

Original Research Article

# Review on traditional uses, phytochemical and pharmacological profiles of *Garcinia kola* Heckel

<sup>1</sup>Olivier Tene Tcheghebe, <sup>1</sup>Martin Signe, <sup>2</sup>Armel Jackson Seukep and  
<sup>3</sup>Francis Ngouafong Tatong

Abstract

<sup>1</sup>Inorganic Chemistry Department,  
Faculty of Science, P.O. Box 812,  
University of Yaounde I.

<sup>2</sup>Biochemistry Department, University  
of Dschang, P.O Box 67 Dschang;  
West Region, Cameroon.

<sup>3</sup>Chemistry Department, University of  
Dschang, P.O Box 67 Dschang; West  
Region, Cameroon.

\*Corresponding Author's Email:  
[tetcholi@yahoo.com](mailto:tetcholi@yahoo.com)  
Tel.: (237) 677381271/698048300

Traditional healing plays an integral role in African culture as it provides primary health care needs for a large majority. *Garcinia kola* Heckel is among the plants abundantly used in traditional medicine to cure diseases. This plant serves in folkloric medicine for the treatment of gastroenteritis, rheumatism, asthma, menstrual cramps, malaria, throat infections, headache, colic, chest colds, cough, liver disorders, diarrhoea, bronchitis, cardiac diseases, as a poison antidote, for oral and dental hygiene. Scientific researches have proved its multiple pharmacological properties: antimalarial, anti-trypanosomal, anti-asthmatic, antihypertensive, antioxidant, antimicrobial, anti-diabetic, anti-inflammatory and analgesic, anti-Candida infections, cardioprotective, gastroprotective, hepatoprotective and nephroprotective activities; its clinical effect in knee osteoarthritis and on the reproductive function, against oral cavity infections and intraocular pressure. Some bioactive constituents such as saponins, tannins, flavonoids, sterols, triterpenoids, alkaloid, and phenol significantly present in the plant extracts, support its multiple properties and uses in traditional medicine, while its rich content in carbohydrate, crude protein, crude fibre, minerals and vitamins validate its high nutritional value. This review study is an effort to give a detailed survey of the literature on the traditional uses, phytochemical and pharmacological profiles of *Garcinia kola* Heckel.


**Keywords:** *Garcinia kola*, Pharmacological, Phytochemical, Traditional uses

## INTRODUCTION

In developing countries, all over the world, 80% of population continues to use traditional medicine in primary medical problems. In the past decade, therefore, research has been focused on scientific evaluation of traditional drugs of plant origin (Giron *et al.*, 1991). *Garcinia kola* is one of such plants that have been frequently used for its nutritional values as well as for its medicinal virtues. All parts of this plant including nut, leaf, stem bark and root have been mentioned in many ethnobotanical and pharmacological studies, although the nut remains the most used part. *Garcinia kola* is a species of flowering

plant which belongs to a family of tropical plants known as Clusiaceae or Guttiferae (Plowden, 1972). It is a cultivated large forest tree, valued in most parts of West and Central Africa for its edible nuts (Hutchinson and Dalziel 1956). The plant grows as a medium size tree, up to 12-14m high and produces reddish yellowish or orange coloured fruit (Okwu 2005; Adesanya *et al.*, 2007). Each fruit contains 2-4 yellow nuts and a sour tasting pulp. Its nuts are commonly called bitter kola (may be because the nuts when chewed have a bitter astringent taste) or false kola (since they often serve as an alternative to true kola nuts,

Table 1. Scientific Classification

<b>Kingdom:</b> Plantae	<b>Genus:</b> <i>Garcinia</i>	
<b>Class:</b> Magnoliopsida	<b>Species:</b> <i>Garcinia kola</i>	
<b>Order:</b> Theales	<b>Scientific name:</b> <i>Garcinia kola</i> Heckel	
<b>Family:</b> Clusiaceae/ Guttiferae		

Nuts images

*Cola accuminata*). Bitter kola is also known as African wonder nut. In Nigerian languages, it is commonly called Namijigoro in Hausa, Agbilu in igbo, and Orogbo in Yoruba. *Garcinia kola* has economic and cultural values across West and Central African countries where the nuts are commonly chewed and used for traditional ceremonies (Eleyinmi, 2006). The seeds are also used in folk medicine in many herbal formulations and have potential therapeutic benefits due largely to the activity of their flavonoids and other bioactive compounds (Akintonwa and Essien, 1990; Okunji, 2002). *Garcinia kola* is highly valued in Cameroon because of its edible nut. In fact, these nuts are sold in the local markets and also at the international level, and constitute an enormous source of incomes for many traders. They are also shared during dowry and wedding ceremonies. (Table 1)

