



(REVIEW ARTICLE)



Dennettia tripetala (Pepper Fruit), a review of its ethno-medicinal use, phyto-constituents, and biological properties

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GSC Advanced Research and Reviews, 2021, 06(03), 035–043

Publication history: Received on 10 January 2021; revised on 21 February 2021; accepted on 26 February 2021

Article DOI: <https://doi.org/10.30574/gscarr.2021.6.3.0024>

Abstract

There has been tremendous growth in field of herbal medicine as therapeutic agents. *Dennettia tripetala*, is known to possess ethnomedicinal properties and has been used for centuries in the Ayurvedic system of medicine for the treatments of various diseases. The present review provides detailed description on the distribution, ethno-medicinal use, phyto-constituents, and biological properties of the plant that justifies its use as a potential therapeutic agent in management of different diseases. The phyto chemical composition of *Dennettia tripetala* include alkaloids, tannins, saponins, flavonoids, terpenoids, steroids and cardiac glycosides while its biological activities include antioxidant, antidiabetic, antibacterial, antihypertensive, anticonvulsant, antitrypanosomal, antimalarial, anti-inflammatory and cytotoxic properties among others. In conclusion, *Dennettia tripetala* contains various nutritional and phytochemicals compositions that make it valuable for pharmacological purposes.

Keywords: *Dennettia tripetala*; Ethno-medicine; Phyto-constituents; Biological properties

1. Introduction

D. tripetala is an important indigenous plant of West Tropical Africa that belongs to the family *Annonaceae* (1). It is found in Nigeria, Ivory Coast and Cameroon. It is commonly called 'pepper fruit' in English, mmimi in Igbo, nkaika in Ibibio, imako in Urhobo, ako in Edo, opipi in Idoma and igberi in Yoruba languages of Nigeria (2,3).

The fruits and leaves are commonly used as a spices or seasonings which are added to prepared food such as meat, sausage, stew, soup and vegetables (4). The bark of the tree is added to food to create variation in the taste and flavour of the foods. The wood is used as fuel (5). The leaves and seeds are used in folk medicine for the treatment of fever, cough, asthma, catarrh, toothache, diarrhea and rheumatism (6) and are also used to enhance appetite, clear throats, check excess saliva, relieve coated tongues and stop nausea (4,7). The seeds serve as important component in the diets of women after childbirth, since it is believed that spices and herbs aid the contraction of the uterus (8). The plant has also been reported for several biological activities including anti-oxidant, antidiarrheal, antimicrobial, antiparasitic, anticonvulsant, antitrypanosomal, antimalarial, anti-inflammatory, anti-snake venom, and antinociceptive properties.

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Studies have shown that *D. tripetala* possesses many phytochemicals in which the type and amount of phytochemical depends on the part of *D. tripetala* plant. Adedayo *et al.*, (9) reported that the fruits possess alkaloids, tannins, saponins, flavonoids, terpenoids, steroids and cardiac glycosides which is slightly different from the study carried out in 2015 (3). The phytochemicals present in the fruits of *D. tripetala* according to Egharevba and Idah, (3) are tannins, alkaloids, steroids, terpenes, flavonoids, balsams (resin) and phenol. The study carried out by Egharevba and Idah, (3) showed that the leaf has a similar phytochemical profile to the fruit except that the leaf lacks balsams (resin) and steroids. The seeds of *D. tripetala* showed the presence of Alkaloids, tannins, saponins, flavonoids, terpenoids, steroids and cardiac glycosides (10). These bioactive compounds are the basis for therapeutic potentials of medicinal plants (5). Herein, we provide a comprehensive review on ethno medicinal use, phyto-constituents, and biological properties of *Dennettia tripetala* (Pepper Fruit).

