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Review Article
Monodora myristica (Gaertn.) Dunal: A Plant with Multiple Food, Health and Medicinal Applications: A Review

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Abstract
Monodora myristica (Gaertn.) Dunal is a useful but neglected tropical tree of the family *Annonaceae* distributed in many countries of the tropics and subtropics. It possesses an impressive range of medicinal and nutritional properties. Different parts of this plant such as seeds, bark and flowers contain important minerals and are a good source of protein, vitamins, β-carotene, amino acids and various phenolics. They also contain bioactive substances that exhibit health-beneficial effects, including stimulation of the cardiac and circulatory system, anti-inflammatory, antispasmodic, diuretic, antihypertensive, cholesterol lowering, antioxidant, anti-diabetic, hepatoprotective, antibacterial and antifungal activities. Crude extracts of the plant are being employed for the treatment of different ailments in the indigenous system of medicine, particularly in South Asia. This review focuses on the phytochemical composition, medicinal uses, as well as the pharmacological properties of different parts of *Monodora myristica.* Prospects for future exploitation of the plant were also discussed.

Key words: *Monodora myristica*, phytochemicals, pharmacological properties, bioactive substances, antibacterial, antifungal activities

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Morphologically, *Monodora myristica* (*M. myristica*) is a perennial plant of the *Annonaceae* or custard apple family of flowering plants[1,2]. The tree grows naturally in the evergreen forests of the sub-Saharan African regions[1] in West Africa: from Liberia to Nigeria, Cameroon and Ghana, as well as in Angola, Uganda and West Kenya[3,4]. Globally, the plant is widely distributed from Africa to Asia, Central and South America and Australia[5,6]. The tree can reach a height of 35 and 2 m in diameter[3]. Fruiting occurs from August-November[5]. The fruit of *M. myristica* is a berry of 20 cm in diameter, smooth, green and spherical and becomes woody at maturity. It is attached to a long stalk, which can be up to 60 cm long. Inside the fruit are the numerous oblong, pale brown seeds which are usually 1.5 cm long and are embedded in a white sweet-smelling pulp[3,7]. It has been observed that an average of 119-122 seeds can be found in one fruit[1].

Monodora myristica is listed presently under Kew's difficult seeds due to its inability to grow easily outside its natural habitat[8]. The plant is largely harvested from the wild and greatly affected by wild fires, urbanization, reckless and uncontrolled felling of trees for timber and firewood without replanting[9]. It is variously known as *Iwor* amongst the Itsekiris; *Ikposa* (Benin); *Ehiri* or *Ehuru* (Ibo); *Gujiya dan miya* (Hausa) and *Ariwo*, *arigbo*, *Abo lakoshe* or *eyi naghose* (Yoruba); *Ehinawosin* (Ikale), *Uyengben* (Edo), *Fausse noix de muscade* (French)[10-13].

Study of Onyenibe *et al.*[7] has shown that almost every part of the tree was important economically and a number of medicinal properties have been ascribed to various parts of this highly esteemed plant. The timber is hard, easy to work with and is used for carpentry, house fittings and joinery while the seeds are also made into necklaces[14]. The most economically important parts are the seeds. After harvesting, various unit operations, such as fermentation, washing, drying and cracking are performed before consumption or storage. The presence of bioactive compounds in the plant makes it possible for the seeds to be used in traditional medicines as well as a spice in local foods[15]. The aromatic seeds are antiemetic, aperient, stimulant, stomachic, tonic and they are added to medicines impart stimulating properties[3,16,17].

So far, no comprehensive review has been compiled from the literature to show the huge socio-economic potential of the plant. This motivated us to bridge the information gap in this area and to write a comprehensive review on the medicinal, phytochemical and pharmacological properties and hence it's high socio-economic value. It is expected that, in the medium to long terms, this review will contribute to increased utilisation of *M. myristica* and thus, an improvement in socio-economic and living standards of the communities living in the regions where it grows.

NUTRITIONAL COMPOSITION

Nutritional value of *M. myristica* centres on its usefulness as a seasoning because of its aromatic flavour[18]. Essential oil from the seed is used as a flavoring agent for food[19,20]. The oil provides a valuable flavor in meal preparations, soups, sauces and canned foods[15,20,21]. The oil could be used as a linolenic-rich salad oil or edible fat or margarine[22]. Its seeds are a popular spice used in cooking to flavour and thicken dishes[23]. It has been reported by many authors that oils containing unsaturated fatty acids especially linoleic and oleic acids can be used to lower plasma cholesterol[24-26]. The oil of *M. myristica*, because of its high level of unsaturated fatty acid is likely to reduce coronary heart disease if consumed[27-29].