### Traditional uses

Extracts of various parts of *Garcinia kola* are used extensively in traditional African medicine (Xu *et al.*, 2013), especially for the preparation of remedies for the treatment of laryngitis, cough and liver diseases (Farombi and Owwoeye, 2011). Other medicinal uses include its use as purgative, antiparasitic, antimicrobial, antiviral, anti-inflammatory, antidote to the effects of *Strophantus gratus*, remedy for guinea-worm infection and for the treatment of gastroenteritis, rheumatism, asthma, menstrual cramps, throat infections, cure headache, relieve colic, chest colds, cough, and liver disorders (Iwu, 1985; Iwu *et al.*, 1987; Iwu *et al.*, 1990; Lewis and Elvin-Lewis, 1977). Oils and fats as well as their hydrolytic products (glycerol and fatty acids) are widely used as raw materials in food, cosmetics, pharmaceutical industries, soap production, synthetic detergents, greases, and several other products (Gunstone, 2004). Oils possessing antimicrobial activities are useful in treatment of wound, formulations of antimicrobial creams and lotions for treating skin diseases, as well as in the area of food preservation. There are claims, that traditional medicine practitioners use *Garcinia kola* seeds for the treatment of hypertension. Traditional African medicinal uses include, treatment of cough, purgative, anti-parasitic, anti-microbial. The seed is used in the treatment of diarrhoea (Braide, 1991), bronchitis and throat infections (Adesina *et al.*, 1995; Kabangu *et al.*, 1987) and liver disorders (Iwu *et al.*, 1990). The seed of

*Garcinia kola* enjoys a folk reputation in Africa as a poison antidote (Iwu *et al.*, 1990; Kabangu *et al.*, 1987). In Cameroon, the nut is chewed against gastroenteritis, worms, cardiac diseases and cough, to ease asthma, menstrual pains as well as for oral and dental hygiene. A decoction of the mixture of its leaf and bark is taken against hypertension, malaria, liver diseases, asthma and gastroenteritis. The nut when chewed is said to be effective against Ebola virus. A *Garcinia kola* nut is given to somebody in sign of friendship and respect for his/her person.

### Phytoconstituents

Esimone *et al.* (2007) documented the phytochemical constituents of *Garcinia kola* seeds which include saponins, tannins, flavonoids, proteins, glycosides, reducing sugar, starch, sterols and triterpenoids, with flavonoids predominating. Other Chemical investigations of the seeds have shown that they contain a complex mixture of phenolic compounds, including GB-type biflavonoids, xanthenes, benzophenones, cycloartenol and triterpenes (Seanego and Ndip, 2012; Antia *et al.*, 2010), Kolaviron (Adaramoye *et al.*, 2005a; Lacmata *et al.*, 2012), biflavonoids, xanthenes, kolanone, ameakoflavone, 2,4,3-methylenecycloartenol, coumarine and prenylatebenzophenones (Narcisi and Sacor, 1996), oleoresin (Onayade *et al.*, 1998), the chromanols, garioic and garcinal (Terashima *et al.*, 2002). In term of percentage, nutritional composition of Bitter kola nut gave: Moisture (60, 48±0,06), dry matter (39,52±0,06), crude fat (4,51± 0,56), crude protein (2,48±0,10), ash (0,79±0,005), crude fiber (5,23±0,16) and total carbohydrates (35,64) (Odebunmi *et al.*, 2009). Mineral composition of bitter kola (mg/kg of dry matter) was: K (722.10±0.00), Ca (67.07±0.1), Mg (114.83±3.47), Fe (6.10±0.43), Zn (6.10±0.43) and P (188.57±0.37) (Odebunmi *et al.*, 2009). Obi and Nwoha conducted another study to evaluate the proximate composition, nutritive properties and phytochemical content of Bitter Kola (Mazi *et al.*, 2013). Carbohydrate (70.31%) was observed to be the most abundant biological molecule. The crude protein (11.27%) and moisture content (9.28%) were significantly high (P<0.05) while ash (4.17%), crude fiber (3.94%) and ether extract/fat (1.03%) were present in appreciable amounts. Vitamins A, C, E, B1, B2, B3 contents of the bitter kola