1.1. *Dennettia tripetala* (Pepper Fruit)

D. tripetala is an important indigenous plant of West Tropical Africa that belongs to the family *Annonaceae* (1). It is found in Nigeria, Ivory Coast and Cameroon. The parts used traditionally for medicine include; the leaves, fruits, seeds, roots and stem. It is commonly called 'pepper fruit' in English, mmimi in Igbo, nkaika in Ibibio, imako in Urhobo, ako in Edo, opipi in Idoma and digberi in Yoruba languages of Nigeria (2,3). *D. tripetala* belongs to the

Kingdom: *Plantae*

Phylum: *Magnoliophyta*

Class: *Magnoliopsida*

Order: *Magnoliales*

Family: *Annonaceae*

Genus: *Dennettia*

Species: *tripetala*

(Source; 11).

1.1.1. Plant Description

D. tripetala is a small woody shrub with a height of about 12-18 m. The wood is soft, white in colour and liable to termite attack. It has a fibrous bark which has a very strong characteristic scent. The leaves are 3 – 6 inches long by 1.5–2.5 inches broad, elliptic in shape, shortly acuminate and broadly connate to round at the base. The plant usually produces fruits between March and May (12). The outside of the flower is light brown while the inside is red and the flower is usually in small clusters on the young or older wood. The fruit appear green when unripe and red when ripe. There is a finger-like carpel constriction between the seeds. The young leaves and fruit when ripe has a peppery and spicy taste when chewed (5).



Figure 1(A) *Dennettia tripetala* tree with leaves and unripe fruits. (B) Ripe (red) and unripe (green) *Dennettia tripetala* fruits. (Source: 12)

1.1.2. Domestic Uses of *Dennettia tripetala*

The fruits and leaves are commonly used as a spices or seasonings which are added to prepared food such as meat, sausage, stew, soup and vegetables (4). The bark of the tree is added to food to create variation in the taste and flavour of the foods. The wood is used as fuel (5). The matured fruits is the edible portion, they are chewed in different forms (fresh green, fresh ripened red, black dry fruit and dry seed) because of its characteristic spicy taste and also serve as a mild stimulant to the consumer (6, 13). The fruits are used in entertaining guest; it is a sign of good reception in

combination with cola nuts, garden egg and palm-wine. It is also used in Igbo land during coronation, the new yam festival and marriage ceremonies (14).

1.1.3. Medicinal Uses of *Dennettia tripetala*

The leaves and seeds are used in folk medicine for the treatment of fever, cough, asthma, catarrh, toothache, diarrhea and rheumatism (6) and are also used to enhance appetite, clear throats, check excess saliva, relieve coated tongues and stop nausea (4,7). The seeds serve as important component in the diets of women after childbirth, since it is believed that spices and herbs aid the contraction of the uterus (8).

1.2. Phytochemical Constituents of *Dennettia tripetala*

Studies have shown that *D. tripetala* possesses many phytochemicals in which the type and amount of phytochemical depends on the part of *D. tripetala* plant. Adedayo *et al.*, (9) reported that the fruits possess alkaloids, tannins, saponins, flavonoids, terpenoids, steroids and cardiac glycosides which is slightly different from the study carried out in 2015 (3). The phytochemicals present in the fruits of *D. tripetala* according to Egharevba and Idah, (3) are tannins, alkaloids, steroids, terpenes, flavonoids, balsams (resin) and phenol. The study carried out by Egharevba and Idah, (3) showed that the leaf has a similar phytochemical profile to the fruit except that the leaf lacks balsams (resin) and steroids. The seeds of *D. tripetala* showed the presence of Alkaloids, tannins, saponins, flavonoids, terpenoids, steroids and cardiac glycosides (10). These bioactive compounds are the basis for therapeutic potentials of medicinal plants (5).

1.3. Nutritional Components of *Dennettia tripetala*

D. tripetala fruits have been reported to contain important nutrients that are required by the body. However, the proportion of the nutrients varies between ripe and unripe fruits. The proximate composition of *D. tripetala* fruits (unripe and ripe) as reported by Ihemeje *et al.*, (15) is shown in table 1. Ihemeje *et al.*, reported that the moisture, fat and carbohydrate contents increases with ripeness while crude fibre and protein contents reduces with ripeness.

