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Tetracarpidium conophorum (African walnut) Hutch. & Dalziel: Ethnomedicinal uses and its therapeutic activities

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The use of medicinal plants to cure many ailments has been a tradition in different parts of the world. *Tetracarpidium conophorum* (African walnut) belongs to the family Euphorbiaceae. It is an edible seed that is widely cultivated for its delicacy. All parts of the plant have been used ethnomedically. This article reviewed the ethnomedicinal, nutritional, phytochemical and some pharmacological activities of *T. conophorum,* because medicinal plants are our hope in achieving sustainable global statutory of health for all and a last resort in healthcare management in African countries. This review reveals previous findings and other pharmacological benefits of the African walnut towards its potential as food and drug development.

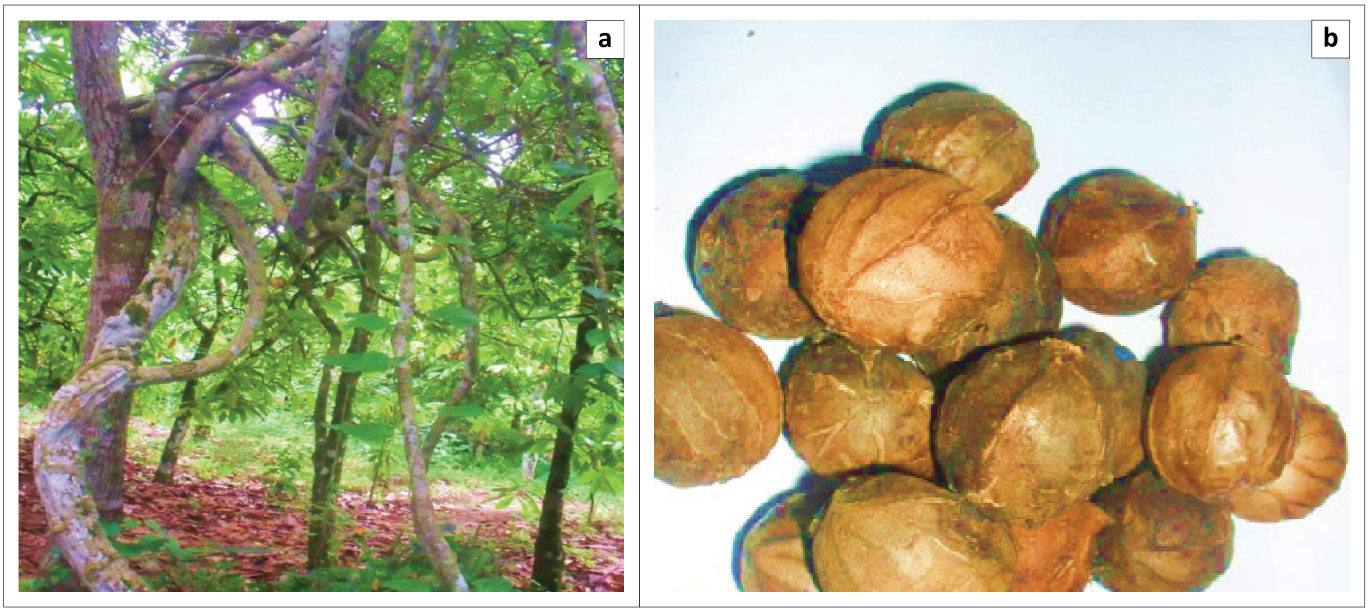
Introduction

Walnuts are edible seeds that are widely cultivated for their delicacy. Prominent species include *Juglans regia* (L.), known as the English walnut and belonging to the family Juglandaceae (Burkill 1985). The tropical African walnut, known as *Tetracarpidium conophorum* or *Plukenetia conophora* (Oyekale et al. 2015), belongs to the family Euphorbiaceae (Edem, Dosunmu & Bassey 2009). Adebona, Ogunsua and Ologunde (1988) stated that some walnut species are found in the family Olacaceae. The walnut is generally referred to as the conophor tree or conophor nut (Janick & Paul 2008). The plant is popularly known as African walnut, black walnut and Nigerian walnut (Ekwe & Ihemeje 2013; Nwaichi, Osuoha & Monanu 2017). In Nigeria, among the Yoruba tribe, the walnut is known as *awusa* or *asala*, *ukpa*, or *oke okpokirinya* in Igbo and *gawudi bairi* in Hausa; and it is known as *okhue* or *okwe* among the Bini tribe of Edo State (Chijoke, Anosike & Ani 2015; Kanu et al. 2015). In Sierra Leone, it is called *musyabassa* and in western Cameroon, it is known as *kaso* or *ngak*, among other local names (Burkill 1985).

However, lack of storage facilities has hampered the market value of the walnut (Kanu et al. 2015) and the nuts must be consumed within 1–2 days when cooked or else they will become foul-smelling and unpleasant for sale and consumption (Kanu et al. 2015). The seeds are consumed as snacks and refreshments. During its season, hawkers relate their walnuts' quality to kola nut maturity (*asala – ogbo koko bi obi*). The buyers also shake each seed nut to ensure that the seed is intact in the hard coat, and sometimes the quality of the seed nut can be seen from the nut colour and size. It is a perennial cash crop and an economic tree that is widely grown for its edible seed nut (Chijoke et al. 2017; Edem et al. 2009; Enujiugha & Ayodele 2003); it is also used as wood in the timber industry.