were assayed. The levels of vitamin C, calcium, potassium and iron were significantly high ( $P < 0.05$ ). The phytochemical assay showed that tannin (0.347%), saponin (0.680%), phytic acid (0.550%), phenol (0.163%), Trypsin inhibitor (2.737Tu/g), sterol (0.093%), flavonoid (2.130%), Alkaloid (0.433%), oxalate (0.433%), caffeine (0.607%) and hydrogen cyanide (1.347 mg/kg) were present in significant amounts. Flavonoids have been implicated as possible bioactive agents responsible for antiulcerogenic and anti-inflammatory effects (Alarcón, *et al.*, 1994; Landberg *et al.*, 2011). Furthermore, many plants containing flavonoids have been shown to have diuretic, laxative, antispasmodic, anti-hypertensive and anti-inflammatory actions (Okuda, 1962), and antimalarial activity (Konziase, 2015). Kolaviron, a biflavonoid complex isolated from the seeds of *Garcinia kola* has been reported to possess neuroprotective, anti-inflammatory, antimicrobial, antioxidant, antigenotoxic and hepatoprotective activities in model systems via multiple biochemical mechanisms (Adaramoye *et al.*, 2005a; Lacmata *et al.*, 2012). Furthermore, a study by Adaramoye *et al.* (2005b) showed that Kolaviron has anti-atherogenic and vasorelaxant effects in animal model and isolated smooth muscle, respectively. This pure compound is also effective against *Plasmodium berghei* (Oluwatosin *et al.*, 2014). Isolated pure form of alkaloids and their synthetic derivatives are used as basic medicinal agents for their analgesic and bacterial effects (Blytt *et al.* 1988), antihypertensive, antiarrhythmic, antimalarial and anti-cancer activities (Wink *et al.*, 1998). Tannin rich medicinal plants are used to heal a lot of illnesses; such as leucorrhoea, rhinorrhoea and diarrhea. More recently, tannins have gained medical interest, because of the high prevalence of deadly ailments such as AIDS and numerous cancers (Ibikunle and Ogbadoyi, 2011). The mineral and phyto-chemical analysis revealed the nutritional and medicinal values of Bitter Kola.

### Pharmacological activities

The research data on *Garcinia kola* indicate that it possesses tremendous pharmacological value (due to its potent phytoconstituents: kolaviron and GB-1) which supports its multiple traditional uses for the management of health problems. The most important are:

#### Antimalarial activity

A scientific work was carried out to investigate the antimalarial potential of kolaviron (KV), a biflavonoid fraction from *Garcinia kola* seeds, against *Plasmodium berghei* infection in Swiss albino mice (Oluwatosin *et al.*, 2014). In addition to its known antioxidant effects, kolaviron, especially at 200mg/kg, exhibited high antimalarial activities in *Plasmodium berghei*-infected

mice. It also ameliorated the parasite-induced anaemia and body weight alterations at the administered doses, possibly through interfering with lipid peroxidation process as well as sparing endogenous primary antioxidant enzymes reserves. In another study, three pure biflavonones (GB-1a, GB-1, and GB-2) from the same plant showed antimalarial potencies *in vitro* and *in vivo* (Konziase, 2015). In fact, they displayed not only potent inhibitory activity *in vitro* against *Plasmodium falciparum* proliferation but also antimalarial potency through oral administration in mice infected with *Plasmodium berghei* without signs of acute toxicity. GB-1 showed the most potent antimalarial activity with a high selectivity index and, therefore could be exploited to identify the molecular target, which subsequently could be helpful to design novel therapeutics against malaria. GB-1 may also be considered as a promising antimalarial candidate for trial *in vivo* using higher animals infected with *Plasmodium falciparum*.

#### Anti-trypanosomal Activity

Treatment options for trichomoniasis are extremely limited. Newer drugs are therefore needed. In this sense, Ogbadoyi *et al.* conducted a study designed to evaluate the therapeutic potentials of methanol extracts of *Garcinia kola* nuts in the chemotherapy of experimental African trypanosomiasis (Ogbadoyi *et al.*, 2011). Mice infected with *Trypanosoma brucei* were treated with 100% and 50% (v/v) methanol extracts of this tree's nut at dose levels of 200, 400 and 600mg/kg body weight per day for 21 consecutive days. Parasitemia in all treated animals continuously increased till death except for the group administered 600mg/kg body weight per day of the 50% v/v methanol extract which maintained very low parasite count for close to four months of treatment. So, 50% methanol extract of *Garcinia kola* nut extract is highly trypanostatic. In another study, researchers found that this plant's extracts are sufficiently trichomonocidal and potentially useful as therapeutic agents in the control of trichomoniasis (Ibikunle and Ogbadoyi, 2011). Hence, *Garcinia kola* extract upon an elaborate pharmacological evaluation and standardization has great potential for use as phytomedicine in the control of trypanosome proliferation in infected animals and can serve as a template for the elaboration of anti-trypanosomal drugs.

#### Anti-asthmatic activity

*Garcinia kola* extract is effective for the management of asthma (Miller 2001; Dorsch and Wagner, 1991; Okwu 2004; Hodek, *et al.*, 2002; Ferguson, 2001; Farquar, 1996; Chen and Kang, 1997). Flavonoid and xanthone present in this plant's extract could be responsible for its beneficial effects for the treatment of asthma. In fact, flavonoids have