Pepper fruits have high carbohydrate content which ranges between 53% - 68% (15, 16, 17). The fruits comprise of sugars such as glucose, sucrose and fructose, hemicellulose and pectin, which act as dietary fibre, add bulk to the diet and may, sometimes, act as a mild natural laxative (14). Okwu and Morah (16) reported that pepper fruits contain a caloric value of 480.24 g cal·100 g⁻¹. The proximate composition of *D. tripetala* fruits is given below (table 2). It has also been reported that *D. tripetala* fruits is rich minerals and vitamins. *D. tripetala* fruits contain mostly water-soluble vitamins such as ascorbic acid, thiamine, riboflavin and niacin (16) which explain its uses for the treatment of the common cold and the control of other diseases such as prostate cancer (18). The fruits of *D. tripetala* contains high amount of potassium (2.48%) and calcium (1.80%) and a low concentration of sodium, Zinc, copper, manganese, cobalt, nickel and cadmium (table 3) (19). Fruits of the plant also contains high (17.75 %) amount of iron (16) which is an essential component of heme moieties of haemoglobin. It helps in oxygen transport and plays a vital role in body metabolism especially in humans (18).

Table 1 Variations in Proximate Composition of *D. Tripetala* Fruit with Ripeness (Pepper Fruit).

% Nutrients	Sample	
	Unripe	Ripe
Moisture content	15.26 ± 0.07	18.73 ± 0.02
Protein	6.59 ± 0.08	4.67 ± 0.08
Fat	5.52 ± 0.3	5.78 ± 0.08
Ash	4.13 ± 0.02	3.18 ± 0.03
Fiber	17.05 ± 0.7	14.32 ± 0.3
Carbohydrate	51.45 ± 0.015	53.32 ± 0.02

Source: (15)

Table 2 Proximate Composition of *D.tripetala* Fruits

Parameters	% composition
Moisture (%)	8-9.08
Ash (%)	3.18- 6.40
Fat (Lipid) (%)	3.47-9.66
Crude fibre (%)	9.00-14.32
Protein (%)	4.67-15.31
Carbohydrate (%)	53.3-68.12

Sources: (15, 16, 17)

Table 3 Nutritional Composition of *D. tripetala* Fruits

Parameters	Composition
Sodium (%)	2.50 ± 0.10
Phosphorus (%)	0.33 ± 0.10
Magnesium (%)	0.42 ± 0.30
Iron (%)	17.75 + 0.30
Calcium (%)	1.80 ± 0.40
Thiamine (vitamin B1) (mg·100 g ⁻¹)	0.12 + 0.10
Niacin (nicotinic acid) (mg·100 g ⁻¹)	10.08 + 0.20
Riboflavin (vitamin B2) (mg·100 g ⁻¹)	0.56 + 0.01
Ascorbic acid (vitamin C) (mg·100 g ⁻¹)	58.48 + 0.20

Source: (16)

1.4. Dietary Supplementation of *D. tripetala* Fruit

Dietary supplements serve a wide range of purposes. Some of these are medically appropriate, while others may do nothing or harm the individual. Reasons for taking dietary supplements include: replacing a necessary substance not found in large enough quantities in the diet, preventing or decreasing the risk of developing a disease or condition, boosting the immune system and improving general health, boosting energy levels, improving mental or physical performance, stimulating weight loss and reducing symptoms of a disease or health condition (20, 21). There has been an increase in the use of dietary supplements and this has necessitated that individuals consult with their physicians so as to get the appropriate supplement without any detrimental effects. IHEMEJEETAL., (22) reported that the nutritional quality of plain yoghurt was improved by the addition of pepper fruits, especially the mineral and vitamin contents. The investigation showed that the therapeutic potency of yoghurt can be improved because consumption of food with high vitamin A, vitamin C and minerals aids in combating deficiency disease, improving cell functioning and body immunity. Pepper fruit has also been used as a substitute for ginger in zobo drinks and the sensory evaluation showed that there was no significant difference between the zobo- ginger drinks and zobo- pepper fruits drinks (15).