Morphology of *Tetracarpidium conophorum*

The plant is a small tropical flowering plant, a woody perennial climber or climbing shrub of about 6 m – 18 m long on attainment of the reproductive phase; its stem can be up to 16 cm in girth and dark grey when old, but is green and glabrous when young (Nwachoko & Jack 2015). The root is fasciculate and the leaf ranges between 10 cm long and 5 cm broad while the petiole may be up to 5 cm long (Ekwe & Ihemeje 2013; Janick & Paul 2008). Furthermore, the leaf is simple, crenate and ovate with a serrated margin. They are rounded at the base with alternate leaf arrangement and abruptly acuminate (Ekwe & Ihemeje 2013; Janick & Paul 2008). Usually, the walnut tree twines around other trees for support, especially the cocoa tree and kola nut tree (Oyekale et al. 2015). The immature fruits are usually green in colour but turn dark brown to black as they reach maturity (Oluwole & Okusanya 1993). The plants have swollen, fleshy, sparsely branched stems and are sometimes candle broid in appearance; the fruit is a capsule 6 cm – 10 cm long by 3 cm – 11 cm wide containing subglobular seeds (Janick & Paul 2008) as shown in Figure 1.



Source: Ayoola et al. 2011

FIGURE 1: *Tetracarpidium conophorum* in its natural habitat (a) and seed nuts (b).

The African walnut is widely grown in the western and eastern parts of Nigeria and is also indigenous to Cameroon, Central African Republic, Congo, Gabon and Niger (Janick & Paul 2008). Sierra Leone and the lower Congo region also consume walnuts (Udedi et al. 2014). Its range in Nigeria includes Uyo, Akamkpa, Akpabuyo, Lagos, Akure, Kogi, Ajaawa, Ogbomosho, Ibadan (Obianime & Uche 2010; Oke 1995), Ife, Ekiti and Ijeshaland; it is abundant in all cocoa-producing states in Nigeria and in the southern part of Nigeria (Nwaichi et al. 2017; Udedi et al. 2014), as shown in Figure 2.

The tree grows on moist, deep, fertile, well-drained loam soils and in silt clay loam soils (Cogliastro, Gagnon & Bouchard 1997). The African walnut is usually cultivated in the hot and humid zones of tropical Africa around gardens and backyards, mainly for subsistence consumption (Oyekale et al. 2015). It grows in coves, bottomlands, abandoned agricultural fields and rich woodlands (Chijoke et al. 2015). The plant climbs up to the tops to benefit from full sunlight and it may bind trees together such that if one of the trees dies, it is held in position until it decays (Bailey 2006). The African walnut usually flowers between November and early January and fruits between February and September with peak production in July (Oyekale et al. 2015). The seed takes 4–6 months to mature (Akpuaka & Nwankwor 2000).

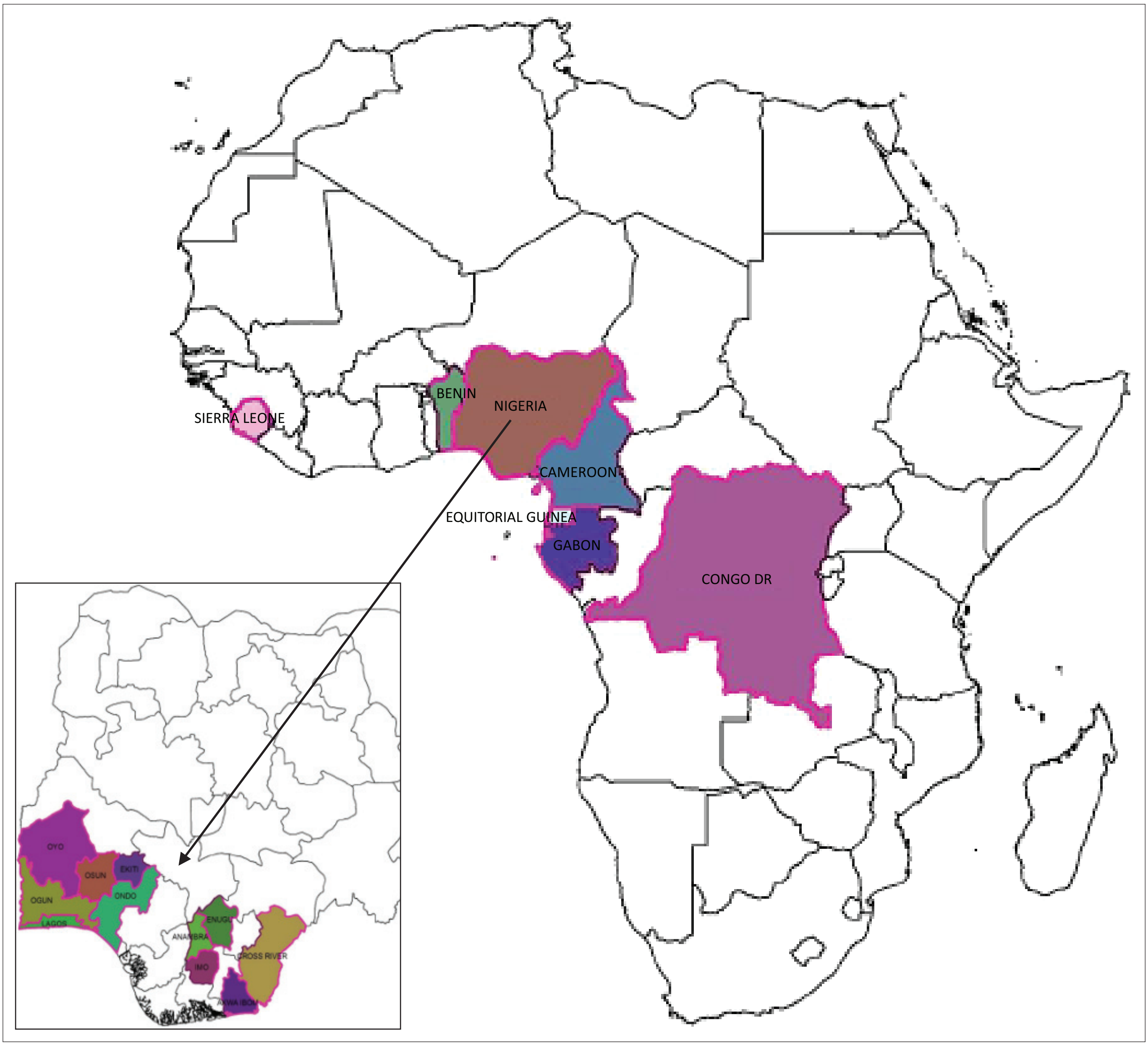
Botanical description of *Tetracarpidium conophorum*

