Introduction

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

Traditional Uses

The kigelia plant have medicinal properties not only because of its perceived characteristics such as bitterness, astringent taste or smell but also because of forces that it seems to emit in connection with its location, orientation and association with other plants. It has a long history of use by rural and African countries particularly for medicinal properties. Several parts of the plant are employed for medicinal purposes by certain aboriginal people. In Malwi during famine the seeds are roasted to eat. Baked fruits are used to ferment beer and boiled ones yield a red dye. Most commonly traditional healers used it to treat a wide range of skin ailments like, fungal infections, boils, psoriasis and eczema. It also has internal application including the treatment in dysentery, ringworm, tape-worm, post-partum haemorrhage, malaria, diabetes, pneumonia and toothache. The tonga women of Zambezi valley regularly apply cosmetic preparation of Kigelia fruits to their faces to ensure a blemish free complexion. In the folk medicine, the fruits of the plant are used as dressing for ulcers, purgative and to increase the flow of milk in lactating women. Roots are said to yield a bright yellow dye. The Shona people tend to use the bark or root as powder or infusion for application to ulcers, drunk or applied in the treatment of pneumonia, as a gargle for toothache, and the leaves in a compound applied for backache. In West Africa, the root and...
unripe fruit is used as a vermifuge and as a treatment for haemorrhoids and rheumatism\(^{14}\).

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

**Chemical Constituents**

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

**Pharmacological Activities**

**Antibacterial and Antifungal**

A biologically monitored fractionation of the methanolic extracts of the root and fruits led to the isolation of the naphthaquinones, kigelinone, iso-pinnatal, dehydro-\(\alpha\)-lapachone, and
lapachol and the phenylpropanoids, 
$p$-coumaric acid and ferulic acid as the compounds responsible for the observed antibacterial and antifungal activity. The compounds isolated were tested for their activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Corynebacterium diphtheriae*, *Aspergillus niger*, *A. flavus*, *Candida albicans* and *Pullularia pullularis* (*Aureobasidium* sp.). The steroids and flavonoids are hygroscopic and have fungicidal properties.

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

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

<table>
<thead>
<tr>
<th>Activity</th>
<th>Iridoids</th>
<th>Naphthoquinone</th>
<th>Meroterpenoid naphthoquinones</th>
<th>Coumarin derivatives</th>
<th>Lignans</th>
<th>Sterols</th>
<th>Flavonoids</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anticancer</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Molluscidal</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
</tr>
<tr>
<td>Syphilis and Gonorrhea</td>
<td>+</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antiarrhythical</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antiulcer</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antifungal</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>Antimalarial</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Anti-inflammatory/analgesic</td>
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<td>+</td>
<td>+</td>
<td>-</td>
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<td>+</td>
<td>+</td>
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<tr>
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<td>-</td>
<td>+</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Postpartum Haemorrhage</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>-</td>
<td>+</td>
<td>-</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>+</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>
C. albicans. The extent of the inhibition of the bacteria was related to the concentration of the plant extract.

**Antineoplastic**

The crude dichloromethane extracts of stem bark and fruit showed cytotoxic activity in vitro against cultured melanoma and other cancer cell lines using the Sulphorhodamine B assay, which was used for bioassay-guided fractionation. TLC examination of the most active fractions of both stem bark and fruits showed the presence of the some major components which were found to be norviburtinal and β-sitosterol. Norviburtinal was found to be the most active compound but had little selectivity for melanoma cell lines while isopinnatal also showed some cytotoxic activity. β-Sitosterol was found to be comparatively inactive. HPLC analysis of the crude extract showed that the amount of norviburtinal present in the plant material did not account for all of the activity of the total extracts. Investigation into the biological activity of K. africana has focused on its antibacterial activity and its cytotoxic effects against cancer cell lines. These are related to the traditional uses of bark and fruit extracts for treating diseases caused by microorganisms and as a remedy for skin cancer. Considerable in vitro cytotoxicity has been demonstrated by extracts of the fruits and barks and the iridoid-related compound norviburtinal and the naphthaquinone isopinnatal have been shown to be two of the compounds responsible. The compounds also show cytotoxicity against mammalian cell lines. Kigelone, 5- or 8-hydroxy-2-(1-hydroxyethyl) naphtha [2, 3-b] furan-4, 9 dione, is a phytochemical analog of naphtha [2, 3-b] furan-4, 9 dione (furanonaphthoquinone [FNQ]) compounds, was isolated from the inner bark of the South American trumpet tree, Tecoma ipe Mart [syn. T. avellanedae Spec., Tabebuia impetiginosa (Mart. ex DC.) Standl., T. cassinoides (Lam.) DC.], or K. africana, which is known to have antitumour activity. Kigelia contains the constituent lapachol that is effective in the treatment of solar keratosis, skin cancer and kaposi sarcoma (an HIV-related skin ailment). Serial dilutions of standardised water, ethanol, and dichloromethane extracts of the stem bark and fruits of K. africana were tested for their growth inhibitory effects against four melanoma cell lines and a renal cell carcinoma line (Caki-2) using two different (MTT and SRB) assays. Lapachol, a possible constituent of these extracts, together with known therapeutic antineoplastic agents, was also tested in the same way. The IC50 of each extract was measured after extracts were diluted to 100 µg/ml in 1% ethanol or water. Significant inhibitory activity was shown by the dichloromethane extract of the stem bark and lapachol (continuous exposure). Moreover, activity was dose-dependent, the extract being less active after one hour exposure. Chemosensitivity of the melanoma cell lines to the stem bark was greater than that seen for the renal adenocarcinoma line. In marked contrast, sensitivity to lapachol was similar amongst the five cell lines. The antitumour activity of Bignoniaceae is probably due mainly to its naphthaquinoids which among them, for example lapachol, have been considered as candidates for clinical use. In vitro cytotoxic activity found in root bark extract of K. africana is attributed to γ-sitosterol which is comparable to standard, lapachol.