anti-asthmatic activity by inhibiting platelet-activating factor (PAF), phospholipase A2 (PLA2) and phosphodiesterase (PDE) (Miller, 2001; Dorsch and Wagner, 1991). Flavonoids also protect against allergies, inflammation, free radicals, and platelet aggregation (Okwu, 2004; Hodek *et al.*, 2002; Ferguson, 2001; Farquar, 1996). Xanthenes on its side have anti-asthmatic activity by dependently inhibiting the Ca<sup>2+</sup> influx induced by either no repinephrine or high K<sup>+</sup>, suggesting that xanthone might act as a blocker of both receptor-operated and voltage-dependent Ca<sup>2+</sup> channels (Chen and Kang, 1997). Furthermore, xanthone causes increase in the level of intracellular cyclic adenosine 3', 5'-monophosphate (cAMP) content (Chen and Kang, 1997). Manimi *et al.* (1994) reported that xanthone showed inhibitory effects on cAMP phosphodiesterase. Intracellular levels of cAMP can be increased by  $\beta$ -adrenoceptor agonists, which increase the rate of its synthesis by adenylyl cyclase (AC) or by phosphodiesterase (PDE) inhibitors such as xanthone, which slow the rate of its degradation. From these studies *Garcinia kola* appears to be very promising in the treatment and management of asthma. There is therefore the need to further examine the effects of its various phytochemical contents on respiratory smooth muscle, with a view to possibly formulating its extracts or active constituents as medicines.

### Antihypertensive activity

A study has been conducted to investigate the effect of *Garcinia kola* on blood pressure. Albino wistar rats were then divided into three groups (Naiho *et al.*, 2009). Groups A rats had normal rat chow and water ad-libitum while groups B and C rats had *Garcinia kola* diet of 10% w/w and 15% w/w respectively. Their blood pressures were monitored weekly for a period of 6 weeks. Secondly, inbred wistar rats weighing on the average 185g were anaesthetized with thiopentone sodium 100mg/kg body weight (b.wt) intraperitoneally and prepared for injection and for blood pressure measurements on a recording device. Significant reduction in blood pressure ( $P < 0.05$ ) was observed in rats given *Garcinia kola* -enriched diets, in the third week. During preliminary investigations it was observed that 5.0mg/kg b.wt dose of extract was lethal after 6 minutes, while 3.0mg/kg b.wt of the extract was tolerated for upwards of four hours. Based on these findings, graded doses of the extract (0.5 – 3.0mg/kg) were used and these doses produced statistically significant ( $P < 0.05$ ) fall in mean arterial pressure and also significant ( $P < 0.05$ ) increase in heart rate. Cholinergic blockade produced no significant attenuation on the effect of extract. However, there was a significant ( $P < 0.05$ ) attenuation to extract effect after Histaminergic blockade. Hence, *Garcinia kola* extract might contain a vasoactive ingredient, which is capable of lowering blood pressure,

although the mechanism of action is yet to be fully understood.

### Antioxidant activity

An *in vitro* study aimed to evaluate the ability of ethanol extract of *Garcinia kola* leaves at concentrations (3.3-40g/ml) to prevent 6 $\mu$ M Fe<sup>2+</sup> induced lipid peroxidation in rat brain and liver homogenate was assessed using Thiobarbituric acid reactive substance assay (TBARS) (Oloyede and Afolabi, 2012). Fe<sup>2+</sup> chelating ability of the extract was also determined. The inhibitory effect of this plant's leaves on lipid peroxidation in both liver and brain homogenate and the iron chelating activity were concentration - dependent exhibiting an antioxidant activity against free radicals. The extract showed its highest inhibition at the same concentration (26.7g/ml) in both liver and brain homogenate with % inhibition of 64.1% and 38.2% respectively. The results of this study demonstrate the efficacy of the ethanol extract of *Garcinia kola* leaves in the inhibition of Fe<sup>2+</sup> induced lipid peroxidation due to its iron chelating. Therefore, the leaves of the plant could be considered to have significant natural antioxidant activity against the initiation of some prevalent diseases and can be used as an accessible source of natural antioxidants. Another study showed that kolaviron (a flavonoid extracted from *Garcinia kola* seeds), was effective at preventing microsomal lipid peroxidation induced by iron/ascorbate in a concentration dependent manner (Olatunde *et al.*, 2008). The latter study attributed the overall antioxidant activity of kolaviron on lipid peroxidation to its properties of scavenging free radicals and active oxygen species and it may relate directly to prevention of propagation of *in vivo* lipid peroxidation.

### Antimicrobial activity

Antimicrobial activity of seed extracts derived from *Garcinia kola* was studied *in vitro* (Madubunyi, 1995). The seeds were successively extracted with petroleum ether, 70% ethanol and water. The ethyl acetate fraction of the ethanol extract, which showed the maximum antimicrobial activity, was recovered in a 2.4% w/w yield. Antimicrobial evaluation of the differential solvent extracts of this plant seeds revealed that the petroleum ether, ethanol, the milky layer and ethyl acetate fractions possessed antimicrobial properties. The observed activity was due to the presence of a polyisoprenyl benzophenone (Kolanone) in the petroleum ether extract as well as the hydroxybiflavanonols present in the ethyl acetate fraction. The hydroxybiflavanonol was found to be the main component exhibiting significant ( $p < 0.005$ ) antimicrobial activity against Gram-positive and Gram-negative bacteria in a bacteriostatic manner and against *Candida albicans* and *Aspergillus flavus* in a fungistatic manner. The MIC of