1.5. Pharmacological Effects of *D. tripetala*

1.5.1. Treatment of Glaucoma

The seeds of *D. tripetala* have been shown to reduce intra ocular pressure (IOP) in humans. IOP is the pressure within the eyeball as a result of the constant formation and drainage of the aqueous humour (23). Timothy and Okere, (23) reported that oral administration of 0.75 g of *D. tripetala* reduces the intraocular pressure for a short period of time, usually not lasting for 30 minutes after administration. The IOP was reduced by 17.30 % (12.90 mmHg) from the mean baseline of 15.60 mmHg. According to Head and Kathleen, (24) flavonoids assist with collagen stabilization and synergize the effect of vitamin C. The effect of flavonoid in IOP reduction is thought to be as a result of the reduction in excessive permeability of blood aqueous membrane within the eye. The presence of lipoic acid (fatty acid) has been

shown to increase glutathione in red blood cells and lacrimal fluid of glaucomatous patients thereby reducing the intraocular pressure (24).

1.5.2. Anti-nociceptive and Anti-inflammatory Effect of *Dennettia tripetala*

D. tripetala possesses significant anti-nociceptive and anti-inflammatory activities (6). The essential oils of *D. tripetala* fruits have been found to possess analgesic effect that is relative to that induced by the powerful opioid morphine as well as aspirin and indomethacin. The anti-inflammatory activity was shown to be effective in both early and late phases of inflammation (25). The essential oil of *D. tripetala* has been shown to also relieve inflammation in rodents with edema to levels similar to that of dexamethasone (25).

1.5.3. Effect on Oxidative Stress and Antioxidant Activities

Reactive oxygen species (ROS) are usually generated as part of metabolism in living organism and the effects of these species are prevented by antioxidants. Some of these antioxidants are endogenous that is produced in the body, while others are obtained from plants in the form of antioxidant nutrients (26). Several studies have shown that *D. tripetala* used in the management of oxidative stress related diseases and infections (27). In 2010, a study carried out at the federal university of technology, Akure, evaluated the changes in the antioxidant contents and potentials of *D. tripetala* fruit with ripening and their result shows that the unripe *D. tripetala* fruits have greater antioxidant activity than the ripe fruits (9). The reduction in the antioxidant activities is due to the physiological changes that accompany ripening which increases total phenol and reduces vitamin C content hence reducing the antioxidant properties of the ripe fruit (9). In 2011, two flavonoid glycosides (avicularin and vitexin-2-O-rhamnoside) were isolated from the ethyl acetate solvent fraction of a 20% aqueous methanol *D. tripetala* leaf extract. These flavonoids were found to instantly bleach the purple color of 1, 1-diphenyl-2-picrylhydrazine (DPPH), thus indicating free radical scavenging potential (27). Another study investigated the ability of the ethanolic extract of the root of *D. tripetala* to inhibit lipid peroxidation in frozen heart muscle slices and the extract showed significantly ($p < 0.05$) higher antioxidant effect when compared with vitamin C which suggest that the root extract of *D. tripetala* is rich in antioxidants and can be used to enhance the preservation of frozen meat (28). Recent studies carried out by Iseghohi and Orhue, (29, 30) revealed that administration of aqueous and ethanolic extracts of *D. tripetala* fruit prevent an increase in the plasma activity of GGT, alanine transaminase (ALT) and alanine phosphatase (ALP) by combating the oxidative stress associated with tetrachloromethane (CCl₄) metabolism.

1.5.4. Antimicrobial Effect of *Dennettia tripetala*

D. tripetala has been reported to have antimicrobial activities due to the presence of some phytochemicals such as flavonoids and some fatty acids such as palmitic acid, eicosanoic acid, ethyl ester and linoleic acid (31). Research carried out at Delta state University, Abraka, showed that the essential oil and phenolic acid extract of *D. tripetala* inhibited the growth of food-borne microorganisms such as *Staphylococcus aureus*, *Salmonella spp.*, *Escherichia coli*, and many others (4). Recently, the leaves of *D. tripetala* have been found to be effective in inhibiting the growth of the rot-causing fungus *Sclerotium rolfsii* in cocoyam both *in vitro* and *in vivo* (32). Several other reports show the antimicrobial activity of *D. tripetala* (33, 34).