**Analgesic and Anti-inflammatory**

The analgesic effect of the stem bark of K. africana has not been previously reported and the mechanism by which it occurs is mostly likely via the inhibition of prostaglandin synthesis as indicated by its inhibition of acetic acid-induced mouse writhing. Also, it is known that centrally acting analgesic drugs elevate the pain threshold of mice towards heat and pressure. The ethanolic extract was evaluated for analgesic property using acetic acid induced mouse writhing and hot plate reaction time and anti-inflammatory property using the carrageenan induced paw edema and its probable mechanism evaluated in mice and guinea pigs. The extract showed a dose dependent significant reduction of the number of writhes (P<0.001) with 500 mg/kg body weight dose giving the highest reduction. The extract showed an insignificant elongation of the hot plate reaction time (P>0.05). In the carrageenan induced paw edema, a dose dependent significant inhibition was observed (P<0.001) between the second and fifth hour. It is clear that the ethanolic stem bark extract has significant analgesic and anti-inflammatory activity. Inhibition of the synthesis of prostaglandins and other inflammatory mediators probably accounts for the analgesic and anti-inflammatory properties. Chemical analysis of a polar extract of K. africana fruit indicated the presence of verminoside, an iridoid, as a major constituent, and of a series of polyphenols such as verbascoside. In vitro assays showed that it had significant
anti-inflammatory effects. Cytotoxicity and cutaneous irritation of the extract and of compounds verminoside and verbacoside were investigated. The crude extract did not affect cell viability in vitro either in cells grown in monolayers (ML) or in the reconstituted human epidermis (RHE, 3D) model; neither caused release of pro-inflammatory mediators or histomorphological modification of RHE.

Supercritical CO₂ extracts of Kigelia have been shown to be more effective than Indomethacin a potent synthetic anti-inflammatory (Table 2). Two different anti-inflammatory assays: inhibition of “oxidative burst” on human neutrophils and inhibition of cyclooxygenase (COX-2) were done. K. africana extracts were tested against a control (buffer, neutrophils and WST-1) and against indomethacin. Absorbance is measured at 450nm.

### Anti-malarial

Four naphthoquinoids isolated from root bark of the plant were assessed in vitro against chloroquine-sensitive (T9-96) and chloroquine-resistant (K1) *Plasmodium falciparum* strains and for cytotoxicity using KB cells. The most active 2-(1-hydroxyethyl) naphtha [2, 3-b] furan-4, 9-dione showed good antiplasmodial activity against both strains; IC₅₀ values were 627 nM for the K1 and 718 nM for the T9-96 strains. The IC₅₀ values were comparable to those of related naphthoquinones isolated from *K. africana* and these compounds also exhibited marked toxicity against endothelial ECV-304 cells due to their antiplasmodial effect. An antimalarial compound known as lapachol has been extracted from the root. Another compound (quinone) obtained from the wood shows anti-malarial activity against drug resistant strains of *P. falciparum* and is superior to chloroquine and quinine.

### CNS stimulant

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

### Antiprotozoal

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

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

<table>
<thead>
<tr>
<th>Plant parts used</th>
<th>Extract</th>
<th>Cox-2 activity(µg/ml)(IC50)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit</td>
<td>Chloroform/ethanol/water</td>
<td>0.8</td>
</tr>
<tr>
<td>Fruit</td>
<td>Chloroform/methanol</td>
<td>0.8</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>-</td>
<td>32</td>
</tr>
</tbody>
</table>
and isokigelinol. Compounds 2-((1-hydroxyethyl)-naphtho-[2, 3-b] furan-4, 9-quinone and isopinnatal possessed a pronounced activity against both Trypanosoma brucei brucei and T. b. rhodesiense bloodstream forms (IC_{50}: 0.12 µM and 0.045 µM, respectively for naphthoquinones and isopinnatal 0.37 µM and 0.73 µM) with a certain selectivity compared to KB cells (IC_{90}: 3.9 µM and 14.8 µM for naphthoquinones and isopinnatal, respectively)\(^51\)-\(^53\). Compounds kigelinol and isokigelinol had a less potent antitrypanosomal activity with IC_{50} values. Although little ethnopharmacological evidence exists, the naphthoquinones are active against several protozoal species associated with disease. Serial dilutions of extracts from the stem bark were tested for their growth inhibitory effects against Entamoeba histolytica. Butanol extract of stem bark exhibited in vitro antiamoebic activity. Three known iridoids specioside, verminoside and minoseide were isolated, purified and identified by comparing their spectral data with the literature values. These compounds were tested against HK-9 strain of E. histolytica for their in vitro antiamoebic evaluation and Metronidazole was used as reference drug to all the biological experiments. It is found that verminoside has two fold antiamoebic activities as compared to the standard drug while specioside showed comparable activity with metronidazole\(^54\).

Antidiarrhoeal

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

Other activities

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

Cosmeceutical Preparations

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

Conclusion

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

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Review Paper


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