this fraction against *Staphylococcus aureus* was  $3.1 \times 10^{-7} \mu\text{g/ml}$  and  $3.0 \times 10^{-3} \mu\text{g/ml}$  against *Escherichia coli*. Similar results was obtained for this plant in other studies against bacteria: *Salmonella typhi*, *Staphylococcus aureus* and *Klebsiella pneumonia*, *Staphylococcus aureus* and *Klebsiella pneumonia* (Indabawa and Arzai, 2011), *Staphylococcus aureus*, *Escherichia coli*, *Bacillus subtilis*, *Salmonella typhi* and *Klebsiella pneumonia* (Aderibigbe, 2012) *Staphylococcus aureus*, *Escherichia coli*, *Klebsiella pneumoniae*, *Bacillus subtilis* and *Pseudomonas aeruginosa* (Arekemase *et al.*, 2012), *Bacillus anthracis* and *Escherichia coli* (Akinpelu *et al.*, 2008); and fungi: *Aspergillus niger*, *Rhizopus stolonifer*, *Penicillium notatum* and *Candida albicans* (Aderibigbe, 2012), *Candida albicans* and *Aspergillus niger* (Arekemase *et al.*, 2012).

### Anti-diabetic activity

The effects of aqueous extract of *Garcinia kola* seed on glucose, superoxide dismutase, catalase and malondialdehyde of normal rats were investigated (Omage *et al.*, 2010). Oral administration of aqueous seed extract of *Garcinia kola* at a concentration of  $200 \text{ mg kg}^{-1}$  body weight over a period of 21 days, significantly ( $p < 0.05$ ) decreased the levels of blood glucose, increased the activity of superoxide dismutase ( $p < 0.05$ ) and that of malondialdehyde ( $p < 0.05$ ). The treatment however had no significant effect ( $p > 0.05$ ) on the activity of catalase. The elicitation of these effects by the plant is a reflection of its hypoglycemic and antioxidative properties. Onyemaechi *et al.* found a similar result in alloxan-induced diabetic male Sprague-Dawley rats (Onyemaechi *et al.*, 2005). Adaramoye conducted another study to evaluate the possible protective effects of kolaviron (KV) isolated from *Garcinia kola* seed on cardiac, renal and hepatic tissues of STZ-diabetic rats, (Adaramoye, 2012). KV offered significant antidiabetic and tissues protective effects in the rats. This study confirmed that cardiac, renal and hepatic function indices were significantly elevated during STZ-induced diabetes, and that oral administration of KV reduced the levels of some of the indices. Therefore, KV may offer protection for tissues of animals during diabetes but more studies are required to define a novel pathway by which KV affects diabetes using pancreatic cell line. This seed can also be chewed to decrease the levels of blood glucose.

### Anti-inflammatory and analgesic activity

In a research work, the analgesic and anti-inflammatory properties of Kolaviron (a pure compound from *Garcinia kola* seed) was investigated using both thermal and chemical models of pain assessment in mice and rats (Olaleye *et al.*, 2000). Varying doses of Kolaviron were

given 30 minutes prior to the induction of abdominal constrictions in mice and the determination of the mean tail immersion duration at water bath temperature of  $50.0 \pm 10^\circ\text{C}$  in mice. Kolaviron exhibited dose-related antinociceptive properties against acetic acid induced abdominal constrictions in mice: at  $50 \text{ mg/kg}$ , it gave 28.92% inhibition ( $P > 0.05$ ) and at  $200 \text{ mg/kg}$  it gave 55.49% inhibition ( $P < 0.01$ ). The compound also increased the mean tail immersion duration at water bath temperature of  $50.0 \pm 1^\circ\text{C}$  in mice. The traditional use of this seed in the management of inflammatory conditions in hepatic and respiratory systems is thus justified.

### Anti-Candida infections

A study aimed at determining the effect of *Garcinia kola* extract on oral Candida infection in non-HIV participants, to assess its side effects and to compare its efficacy with chlorhexidine (CHX) mouth wash was carried out (Abah *et al.*, 2014). A double blinded clinical trial was carried out in non-HIV participants with clinically diagnosed Candida infection. *Garcinia kola* extract and chlorhexidine mouth wash were administered to the participants after randomly selected into the two treatment groups. The lesion was cleared in 96.4% participants who used *Garcinia kola* (without any side effect), while it was cleared in 80.6% participants who used chlorhexidine at the end of the 3<sup>rd</sup> week. Thus, *Garcinia kola* can be used against candidal infections of the oral cavity in patients with compromised immunity, extremes of ages and in healthy people with local factors that can precipitate the infection. Antwi-Boasiako and Abubakari also proved the effectiveness of aqueous extracts from the stem-wood and bark of *Garcinia kola* against *Bacillus subtilis* and *Escherichia coli* bacteria which infect oral cavity (Antwi-Boasiako and Abubakari, 2011).