Tetracarpidium conophorum is a monoecious plant that has separate male and female flowers on the same plant (Janick & Paul 2008). The male flowers are in a narrow raceme-like panicle that is as long as the leaves, with one or two female flowers near the base. The flowers are arranged alternately on the axis of the raceme inflorescence. The style is stout and quadrangular with four spreading stigmas. There are many stamens, about 40 in number (Janick & Paul 2008). They are found in the forest zones as climbers and the seed is surrounded by a thick, hard testa, while the seeds are round and dark brown at maturity. The plants are found in both primary and secondary forests (Okujagu et al. 2005). The seed is about 2.5 cm in diameter and the fruit (7 cm across) is light green to brown when ripe (Janick & Paul 2008).

Ethnomedicinal uses of *Tetracarpidium conophorum*

All parts of *T. conophorum* have been used ethnomedically, including the stem bark, leaves, seeds and roots. The bark is used by local people as a mild laxative (Janick & Paul 2008). The seed kernel, when eaten raw, has a bitter taste like the kola nut and is considered to be a tonic and aphrodisiac (Aiyeloja & Bello 2006). Customarily, drinking water immediately after eating the edible nut has a bitter taste principle, which might be due to the presence of some alkaloid-containing compounds in the plant. Nwauzoma and Dappa (2013) reported ethnobotanical uses of *T. conophorum* seed in the treatment of fibroids; the boiled seeds are also eaten to improve sperm count in men while the leaf juice is used to improve fertility in women and regulate menstrual flow.

Ayoola et al. (2011) reported the use of *T. conophorum* in the treatment of stomach disorders and for controlling high blood pressure. The bark is brewed as a tea for use as a laxative and is chewed for toothache. The fruits are edible and used for various purposes, including masticatory, thrush, anti-helminth, syphilis and also as an antidote against snake bites (Obianime & Uche 2010). They are said to tonify the kidneys, strengthen the back and knees and



Source: Nkwonta 2015

FIGURE 2: Geographical distribution of walnut-producing countries in Africa and Nigeria.

moisten the intestines. They are believed to stop asthma and are prescribed to be taken between bouts of asthma but not for acute asthma. They are used by the elderly to cure constipation and flatulence (Ayoola et al. 2011; Ogundolie et al. 2017). The leaves and young shoots are occasionally eaten with cooked rice in some parts of West Africa. The oil from the nut has been used in the formulation of wood varnish, stand oil, vulcanised oil for rubber and leather substitutes (Oyenuga 1997). Brown dyes have been extracted from the husk and the leaf extracts were used to reduce hiccups (Hogue 2000).

Chemical constituents of *Tetracarpidium conophorum*

The African walnut contains protein, vitamins, magnesium and is a good source of antioxidants (Kim & Lee 2002). The nut oil contains 48% – 50% dry weight of oil, is golden yellow in colour, with a taste and odour resembling linseed oil (Enujiugha 2003; Enujiugha & Ayodele 2003; Negi et al. 2011). The oil is highly rich in linolenic acid (64%), palmitic and stearic acids (15%) and oleic acid (11%). It is also rich in polyunsaturated fatty acids such as α-linolenic acid and it contains mono-saturated fatty acids (Kanu et al. 2015). Animashaun, Togun & Hughes (1994) used affinity chromatography techniques to isolate the agglutinin I and II of disulphide-bonded 70 kDa and 34 kDa of monomeric protein, respectively, which are referred to as isolectins from *T. conophorum* seed extracts. Asaolu (2009) quantified the amino acid composition of *T. conophorum* seed nuts and the total essential amino acid (274 mg/g) crude protein out of the total amino acids (573 mg/g). Glutamic acid (134 mg/g) had the highest amino acid and leucine (0.32) had the lowest essential amino acid score. Nkwonta (2015) indicated the presence of essential and non-essential fatty acids, namely palmitate, oleate, stearate, linoleate, arachidate and α-linoleate. The physicochemical characteristics, fatty acids and triglycerols (TG) of the nut oil (Type 1 and Type 2) content varied between 55.75% and 61.62%, while the ash values varied between 8.40% and 9.68% (Tchiegang, Kapseu & Parmentier 2001). The main fatty acid was linolenic acid (69.47% – 70.39%) as determined by capillary gas chromatographic analysis and the triacylglycerol profile obtained by reversed phase liquid chromatography showed 10 TG, with three major ones identified as trilinolenin (33.39% – 47.67%), dilinolenic-linoleic (12.19% – 27.15%) and dilinolenic-olein (18.46% – 37.71%) (Tchiegang et al. 2001).

