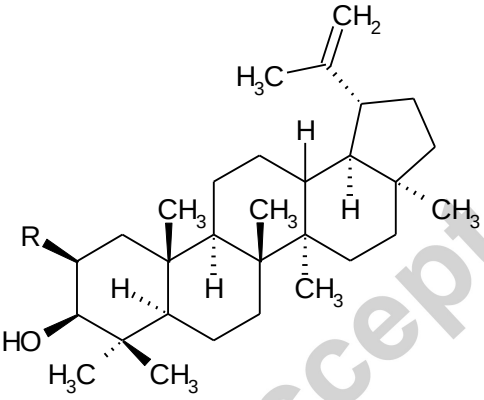
86 fibrarecisin



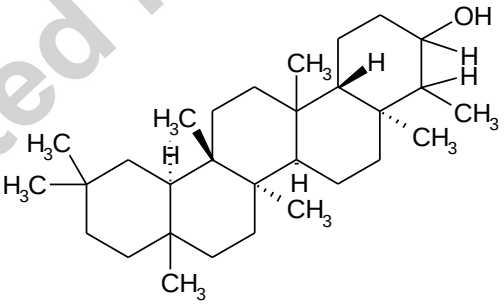
86 Canophyllol



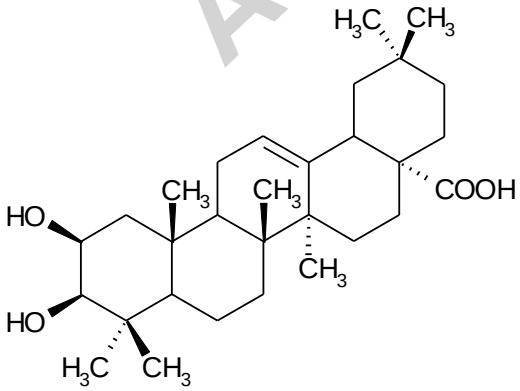
87 R = H, Pomolic acid
88 R = OH, 2ß-hydroxy-pomolic acid