### Cardioprotective activity

The effect of kolaviron (a flavonoid complex) extracted from *Garcinia kola* seeds on the organ weights (lungs, kidneys, heart, spleen and liver) of rats administered with cholesterol, five times a week, for eight consecutive weeks was investigated (Nwaneri-Chidozie *et al.*, 2014). The results revealed that cholesterol administration at a dose of  $30 \text{ mg/day}$  for eight consecutive weeks caused a significant increase ( $p < 0.001$ ) in relative heart weights of the cholesterol-fed rats when compared with the control. However, co-treatment with kolaviron at doses  $100$  and  $200 \text{ mg/kg}$  significantly ( $p < 0.001$ ) reduced the cholesterol induced enlargement of the heart. This is a pointer to the cardioprotective potential of kolaviron; and thus, suggests a possible use as a dietary supplement for the prevention and management of coronary heart diseases.

### Gastroprotective activity

The antiulcer effect of petroleum ether extract of *Garcinia kola* (GK) has been reported (Olaleye *et al.*, 2006). Similarly, the antiulcer effect of diet containing GK has been documented (Ibironke *et al.*, 1997). More recently, Ige *et al.* conducted a study aimed at evaluating the efficacy of the methanolic extract of GK (mGK) in the management of gastritis and gastric ulcerations in rat model (Ige *et al.*, 2012). In the latter study, treatment with mGK abrogated ethanol-induced gastric damage: it reduced the morphological damage score, ulcer score, gastric wall thickness, and lipid peroxidation ( $p < 0.05$ ), and also improved the cyto-architecture of the gastric mucosa. This study substantiated the gastroprotective potentials of mGK. The mechanism of action could be associated with the anti-oxidative activities of the flavonoid constituents (Ige *et al.*, 2012).

### Hepatoprotective activity

A research work was conducted to evaluate the hepatoprotective effect of aqueous extract of *Garcinia kola* seeds on carbon tetrachloride (CCl<sub>4</sub>) induced liver damage in adult wistar rats (Dauda Zainab, 2014). 36 animals (male and female) weighing between 150-250g were randomly divided into six groups. Each group comprised of 6 rats and was labelled as groups I, II, III, IV, V and VI. Group I (control) animals were administered distilled water orally daily for 2 weeks (volume per body weight) while group II (CCl<sub>4</sub> control) animals were administered distilled water orally daily for 2 weeks (volume per body weight) and carbon tetrachloride (CCl<sub>4</sub>) 0.4 ml/kg intraperitoneally as a single application. Group III rats were administered 100 mg/kg body weight of silymarin (a standard drug) once daily for 2 weeks followed by a single dose of CCl<sub>4</sub> (0.4 ml) on day 14 of the experiment. Group IV rats were administered 800 mg aqueous extract *Garcinia kola* / kg body weight orally once daily for 2 weeks. Group V and VI rats were administered 800 mg and 400 mg aqueous extract of *Garcinia kola* orally once daily for 2 weeks followed by a single dose of CCl<sub>4</sub> (0.4 ml) on day 14 respectively. At the end of the experiment, blood samples were collected for serum analysis of levels of alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), superoxide dismutase (SOD), reduced glutathione (GSH) and catalase (CAT). Hepatic tissues were also collected for histopathological assessment of liver damage. Results obtained showed that the CCl<sub>4</sub> treated group caused significant increase in the levels of liver enzymes (AST, ALP and ALT). *Garcinia kola* seed aqueous extract caused significant decrease in the aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) levels in the serum of the extract treated groups. Histopathological and histochemical

examinations of liver sections revealed distortion of histoarchitecture of the liver tissue such as sinusoidal congestion, necrosis, steatosis and fibrosis in group II. The administration of aqueous extract of *Garcinia kola* seed remarkably inhibited histoarchitectural distortion induced by CCl<sub>4</sub> administration. Hepatoprotective activity of the extract at dose of 400mg/kg was comparable to the reference drug. *Garcinia kola* aqueous seed extract showed a remarkable hepatoprotective and antioxidant activity against CCl<sub>4</sub>-induced hepatotoxicity as observed from the serum marker enzymes and antioxidant levels in liver tissues. CCl<sub>4</sub>-induced a significant rise in AST, ALT, ALP with a reduction of superoxide dismutase (SOD), catalase (CAT) and reduced glutathione (GSH). Treatment of the rats with the extract significantly ( $p < 0.05$ ) altered serum marker enzymes and antioxidant levels to near normal compared with CCl<sub>4</sub>-treated rats (group II). The activity of the extract at dose of 400mg/kg (group VI) was comparable to the standard drug confirmed by histopathological examinations of liver sections. Hence, *Garcinia kola* seed aqueous seed extract has hepatoprotective and antioxidant properties against CCl<sub>4</sub>-induced hepatotoxicity in Wistar rats and can serve as an affordable remedy against liver diseases.