Nutritional and phytochemical constituents

Nwaoguikpe, Ujowundu and Wesley (2012) established the phytochemical and biochemical composition of varieties of walnut (boiled and mashed wet nuts and dried powdered nuts). Saponins (8.37, 5.03 mg/kg) were the highest constituent of the mashed wet nuts and the dried powdered nuts, respectively. This suggested a role of the seed nuts in health and nutrition. Ekwe and Ihemeje (2013) reported the proximate composition of the African walnut (*T. conophorum*) on wet basis, which revealed protein (14.92%), oil (45.84%), crude fibre (1.14%), ash (3.52%) and carbohydrate (15.38%), while the anti-nutritional factors revealed tannins (0.89 mg/100 g), oxalate (1.28 mg/100 g), phytic acid (3.105 mg/100 g), trypsin inhibitors (1.84 mg/100 g), saponin (985.0 mg/100 g) and alkaloid (40.91 mg/100 g). Arinola and Adesina (2014) stated that the seed nut is a rich source of protein and fat but high heat could reduce the protein, ash and crude fibre content of the nut.

In addition, Akpoghelie et al. (2016) evaluated the nutritional content of walnut seed (*P. conophora*) and revealed that the raw seed contains ash (3.18%), moisture (39.27%), crude fibre (8.40%), fat (5.19%), protein (20.74%) and carbohydrate (23.22%), while the mineral content revealed K (4029.14 mg/kg), Na (3480.00 mg/kg), Ca (3014.28 mg/kg), Mg (726.11 mg/kg), Fe (68.00 mg/kg), Zn (24.01 mg/kg), Mn (19.00 mg/kg) and Cu (14.00 mg/kg). Chijoke et al. (2015) reported the seed nut contains alkaloids (2.29 mg/100 g), glycoside (2.19 mg/100 g), saponins (8.07 mg/100 g), flavonoids (0.02 mg/100 g), tannins (0.89 mg/100 g), reducing sugars (4.10 mg/100 g) and soluble carbohydrate (1.06 mg/100 g). The seed nut also revealed high moisture content (31.40%), ash (6.01%), fibre (8.66%), protein (28.85%), carbohydrate (21.30%) and high energy value (234.57 kcal). The mineral and vitamin constituents of the seed were also documented by Nnorom, Enenwa and Ewuzie (2013).

Udedi et al. (2013, 2014) reported comparative proximate analyses of raw and cooked walnut and noted that the nut is an excellent food material with potential in combating food insecurity in rural communities. They suggested the nut as a supplement to schoolchildren feeding programmes. The reported major bioactive compounds found in *T. conophorum* include phenols (7.44 mg/mL and 7.04 mg/mL), flavonoids (3.5 mg/mL and 1.66 mg/mL) and ascorbic acid (54.56 mg/kg and 44.00 mg/kg) for raw and cooked walnuts, respectively. Apeh et al. (2014) reported the effect of cooking on the proximate, phytochemical constituents and haematological parameters of *T. conophorum* in male rats. The results showed that the crude protein, carbohydrate and crude fibre contents of the raw seed were significantly higher than for cooked seed nuts but the hydrogen cyanide and steroid content of raw seed nuts was higher than for cooked seed nuts. The haematological parameters in the rats had a significant decrease in white blood cell (WBC) and lymphocytes when compared with the control group.

In a study, Oyekale et al. (2015) attempted to determine the bioactive agents groups that could be responsible for the diverse growth characteristics and medicinal uses of *T. conophorum* and the findings showed that alkaloid and saponin concentrations were highest in the foliage, terpene concentration was abundant in the regenerative hypocotyl segment while tannins, phenolic compounds and phlobatannin concentrations were abundant in the non-regenerative hypocotyl segment. The study concluded that the foliage can be used as an anti-venom agent based on its relatively high content of cardiac glycosides, alkaloids, saponins and phenols, which are active substances for detoxification of venoms in the human system (Bowsher, Steer & Tobin 2008). Chikezie (2017) also examined the phytochemical and proximate composition of boiled walnut seeds and the findings revealed a high concentration of alkaloids, steroids and a moderate concentration of tannins with no traces of saponins, phlobatannins, flavonoids, phenols or glycosides. Barber and Obinna-Echem (2016) assessed the nutritional composition, physical and sensory properties of wheat–African walnut cookies and recommended that the African walnut flour could be used successfully as a partial substitute for wheat flour at a range of 5% – 15%.