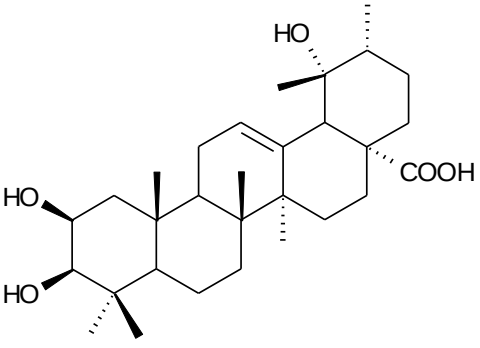
89 Lupeol



90 friedelinol



91 2b-hydroxyoleanolic acid



92 2b, 3b, 19a-trihydroxy-urs-12-en-28-oic acid

Steroids

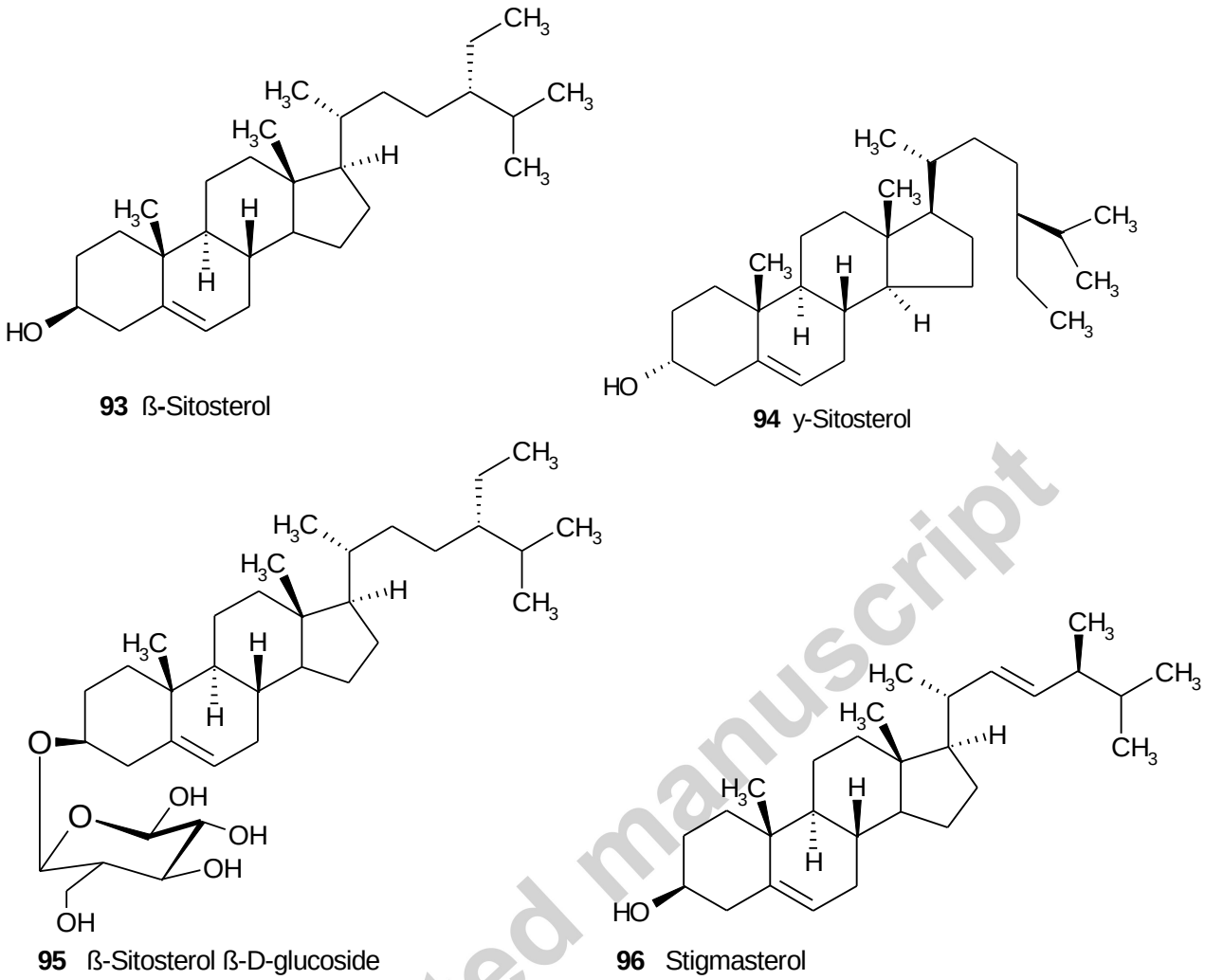
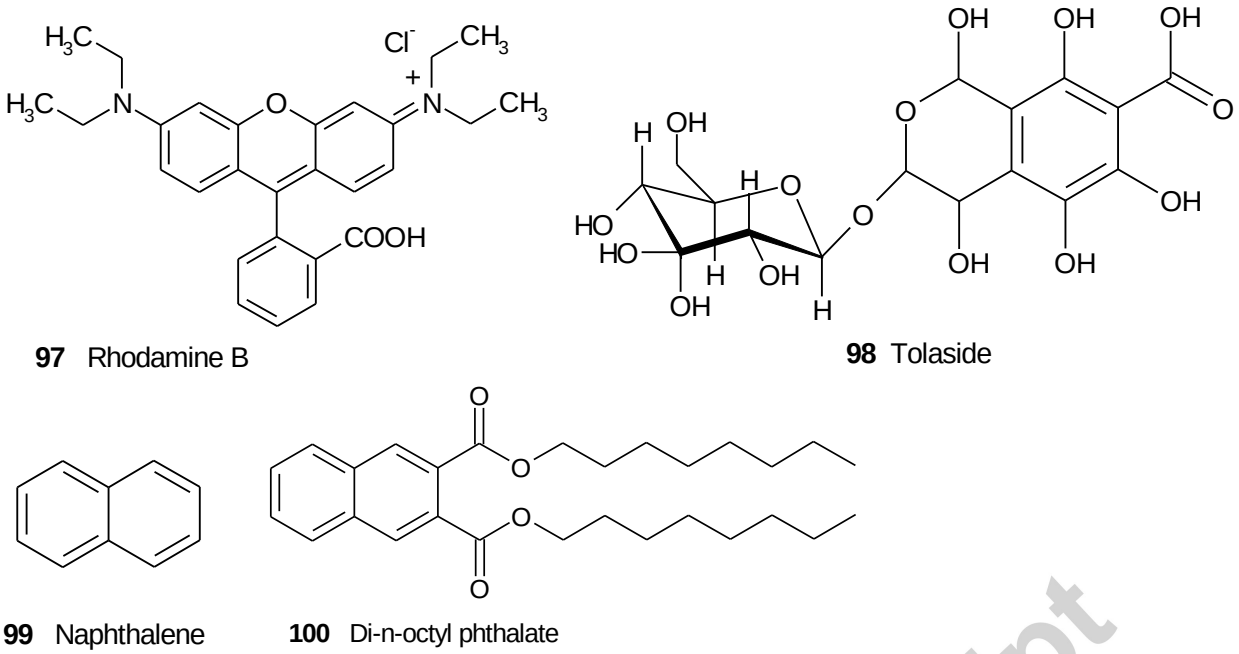


Figure 6: The chemical structures of terpenes, terpenoids and steroids isolated from K. africana.



97 Rhodamine B

98 Tolaside

Figure 7: Chemical structure of miscellaneous compounds from K. africana.

Review

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