### Nephroprotective activity

The effect of *Garcinia kola* extract on cisplatin-induced renal insufficiency in rats was studied (Okoko *et al.*, 2007). A total of fifteen rats were used for the study and were split into three groups of five rats each. Renal insufficiency was induced in rats of groups II and III by a single intraperitoneal administration of cisplatin (5mg/kg body weight), while rats in group I were normal controls. After three day, rats in group III received a daily dose of 10mg/kg body weight orally for another seven days. Renal deficiency was later assessed by serum urea, serum creatinine and urine protein levels. The results showed that the levels of measured parameter which were elevated as a result of cisplatin administration in group II were brought to near normal level by *Garcinia kola* seed extract in group III. This indicates that the plant possesses significant potential of ameliorating mild renal insufficiency induced by anticancer drug, cisplatin.

### Effect on the reproductive function

The effects of kolaviron (isolated from *Garcinia kola* seed) on the histology of organs of the hypothalamic-pituitary-gonadal axis, mainly the hypothalamus, pituitary and testis was studied (Obi and Nwoha, 2014). The aim was to ascertain if its consumption has deleterious effects on these organs. Thirty-six adult Wistar rats divided into six groups of six animals each were used and kolaviron administered at 100, 200, 400 and 800 mg/kg body weight.

The results showed that gross cellular depletion and desquamation of cells of testis significantly reduced number of cells in the hypothalamus and pituitary ( $P < 0.05$ ). It significantly reduced the relative brain weight ( $P < 0.05$ ). The results also showed that kolaviron at 800 mg/kg body weight alter the microanatomy of the hypothalamus, pituitary and testes thereby affecting the hypothalamic-pituitary-gonadal axis. This histological alteration suggests that kolaviron at high dose may impair reproductive functions in the male adult. In another study, the effects of *Garcinia kola* seed extract on oestrous cycle, ovulation and foetal development were studied in adult female Sprague-Dawley (S-D) rats (Akpantah *et al.*, 2005). Cyclic female rats weighing 150 to 200g were divided into three experimental groups and a control group. Group 1 was fed with 200mg/kg body weight of the extract on proestrous. Group 2 received 200mg/kg body weight of the extract daily for six weeks, while group 3, consisted of pregnant rats which received the same dose of the extract on days 1-5, 7-9th, 13<sup>th</sup> and 14<sup>th</sup> day of gestation. In groups 1 and 2, vaginal lavage was taken daily to monitor the oestrous cycle and ovulation. In group 3, gestational parameters monitored were number of total implants, resorption and dead fetuses. Live fetuses were weighed and examined for external malformation and variation. The results showed that the oestrous cycle was altered for the first two weeks after commencement of extract but returned to normal from the third week. This was indicated by the irregular pattern of oestrous with a prolonged dioestrus observed in the treated rats. Ovulation was partially blocked as shown by the reduced number of ova observed in the oviduct from the treated rats compared with control ( $p < 0.05$ ). There was a significant decrease in the weight of fetuses from the treated rats ( $p < 0.05$ ) while 7% of the fetuses from pregnant rats, which received treatment for the first five days of gestation, had malformed left upper limb. Results suggest that this plant seed at 200mg/kg body weight administered alters oestrous cycle in rats partly inhibits ovulation and may produce duration dependent teratogenicity in foetal rats. *Garcinia kola* is then to be consumed moderately, especially for pregnant women.

### Clinical effect in knee osteoarthritis (KOA)

A study was carried out to assess the clinical effects of *Garcinia kola* in KOA patients (Nwaneri-chidozie *et al.*, 2014). The patients were grouped into four (A = Placebo, B = Naproxen, C = *Garcinia kola*, D = Celebrex). The drugs and placebo were given twice a day per oral route. Each dose consisted of 200 mg of *G. kola*, Naproxen (500 mg), Celebrex (200 mg) and Ascorbic acid (100 mg). The primary outcome measure over six weeks' study period was the change in mean WOMAC pain visual analogue scales (VAS). Secondary outcome measures included the mean change in joint stiffness and physical function

(mobility/walking). The effect of knee osteoarthritis bilaterality among the subjects was not significant on their outcome ( $p > 0.05$ ). The change in the mean WOMAC pain VAS after six weeks of *Garcinia kola* was significantly reduced compared to the placebo ( $p < 0.001$ ). Multiple comparisons of the mean VAS pain change of *Garcinia kola* group was not lowered significantly as compared to the naproxen and celebrex groups ( $p > 0.05$ ). The onset of *Garcinia kola* symptomatic pain relief was faster than the placebo ( $p < 0.001$ ). However, it was slower than the active comparators ( $p > 0.05$ ). The duration of therapeutic effect of *Garcinia kola* was longer than the placebo ( $p > 0.001$ ) but less than naproxen and celebrex ( $p < 0.001$ ). *Garcinia kola* subjects had improved mean change mobility/walking after six weeks better than the control group ( $p < 0.001$ ). The mean change in mobility of the *Garcinia kola* group when compared to the active comparators was not significantly better ( $p < 0.05$ ). The mean change of knee joint stiffness ( $p < 0.001$ ) and the change of mean WOMAC score ( $p < 0.001$ ) were improved on *Garcinia kola* as compared to the placebo. The mid-term outcome of *Garcinia kola* subjects after cessation of use had a mean pain relief period of 17.27  $\pm$  5.15 days (range: 9–26 days). There was no significant cardiovascular, renal or drug induced adverse reaction to *Garcinia kola*. This plant's seed can then be consumed to manage some joint pains.