Onawumi, Faboya and Ayoola (2013) carried out proximate analysis on the leaf *T. conophorum*, which contained moisture (29%), fat (5.63%), fibre (14.92%), protein (16.62%), ash (12.89%) and carbohydrate (20.94%). The secondary metabolites revealed high alkaloid content (2.670 mg/kg) and low tannin content (0.56 mg/kg). Ayoola, Faboya and Onawumi (2013) reported on a comparative analysis of the phytochemical and nutrient composition of the leaves and seeds of *T. conophorum* and noted that the seeds have more nutritional and elemental composition than the leaves. The phytochemical constituents present in the seeds are also present in the leaves. Suara et al. (2016) evaluated the nutraceutical properties of the methanol extract of *P. conophora* leaves and reported some vital mineral elements; the proximate analysis revealed 6.86% moisture content, 11.78% protein, 8.57% total ash, 20.12% crude fibre, 1.56% total fat and 51.8% total carbohydrate. Uhunmwangho and Omoregie (2017) evaluated the nutrition and anti-nutrition as well as mineral content of walnut seed oil at different stages of fruit maturation. This study revealed the nutritional profile of the fruit-nut as a good source of plant protein, carbohydrate and fat, with a reduction in the level of some anti-nutrients in matured fruits. Findings from a study carried out by Isong, Alozie and Ekwere (2013) on conophor nut oil suggests that it is a non-drying oil suitable for paint and soap making as well as other industrial purposes. The results revealed that the oil has potential as a source of biofuel when compared with commercial graded diesel. Also, the free fatty acid (9.47%) and ester (89.74 mg KOH g^{-1}) content suggests its suitability as an edible oil while the high acid (87.22 mg KOH g^{-1}) and low peroxide (9.67 meq O_2 g^{-1}) content indicates high susceptibility to rancidity and low antioxidant levels.

Some reported pharmacological activities of *Tetracarpidium conophorum*

Anti-diarrhoea activity

Nwachoko and Jack (2015) reported that the *T. conophorum* nut hot aqueous extract protected rats against castor oil-induced diarrhoea; the inhibitory effect was attributed to the presence of some secondary metabolites and also justified ethnomedicinal use.

Male fertility enhancing activities

Ikpeme et al. (2014) reported that *T. conophorum* seed extract increased the viability and sperm output of male albino rats and suggested that the seed should be included in the formulation of male fertility drugs. Results from a study conducted by Obianime and Uche (2010) on the effect of aqueous extract of *T. conophorum* seed on the hormonal parameters of male guinea pigs showed a significant dose–time-dependent increase ($p \leq 0.05$) in the level of testosterone; the highest increase was recorded after the seventh day of the treatment (3.40 ng/mL) when compared with standard drugs (Proviron). However, Akpan and Anietie (2014) had contrary findings on the use of an aqueous extract of *T. conophorum* seed nut as a fertility enhancer in male albino Wistar rats. It was reported that 14.14 mg/kg and 21.21 mg/kg significantly decreased the percentage of sperm concentration but increased the follicle stimulating (FSH) and luteinising hormones (LH), which implies that it stimulates biosynthesis and secretion of fertility hormones and also is clear evidence of toxic damage to the spermatozoa. However, it was concluded that there is a need for caution on excessive consumption of *T. conophorum* seed nuts among males with infertility problems. Dada and Aguda (2015) reported that the *T. conophorum* seed powder has potential pro-fertility properties in male *Clarias gariepinus* that could be exploited in fish production as a feed additive for the improved reproductive performance of male African catfish.

Chijoke et al. (2017) stated that the leaf extract significantly increased testosterone levels and had an effect on the reproductive pathway of the rats that was dose-dependent and that the histopathological tissues were not distorted across the treatment groups.

Akomolafe et al. (2017a) established the modulatory effects of *T. conophorum* aqueous leaf extracts on oxidative stress-induced penile damage and key enzymes associated with erectile dysfunction. The highest inhibitory effect was obtained in the penis at a concentration of 0.50 mg/mL while the extract inhibited arginase activity in a dose-dependent manner and the IC_{50} (130.96 µg/mL) revealed higher inhibitory activity in the penile tissue than the testicular tissue homogenate (179.02 µg/mL). It was suggested that the inhibitory activities could be linked to the presence of phenolic constituents in *T. conophorum*.

In a similar study conducted by Akomolafe and Oboh (2017b), at the highest concentration the extract showed a more pronounced effect than the standard drug. The testicular biochemical parameters in all the treated groups showed significant ($p < 0.05$) increase in lactate dehydrogenase (LDH), glucose-6-phosphate dehydrogenase (G-6PDH), glycogen content, 3β and 17β hydroxysteroid dehydrogenase (HSD) activity and testicular and epididymal Zn and Se content, with a significant decrease in cholesterol content. Also, a significant ($p < 0.05$) increase in the level of serum testosterone, LH, FSH, sperm count, motility, viability and a decrease in sperm abnormality were observed when compared with the control group, indicating useful effects on spermatogenesis and sperm parameters in rats. Akomolafe et al. (2017c) investigated the effects of *T. conophorum* aqueous leaf extract on ethanol-induced infertility in male rats. The ethanol treatment group showed a significant ($p < 0.05$) decrease in LDH activity, G-6PDH activity, glycogen content, 3β and 17β HSD activity and testicular and epididymal Zn and Se content; furthermore there was a decrease in testicular sperm count, viability and marked increment in total sperm abnormalities, rate of sperm analysis parameters and consequently decreased reproductive hormone levels. It was concluded that co-administration of ethanol with either *T. conophorum* extract or standard drug almost improved the toxic assault imposed by ethanol on the reproductive organs and seminal quality of the rats.