The whole seed together with its seed coat is either ground and used as a seasoning for West African soups or stews or is ground and used as a nutmeg-like flavouring in cakes and desserts[30-32]. There is wide variation in the proximate composition of *M. myristica* seeds reported in the literature as shown in Table 1.

Its moisture content is low[33] making them suitable for long-term storage[34] without deterioration in quality or microbial spoilage since microbial activity will be reduced to a minimum. This will be of benefit to rural communities which lack access to basic storage facilities and electricity as it will reduce the cost of handling and ensure long term storage[35]. Its ash content is moderately high (2.3-6.49%) implying that it has good mineral content and thus serves as a viable tool for nutritional evaluation[36]. Minerals are a group of essential nutrients which serve a variety of important metabolic functions and are parts of molecules such as haemoglobin, adenosine triphosphate (ATP) and deoxyribonucleic acid (DNA)[37].

Table 1: Proximate compositions (% dry weight) of *M. myristica* seeds

Moisture	Ash	Crude fat	Crude fibre	Crude protein	Carbohydrate	Source
3.48	4.50	47.09	8.38	27.57	8.96	Enwereuzoh *et al.*[33]
14.7	2.30	29.10	25.90	9.10	18.90	Burubai *et al.*[1]
13.15	3.90	29.10	25.90	10.13	21.20	Ekeanyanwu *et al.*[31]
9.72	6.49	13.24	7.38	21.69	41.02	Zaragoza[38]

Values are mean of triplicate determinations

Crude fat is high which indicates that it is a good source of flavour since it is rich in essential oil and also suggests possible sources of oil-soluble vitamins. Crude fibre content shows that when it is incorporated into food, it will help to prevent many metabolic or digestive disorders such as constipation and irritable bowels as this is the work of fibre in the body. Fibre has long been known to aid digestive health and can help one lose or maintain weight because eating fibre-dense wheat bread helps one feel full[39]. Recently, the hypoglycemic and hypocholesteremic effect of dietary fiber has been reported[40]. It is generally known that any plant food that provides more than 12% of their caloric value from protein is considered to be a good source of protein[33]. This signifies the healing properties of *M. myristica* as proteins are essential for the synthesis/repair of body tissues and as enzymes. *Monodora myristica* could be used as a good source of protein supplement in the human diet[41]. Its low carbohydrate content (8.96%) suggests low caloric value and is indicative of its low sugar concentration[33].

Mineral composition: The seeds possess magnesium, calcium, potassium, phosphorus, manganese, iron, sodium, copper, aluminium and zinc[31,1]. Minerals are known to play important metabolic and physiological functions in living cells[42]. The calcium/phosphorus ratio is greater than 1, indicating that it would serve as good source of mineral for bone formation. The ratio of sodium to potassium in the body is of great concern for prevention of high blood pressure. Sodium/potassium ratio of less than 1 is recommended[43]. This is an indication that the inclusion of African nutmeg in the diet would probably reduce high blood pressure diseases since its sodium/potassium ratio is less than 1[31].

PHYTOCHEMISTRY

Feyisayo and Oluokun[44] identified phenolics present in the seeds of *Monodora myristica* by gas chromatography (GC) coupled to flame ionization detector (FID). They estimated the total phenolic content as 1478.32 mg/100 g and concluded that *M. myristica* is a good source of phenolics. The seed is rich in Myristicin (42.60%), Caffeic acid (23.39%), Elemicin (3.82%) and Eugenol (1.02%)[45] and contains 5.9% colourless essential oil[46]. Other reports on the phytochemical screening of the seeds of this plant revealed the presence of phenolic compounds, including flavonoids and tannins, cyanogenic glycosides, alkaloids, arocine, lactose, terpene, resins, fiberro-latic oils, anthraquinones, saponins, steroids, oxalates and phytates[31,47,48].

Almond contains six non-essential amino acids (aspartate, glutamine, alanine, proline, arginine and glycine) and nine essential amino acids (histidine, valine, methionine, cysteine, isoleucine, leucine, phenylalanine, lysine, tyrosine)[13]. Based on this, it is qualified as a good source of protein because the quality of protein in food is determined by the content of amino acids especially the essential amino acids[49]. The amino acids phenylalanine (Phe), tyrosine (Tyr), arginine (Arg), glutamic acid (Glu) and asparagine (Asn) have been found to exhibit anti-sickling properties[50-52]. The crude aqueous extracts (CAE) of *M. myristica* exhibited anti-sickling potency due to the preponderance of these anti-sickling amino acids and other Vitamins like Vitamin C, E and sugars which are also identified in the extracts[45,47].