### Against dental problems

In a study, the crude ethanol extract, chromatographic fractions and isolated constituents of *Garcinia kola* seed against clinical strains of dental caries-causing and related microorganisms was evaluated (Ajayi *et al.*, 2014). Antimicrobial evaluations were done by testing different concentrations of the crude extract, vacuum liquid chromatographic (VLC) fractions and pure isolates against *Streptococcus mutans*, *Streptococcus viridians* and *Staphylococcus aureus* in already set blood agar with gentamicin as the reference standard. The zones of inhibition and minimum inhibitory concentrations (MIC) were determined as appropriate. Fraction N, eluted with (hexane: ethyl acetate 70: 30), exhibited the highest activity with MIC's of 1.50 mgml<sup>-1</sup> and 0.33 mgml<sup>-1</sup> while the pure isolates 1 (cycloartenol) and 2 (24-methylenecycloartenol) gave MIC's of 0.17mgml<sup>-1</sup> and 0.38 mgml<sup>-1</sup> against *Streptococcus mutans* and *Streptococcus viridians* respectively. Isolate 3 (garcinianin) gave MIC of 1.0 mgml<sup>-1</sup> against *Streptococcus mutans* but there was no significant activity against *Streptococcus viridians* and *Staphylococcus aureus*. This result provides justifications for the folkloric use of *Garcinia kola* for dental caries-related health problems while the isolated compounds may also serve as templates for future antimicrobial drug development.

### Intraocular pressure lowering efficacy

To evaluate the intraocular pressure (IOP) lowering efficacy of *Garcinia kola* 0.5% aqueous solution eye drops in patients with newly diagnosed primary open-angle glaucoma or ocular hypertension (POAG/OH) were studied (Adefule-Ositelu *et al.*, 2010). A total of 178 patients were randomly assigned to *Garcinia kola* and Timolol groups. At baseline, there were no differences in mean IOP between groups, based on age, sex, or diagnosis. At the end of the study period (24<sup>th</sup> week), the mean ( $\pm$  SD) reduction in IOP was  $12.93 \pm 2.3$  mmHg (47.8%  $\pm$  0.8% reduction) in *Garcinia kola* group and  $13.09 \pm 2.8$  mm Hg (48.2%  $\pm$  1.03% reduction) in the Timolol group ( $P > 0.05$ ). Adverse events were mild in nature with no statistically significant differences between groups ( $P > 0.05$ ). *Garcinia kola* ophthalmic solution significantly reduces IOP as compared to baseline. The IOP lowering effect of both treatments was equivalent. Topical *Garcinia kola* 0.5% aqueous eye drops are as effective as timolol maleate 0.5% eye drops in lowering IOP in newly diagnosed glaucoma and ocular hypertensive patients. The mean IOP reducing efficacy after six months of use was similar in both groups. *Garcinia kola* extract may then represent an alternate topical medication for patient with open angle glaucoma and ocular hypertensive in a resource limited population.

### CONCLUSION

Many people, mostly from developing countries now depend on herbal medicine for health care, possibly because standard treatments modalities are becoming more expensive and often carry severe side effects. It is now urgent that options in folklore medicine for the management of diseases should be investigated. *Garcinia kola* is one of such natural products involved in the treatment of several diseases. Some pharmacological tests carried out on the plant for its antimalarial, anti-trypanosomal, anti-asthmatic, antihypertensive, antioxidant, antimicrobial, anti-diabetic, anti-inflammatory and analgesic, anti-candida infections, cardioprotective, gastroprotective, hepatoprotective and nephroprotective activities; its clinical effect in knee osteoarthritis and on the reproductive function, against oral cavity infections and intraocular pressure, revealed positive results without significant adverse side effects. Bioactive constituents such as saponins, tannins, flavonoids, sterols, triterpenoids, alkaloid, and phenol significantly present in the plant extracts, support its multiple properties and uses in traditional medicine, while its rich content in carbohydrate, crude protein, crude fibre, minerals and vitamins validate its high nutritional value. We sincerely hope that the information provided in this review on *Garcinia kola* will serve as a data base for proper evaluation of this plant extracts which could lead to the

discovery of new and more effective drugs.

### Conflict of Interest Statement

None declared

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