Antioxidant activities

Amaral et al. (2004) and Periera et al. (2007) reported that polyphenolic compounds identified in walnut leaf extract included 3-galactoside, lactoside, 3-pentoside, 3-arabinoside, quercetin, *p*-coumaric-acid and 3- and 5-caffeoylquinic acids, which could be responsible for its antioxidant activity. Amaeze et al. (2011) reported the *in vitro* antioxidant activity of *T. conophorum* leaf extract and revealed that the dried leaves have more antioxidant activity than fresh leaves but the methanol extract possesses a high amount of plant bioflavonoids that are responsible for the antioxidant activity of many plant families. Udedi et al. (2014) evaluated the antioxidant activity of *T. conophorum* nut extract. The extracts have hydrogen ion donating potential while the free radical scavenging ability of the raw walnut was found to be higher than that of the cooked. Both the raw and cooked walnut extracts had potent lipid peroxidation inhibition capacity with EC_{50} values of 4.0 µg/mL and 6.50 µg/mL, respectively. The study concluded that the plant could be useful in boosting food security and reducing malnutrition in Africa countries. Akomolafe et al. (2015a) reported anti-peroxidative activity of *T. conophorum* leaf extract in the reproductive organ of male rats. The leaf extract caused a significant ($p < 0.001$) dose-dependent reduction in the lipid peroxidation levels when compared with the control group. The anti-peroxidative activity in the testes was associated with an increase in total protein, non-enzymatic (glutathione [GSH], vitamin C) and enzymatic superoxide dismutase (SOD), catalase (CAT), glutathione s-transferase (GST), glutathione peroxidase (GPX) antioxidant levels, by means of which the leaf extract may be useful in the treatment of reproductive cellular damage involving reactive oxygen species (ROS). A similar study was carried out by Akomolafe et al. (2015b) on the ameliorative oxidative effect of *T. conophorum* aqueous leaf extract on ethanol-induced reproductive toxicity in male rats; the authors concluded that the ameliorative effect could be a result of its antioxidant property, which may be attributed to the scavenging of radical species generated by ethanol and may also be linked to its phytochemical constituents. Ademiluyi et al. (2015) established that walnuts cooked with the shell contained more antioxidant phytoconstituents than those cooked without the shell. Cooking walnuts with the shell might, therefore, protect the antioxidant constituents. It is hence recommended to cook African walnut fruits with the shell to enhance its health protective properties. Abam et al. (2013a) reported on the effect of walnut oil on cadmium-induced oxidative stress in male rats and concluded the nut could be effective as an antioxidant in ameliorating the toxic effect of cadmium in the kidney, liver and brain tissues. A study from Akomolafe et al. (2015c) reported inhibitory effects of the aqueous extract of *T. conophorum* leaves on $FeSO_4$-induced lipid peroxidation in rat genitals; the findings were attributed to the high levels of quercetin, quercitrin and luteolin and the metabolic pathways in which these compounds may be associated with the free radical scavenging properties.

Anti-chelating activity

Olabinrin et al. (2010) evaluated the *in vitro* chelating ability of the aqueous extracts of *T. conophorum* nuts and concluded that the seed nut extract showed a dose-dependent decrease in chelating ability and a 2% w/v graded dose had the highest chelating ability.

Anti-ulcer and wound healing activities

Ezealisiji et al. (2014a) evaluated the methanol extract of the *T. conophorum* nut using pyloric ligation induced and ethanol-induced gastric ulceration methods. The extract reduced the ulcer index, gastric volume, total free and free acidity but increased the pH significantly ($p < 0.05$) when compared with the control group. It was established that the presence of some phytochemicals such as tannins, terpenoids and flavonoids were indicated for the cytoprotective properties as well as the wound healing activity. The result from a similar study carried out by Anosike, Abonyi and Etaduovie (2015) reported that the methanol extract of the seed nut showed significant anti-ulcer activity in the indomethacin-induced ulcer and there was significantly reduced ulceration ($p < 0.001$) when compared with the control group but it was not dose-dependent.

Results from the findings of Ezealisiji et al. (2014b) reported that the n-hexane and methanol extracts of the *T. conophorum* seed nut established accelerated dose-dependent wound healing activity of the extracts. This was attributed to the presence of some secondary metabolites like flavonoids with repeated antioxidant and immunostimulating activities. Bello et al. (2013a) investigated the healing properties of the walnut leaf in catfish (*Clarias gariepinus*), and it was concluded that a 1.50% addition of walnut leaf residue in the catfish diet could significantly aid the aquaculture industry and reduce mortality associated with wound infection.

Anti-inflammatory activity

Olaniyi et al. (2016) reported on the chloroform extract of the *T. conophorum* fruit and noted that a 400 mg/kg dose significantly inhibited inflammation when compared with diclofenac but 200 mg/kg of the extract was pro-inflammatory.