The seeds also contain about 35-36% of a reddish brown fixed oil which is mainly linoleic acid (46.9%), oleic acid (35%), arachidic acid (9.52%), palmitic acid (8.78%) and butyric acid (3.74%)[1,53-55]. Linoleic acid helps to relieve flaky or rough skin and maintain smooth moist skin[56].

The monoterpenoid content of *M. myristica* is mainly hydrocarbons comprising α-phellandrene (29.2%), *p*-cymene (11.2%), α-pinene (9.7%), *cis*-sabinol (6.9%), 0.10% camphene, geraniol 0.34%, eugenol 0.42%, 0.40% myrcene, thujene 0.22% and limonene (6.8%)[57,21]. Bakarnga-Via *et al.*[58] reported that *Monodora myristica* seed oils from Chad and Cameroun contain mainly α-phellandrene at 52.7 and 67.1%, respectively. The essential oil is associated in the seeds with solid fat. The seeds have a pungent, peppery taste due to aromatic ketones such as gingerol and paradol[48]. This oil can be used as a counter-irritant and in the treatment of rheumatism and as carminative[59]. The essential oil that can be obtained from the leaves contains β-caryophyllene, α-humulene and α-pinene[60]. Structures of some active compounds of *M. myristica* are shown in Fig. 1.

Adewole *et al.*[61] extracted the oil of *M. myristica* using Soxhlet extractor and petroleum ether as solvent and characterized the oil using gas chromatography-mass spectrophotometer. The compounds they identified are shown in Table 2.

Feyisayo and Oluokun[44] estimated the total phenolic content of seeds of *M. myristica* as 1478.32 mg/100 g and used GC-FID (Gas Chromatography-Flame Ionization Detector) analysis to identify about fifty-three different types of phenolics.

These are shown in Table 3. The GC-MS analytical report for the chloroform fraction of the seed showed the presence of o-Cymene, Trans-2-caren-4-ol, 4-methylene-1-(1-methylethyl)-, (1α, 3α, 5α), Thymol, Cyclohexene, Carbamic

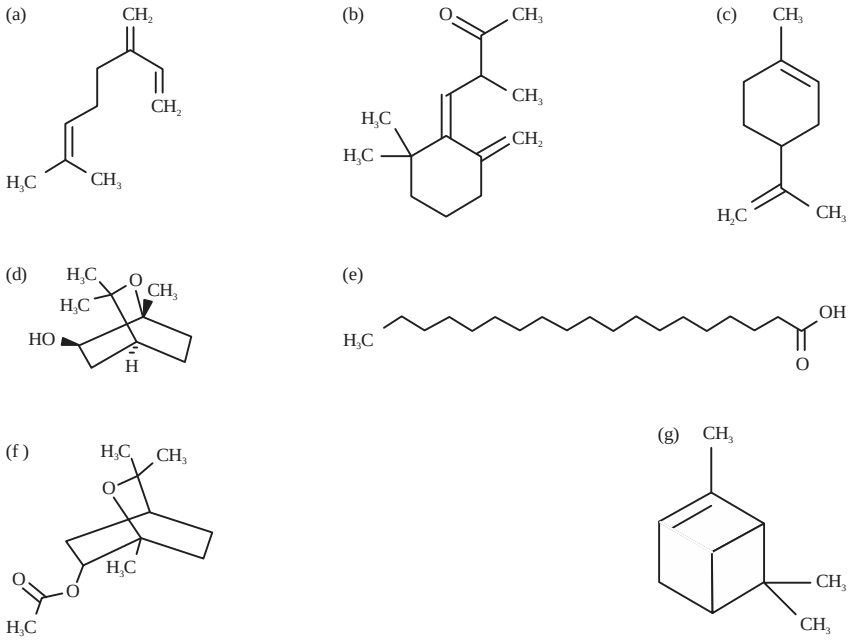

Fig. 1(a-g): Structures of selected phytochemicals from *M. myristica*: (a) Myrcene, (b) 4-(2,2-Dimethyl-6-methylenecyclohexylidene)-3-methyl-2-butanon, (c) Limonene, (d) 1,3,3-Trimethyl-2-oxabicyclo[2,2,2] octan-6-ol, (e) Nonadecylic acid, (f) 1,3, 3-Trimethyl-2-oxabicyclo[2,2,2] oct-6-yl acetate and (g) Pinene

Table 2: Properties of some identified compounds in the oil of *Monodora myristica*