1.5.5. Insecticidal Effect of *Dennettia tripetala*

D. tripetala has been shown to have protective ability on cowpea against storage insect pest. Anyaele and Amusan (33) observed that hexane extract of *D. tripetala* has larvicidal activity against the mosquito larvae of *Aedes aegypti*. It was reported by Ukehet *al.*, (7) that the insecticidal activity of the pepper fruit increases as concentration and days of exposure increases. Also, the emergence of the adult and the destruction of the larval stages of the cowpea weevil (*Callosobruchus maculatus*) and maize weevil (*Sitophilus zeamais*) was completely controlled by *D. tripetala* (35). According to Asawalamet *al.*, (36), the bioactive components responsible for the insecticidal activity of *D. tripetala* are 2-nitroethyl-benzene and beta-phenyl nitroethane.

1.5.6. Anti-hyperglycaemic Effect of *Dennettia tripetala*

Anaga and Asuzu (37) observed that the chloroform, ethyl acetate and methanolic extract of *D. tripetala* can reduce the plasma glucose level in alloxan- and streptozotocin-induced hyperglycemic rats to levels similar to that of normal rats. In 2011, the same researchers used 3T3-L1 adipocytes and brefeldin to investigate the possible mechanism for the antihyperglycaemic effect of *D. tripetala* and it was discovered that *D. tripetala* exerts its effect partly by mobilising glucose uptake proteins from the interior of the cell to the plasma membrane through the Golgi apparatus (38)

1.5.7. Effects of *Dennettia tripetala* on the Nervous System

A component of the essential oil (1-nitro-2-phenyl ethane) of the fruits, leaves, and seeds of *D. tripetala* has been discovered and said to be responsible for the observed neuropharmacological effects of the oil. This compound has hypnotic, anticonvulsant, and anxiolytic effects in mice (25).

1.5.8. Effect of *Dennettia tripetala* on Cancer

A study from the University of Illinois at Chicago showed that *D. tripetala* extract inhibits the growth of prostate cancer cells. The efficacy of the ethanolic extract of *D. tripetala* seeds was tested on prostate cancer cell lines PC3 and LNCaP and the result showed that the extract has growth-inhibitory and cytotoxic effects on the prostate cancer cell lines *in vitro* (39).

1.6. Toxicity of *Dennettia tripetala*

A number of studies have been carried out to investigate the toxic effect of *D. tripetala*. *D. tripetala* has been shown to contain uvariopsin, an alkaloid that helps to improve bile secretion and reduces hepatic disorders (26, 40). However, a study by Ofemet *et al.*, (26) discovered that the ethanolic extract of *D. tripetala* fruits given at a certain dose reduces bile production in normal healthy rats. The extract has also been reported to cause an increase in sodium, potassium, and bicarbonate ions in bile and reduce the chloride and unconjugated bilirubin content of bile (26). The LD₅₀ of the ethyl acetate root extract of *D. tripetala* was reported to be 1120 mg/kg when given intraperitoneally with no remarkable change observed in the major organs at postmortem (37).

Natural products, particularly medicinal plants have been used from time immemorial for the treatment of various diseases (41-43) and various studies have recommended the evaluation of medicinal plants in order to accept their use for medicinal purposes (44-50). It is therefore noteworthy that *Dennettia tripetala* demonstrated safety profile in toxicity study, in addition to its various biological activities, and thus serve as an important medicinal plant worthy of further preclinical evaluation

2. Conclusion

In conclusion, *Dennettia tripetala* contains various nutritional and phytochemicals compositions make this plant valuable for pharmacological purposes. Thus, the importance of this beneficial plant should be emphasized and the bioactive components of *Dennettia tripetala* should be analyzed further and, an extensive research and development work should be undertaken on the plant and its products for better economic and therapeutic utilization.

Compliance with ethical standards

Acknowledgments

We acknowledge the support of the entire staff of the Southern Guinea Research Station-Forestry Research Institute of Nigeria, Mokwa, Niger State, Nigeria.

Disclosure of conflict of interest

The author disclosed that no conflict of interest exists.

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