Anti-lipidemic activities

Ezealisiji et al. (2016) reported on the anti-cholesterol activity of the ethyl acetate and n-hexane extracts of the *T. conophorum* seed and showed that a 2.00 mg/kg dose of both extracts decreased low density lipoprotein (LDL) and increased high density lipoprotein (HDL) cholesterol when compared with atorvastatin (a standard cholesterol-lowering agent), which could be attributed to the oleic acid and α-linolenic acid. Analike et al. (2017) investigated the effects of cooked walnuts on blood lipids, lipoprotein and glucose among adult Nigerians. There was a significant reduction in plasma cholesterol, triglycerides, LDL-C and the LDL-C/HDL-C ratio of the subjects when compared with their baseline values. It was concluded that the reduction could prevent hyperlipidaemia complications and also improve lipid metabolism. Nwaichi et al. (2017) also reported on the nutraceutical potential of *T. conophorum* and *Buchholzia coriacea* in diet-induced hyperlipidaemia. The hyperlipidaemic rats were subsequently treated with normal feed supplemented at 500 mg/kg and 1000 mg/kg of *T. conophorum* and *B. coriacea* for two weeks. In comparison to test control animals, there was a reduction in weight gain, total cholesterol (TC), triglycerides (TG), aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), plasma contents of LDL, very low density lipoprotein (VLDL), non-HDL and atherogenic indices in a dose-dependent fashion. Clarisse, Kenfack and Angele (2017) assessed some effects of consumption of defatted flours of *Ricinodendron heudelotii* and *T. conophorum* on some biological and biochemical parameters in adult male rats. The study revealed that HDL cholesterol for experimental diets was comparable with the control diet and LDL cholesterol was higher in rats from the casein group. Abam et al. (2013b) concluded that walnut oil administered at 2.00 g/kg and 4.00 g/kg doses restored some lipid aberrations but caused an increase in total and LDL cholesterol. This suggested that the walnut oil could be linked with some cardiovascular risk despite its beneficial importance in lowering cadmium levels in the blood. Leudeu et al. (2009) evaluated *T. conophorum* and *R. heudelotii* oil fed to male Sparague–Dawley rats to lower blood lipids and there was significant reduction in the cholesterol and triglycerides levels when compared with control group. Sebate et al. (1993) established the effects of walnut on serum lipid levels and blood pressure in normal men; they concluded that moderate quantities of walnuts could be recommended as cholesterol-lowering diet. Mahmoodi et al. (2011) evaluated the effects of walnut on some blood biochemical parameters in hypercholesterolaemic rats and it was concluded that consumption of 5% walnut leaf significantly decreased cholesterol ($p < 0.05$); LDL-C, triglycerides and HDL-C were increased. Oladiji, Abodunrin and Yakubu (2010) reported significantly reduced ($p < 0.05$) serum concentration of TC and HDL-C while TG and the atherogenic index increased with a *T. conophorum* nut oil–based diet in rats. Similar alterations in the serum lipid of the animals suggested cardiovascular risk and that it was not completely safe for consumption.

Anti-diabetic activities

Onwuli, Bown and Ozoani (2014) and Ogunyinka et al. (2015) reported that the nuts have the potential to reduce hyperglycaemia; the authors also reported that the nuts increased the haemoglobin level and decreased urine output in the test group when compared with controls and could prevent diabetes associated with renal damage.

A study carried out by Ogbonna et al. (2013) indicated a significant reduction in blood glucose level and suggested that the leaf and the root extracts of *T. conophorum* are more potent in lowering blood glucose in alloxan-induced diabetic rats when compared with oral hypoglycaemic agents. Similar studies were carried out by Ogbonna et al. (2015) on the effect of root and leaf extracts of *T. conophorum* in alloxan-induced diabetic rats and showed a significant increase ($p < 0.001$) of ALP, AST and ALT, which indicated that the leaf and root extracts possess anti-diabetic and hepatoprotective activity. Lepzem and Togun (2017) established the anti-diabetic and antioxidant effects of the methanolic extracts of leaf and seed of *T. conophorum* on alloxan-induced diabetic Wistar rats. The leaf and seed extract when mixed together as a diet had great anti-hyperglycaemic and superior antioxidant potential to the standard drugs. Zibaeenezhad et al. (2017) showed that with the addition of 15 mL walnut oil to the foregoing diet of diabetes patients aged 35–75 years for 90 days, there was a significant decrease in TC, LDL-C, TG and the TC/HDL ratio when compared with the control group. It was assumed that these effects might have an impact on the reduction of cardiovascular risk diseases and other related complications in diabetes patients. Pan et al. (2013) also attributed consumption of walnut to lower risk of type II diabetes among women but it was insignificant to control body mass index.