Compound S/NO	Compound names	Molecular formula	Molecular weight	CAS
A	1,3,3-Trimethyl-2-oxabicyclo[2,2,2] octan-6-ol	$C_{10}H_{18}O_2$	170	18679-48-6
B	1,3,3-Trimethyl-2-oxabicyclo[2,2,2] oct-6-yl acetate	$C_{12}H_{20}O_3$	212	57709-95-2
C	4-(2,2-Dimethyl-6-methylenecyclohexylidene)-3-methyl-2-butanon	$C_{14}H_{22}O$	206	93175-74-7
D	n-Hexadecanoic acid (palmitic acid)	$C_{16}H_{32}O_2$	256	57-10-3
E	n-Pentadecanoic acid	$C_{15}H_{30}O_2$	242	1002-84-2
F	n-Octadecanoic acid(stearic acid)	$C_{18}H_{36}O_2$	284	57-11-4
G	Eicosanoic acid	$C_{20}H_{40}O_2$	312	506-30-9
H	Nonadecylic acid	$C_{19}H_{38}O_2$	298	18281-05-5
I	9-Octadecenoic acid, ethyl ester (oleic acid)	$C_{20}H_{38}O_2$	310	111-62-6
J	Cis-9-Hexadecenal	$C_{16}H_{30}O$	238	56219-04-6

CAS: Chemical abstracts service, Source: Adewole *et al.*[61]

acid, phenyl ester, 2-Cyclohexen-1-one, 2-Cyclohexen-1-one, 4-(2,2-Dimethyl-6-methylenecyclohexylidene)-3-methyl-2-butanone, α-cadinol, 1, 4-Methanoazulen-3-ol, Quercetin, n-hexadecanoic acid, 9-Octadecamide, cis-9-hexadecenal, Acetic acid, Cis-vaccenic acid, Campestrol and Butyl-9-octadecenoate amongst others[61].

MEDICINAL AND PHARMACOLOGICAL PROPERTIES AND APPLICATIONS

As stated earlier, *M. myristica* has several applications in traditional medicine, which is primarily based on indigenous knowledge systems (IKS). Some of the common traditional medicinal applications of *M. myristica* are shown in Table 4. Modern science research has revealed several medicinal and pharmacological properties of the plant. Most of these properties are likely to have been known a very long time ago through IKS and probably are the basis for the traditional medicinal applications of the plant. Several bioactive compounds have been identified and suggested to be responsible for the various medicinal and pharmacological properties of *M. myristica*. The next sections reviewed the reported medicinal and pharmacological properties of *M. myristica*.

Antimicrobial activities

Antibacterial and antifungal activities: The phenolic compounds in *M. myristica* are responsible for the anti-septic, antifungal or bactericide properties of the plant[62]. The mechanism of inhibitory action of these alkaloids and phenolic

Table 3: Phenolic compounds identified in *Monodora myristica* seeds by GC-FID

pK	Retention time (min)	Area (pA*s)	Amount (mg/100 g)	Names
1	3.63	207.97	72.21	Catechin
2	6.78	18.53	1.48e-4	Phenol
3	7.35	9.52	7.59e-5	Phenylacetic acid
4	7.65	21.18	1.69e-4	Salicylic acid
5	7.96	8.61	6.86	Myrcene
6	8.78	4.00	3.19e-5	Cinnamic acid
7	9.69	48.59	13.21	Protocatechuic acid
8	10.01	1.91	1.28e-2	Carvacrol
9	10.11	2.97	2.36e-5	Gentisic acid
10	10.79	1.64	1.98e-2	ρ-coumaric acid
11	11.17	3.38	4.00e-2	Vanillic acid
12	11.37	101.88	165.39	Safrole
13	11.70	3.75	15.08	Eugenol
14	11.96	4.11	3.27e-5	Isoeugenol
15	12.32	4.28	79.76	Methyl Eugenol
16	12.69	3.44	20.49	Methyl Isoeugenol
17	13.21	10.02	7.98e-5	Gallic acid
18	13.69	23.50	56.50	Elemicin
19	13.78	5.24	629.72	Myristicin
20	14.16	42.60	345.79	Caffeic acid
21	14.94	15.48	5.60e-2	Ferulic acid
22	15.39	35.18	2.80e-4	Syringic acid
23	15.50	4.87	7.87e-3	Piperic acid
24	16.14	16.35	1.17e-2	Sinapinic acid
25	16.55	24.36	9.82e-3	Daidzein
26	17.52	4.06	1.10e-3	Coumestrol
27	18.39	3.33	3.25e-3	Genistein
28	18.77	5.36	1.10e-2	Apigenin
29	19.00	6.35	5.06e-5	Naringenin chalcome
30	19.31	3.77	3.77e-5	Naringenin
31	19.67	9.39	2.88e-2	Shogaol
32	20.61	2.34	1.92e-3	Glycitein
33	21.52	3.40	32.95	Kaempferol
34	21.83	1.03	1.11e-3	Luteolin
35	22.39	1.92	2.98e-3	Capsaicin
36	22.70	2.06	1.64e-5	Epicatechin
37	23.22	3.37	2.92e-5	Epigallocatechin
38	23.34	9.30e-1	9.01e-4	Gingerol
39	24.14	9.74e-1	9.44e-3	Myricetin
40	24.50	8.44e-1	2.50e-3	Isorhamnetin
41	25.05	49.42	40.11	Quercetin
42	25.26	3.63	2.96e-4	3-o-caffeoylquinic
43	25.53	3.90	6.25e-3	Chlorogenic acid
44	26.24	4.46	7.01e-3	Rosmarinic acid
45	26.93	3.49	2.83e-3	Curcumin
46	27.20	1.72	2.76e-3	Miquelianin
47	27.48	9.09e-1	1.44e-3	Eriocitrin
48	28.25	2.48	4.03e-3	Rutin
49	29.00	5.27	4.29e-6	Papain
50	29.31	4.08	3.25e-5	Phenyl-6-o-malonyl-beta-D-glucoside
51	29.48	9.21	7.33e-5	4-o-methyl-epi-gallocatechin
52	30.06	48.07	3.83e-4	Epi-gallocatechin-3-o-gallate
53	30.26	19.03	1.52e-4	Lupeol