Antimicrobial activities

Akinwande (2015) reported antimicrobial activity of the leaves and isolated phytosterols (triterpenoids) – 3β, 22E-stigmata-5, 22-dien-3-ol and 3β-hydroxyolean-12-en-28-oic acid from petroleum ether fraction of *T. conophorum* leaves, which has high potential as an antimicrobial agent. Suara et al. (2016) also established an antibacterial assay of *P. conophora* methanol leaf extract and showed a concentration-dependent effect against *Bacillus subtilis* and *Proteus mirabilis* that could be formulated and used as cream in the management of susceptible bacteria skin infection. Ogbolu and Alli (2012) suggested that the walnut had no *in vitro* antibacterial activity (leaf, stem bark, cooked or uncooked kernel) on Gram-positive and Gram-negative bacteria. These findings contradicted similar reports of Ajaiyeoba and Fadare (2006) that methanol extract and its fractions exhibited concentration-dependent antimicrobial properties, which were carried out in the same geographical areas. Bello et al. (2013b) established the potential of walnut and onion bulb extracts as antimicrobial agents for fish. It was recorded that 500 µg/mL of both extracts had the best minimum inhibitory concentration on the pathogens and could prevent the growth of microorganisms in fish feed production.

Toxicological studies

Akomolafe et al. (2017d) reported that the aqueous extract of *T. conophorum* leaves in rats did not reveal any pathological changes even at 2000 mg/kg. Agbaje et al. (2016) studied the acute and sub-chronic toxicity studies of the aqueous extract of the fresh nuts of *P. conophorum* and reported there was no mortality at a 2 g/kg dosage. However, ALT and AST were significantly reduced ($p < 0.05$) at 500 mg/kg and 750 mg/kg when compared with the control group and the haematological assessment was significant in all the treatment doses. It was concluded that the extract could be hepatoprotective and possibly serve as an immunostimulant. In a study carried out by Oladiji et al. (2010) on the toxicity of a *T. conophorum* nut oil–based diet in rats, there was a reduction in the activity of ALP, glutamic oxaloacetic transaminase (GOT) and glutamic pyruvic transaminase (GPT) in the liver and heart of the animals fed the nut oil–based diet. Bello et al. (2014) assessed the haematological and biochemical changes in African catfish fed a diet supplemented with *T. conophorum* leaf and onion bulb and reported no traces of infections such as anaemia during the fish culture, suggesting that the extract of the walnut leaf and onion bulb could be useful in stimulating immune responses.

Anti-malarial activity

Dada and Ogundolie (2016) evaluated the *in vivo* anti-plasmodial activity of the raw seed extract of *T. conophorum* in Swiss albino mice infected with *Plasmodium berghei*, revealing dose-dependent activity on chemo-suppression. Similarly, a dose of 600 mg/kg had the highest at 47.22%, while chloroquine at 5 mg/kg produced 55.50% chemo-suppression. This suggested that the seed nut could be useful in the treatment of malaria. A similar study conducted by Ogundolie et al. (2017) on the effects of the raw ethanolic seed extracts of *T. conophorum* on the haematological and histopathological parameters of Swiss albino mice infected with *P. berghei* (NK65) suggested an increased in the haematological parameters packed cell volume (PCV), red blood cells (RBC), hemoglobin (HGB) and platelet (PLT) of all treated groups. The histology of the seed extract at 400 mg/kg showed a restorative effect on the liver and kidney of the mice but at 600 mg/kg there was a regenerative tissues on the kidney but had adverse effects on the liver. It was concluded that 400 mg/kg of the seed extract of *T. conophorum* might be considered suitable to treat human malaria infection.

Anticancer activity

Carvalho et al. (2010) reported that the methanol extract showed concentration-dependent growth inhibition towards human kidney and colon cancer cells. However in A-498 renal cancer cells all extracts exhibited similar growth inhibition activity (IC_{50}) values (between 0.226 mg/mL and 0.291 mg/mL), while for both 769-P renal and Caco-2 colon cancer cells, walnut leaf extract showed a higher anti-proliferative efficiency (IC_{50} values of 0.352 mg/mL and 0.229 mg/mL, respectively) than green husk or seed extracts. The results obtained herein strongly indicate that walnut tree constitutes an excellent source of effective natural antioxidants and chemopreventive agents.

Antidepressant activity

Aladeokin and Umukoro (2011) evaluated the psychopharmacological properties of an aqueous extract of the *T. conophorum* nut in mice and oral administration at 50 mg/kg – 200 mg/kg produced a significant dose-related decrease in the duration of immobility in the forced swim test. The test doses did not prolong the duration of sleep produced by thiopentone nor alter the pattern of the stereotyped behaviour induced by the amphetamine. It was concluded that the nut extract demonstrated antidepressant-like activity.

Other therapeutic and health benefits

Tetracarpidium conophorum promotes quality sleep, can be used for treatment of the gastrointestinal tract, is ideal to help pregnant women avoid miscarriages, has culinary purposes such as soup preparation, can boost cognitive function because of the presence of vitamin B_6 and omega-3 fatty acids and also helps as an anti-ageing agent (Global Food Book 2015).

Conclusion

The African walnut (*T. conophorum*) should be explored for the production of walnut flour and cake for diet-based (diabetes, hypertensive) patients because of its great potential. The production, propagation and cultivation should be extended to other parts of Nigeria and Africa, which could boost food security and reduce poverty in Africa. Also, its isolation, characterisation and structural elucidation of the chemical compounds in the leaf, stem bark and seed nut should be assayed in view of producing drugs that could be useful in fighting many diseases and illnesses.

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Competing interests

The authors declare that they have no financial or personal relationships which may have inappropriately influenced them in writing this article.

Authors' contributions

A.E.A. designed the study and gave directions, gathered information and wrote the first draft of the article. N.A. gathered information, edited and proofread the draft of the article and put it into the journal format.

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