Source: Feyisayo and Oluokun[44]

compounds on micro-organisms may be due to impairment of variety of enzyme systems, including those involved in energy production, interference with the integrity of the cell membranes and structural component synthesis[63-64].

These antimicrobial agents include different forms of alkaloids, sesquiterpenes, diterpenes, triterpenes saponins, triterpen aglycous, flavonoids, sterols, coumarin, quinines, monoterpenes, different proteins as well as lipids and

Table 4: Common traditional medicinal uses of the bark and seed of *M. myristica*

Plant parts	Medicinal uses	References
Bark	Treatment of stomach-aches, febrile pains, eye diseases and haemorrhoids. Combined with the bark of *Monodora tenuifolia* a lotion is prepared for use in various eye-troubles. Used in a vapour-bath as a defatigant and to relieve febrile lumbago.	Weiss[3] and Cimanga *et al.*[65]
Seed	Used to relieve constipation and control passive uterine haemorrhage in women immediately after child birth. Treatment of headache, hypertension, candidiasis, treatment and management of pain. Roasted and ground, they are rubbed on the skin for skin diseases. Chewed and used as insecticides, widely used to relieve toothache, dysentery, dermatitis and as worm expeller. Used for the treatment of body aches, chest pains and rashes due to river blindness and leprosy. Administered for quick relief from mild fever and headache. Traditionally, used in the treatment of arthritis, cutaneous and subcutaneous parasitic infection, eye infection, diabetes mellitus and stomach pain. Used in the treatment of malaria, anemia and sexual weakness.	Okafor[4], Udeala *et al.*[16], Koudou *et al.*[66], Addo-Fordjour *et al.*[67], Iruvine[68], Oguntimein *et al.*[69], Akinwunmi and Oyedapo[70], Iwu *et al.*[71], Gill[72], Feyisayo and Oluokun[11] and Nwaozuzu and Ebi[73] Okafor[4]

tannins (Sofowora)[74]. Its phenolic content has been reported to be potent in killing *Staphylococcus aureus*, *Bacillus subtilis* and *Canadidia albicans*[75,76]. Also Oluwafemi and Taiwo[77], reported on the reversal of toxigenic effects of aflatoxin by alcoholic extracts of *Monodora myristica*.

Nwaiwu and Imo[78] screened *M. myristica* for the fungicity of their essential oils against mycelial growth of three foodborne fungi; *Aspergillus fumigatus*, *Aspergillus nidulans* and *Mucor hiemalis*. The essential oils from all the spices were fungi-toxic at varying degree to all the organisms. Ethanolic extract of *M. myristica* seed possesses antimicrobial activity against *Klebsiella* and *Bacillus* species[79] and possess broad spectrum antibacterial activities against selected gram positive and negative bacteria[80]. It also inhibited *Aspergillus niger* in "Kunun" beverage[81]. This generally confirmed that this seed is highly potent to activities of many microorganisms.

Monodora myristica extracts inhibited the growth of mycelium, the formation of conidial spores and chlamydospores of *Sclerotium rolfsii*, thereby reducing the number of propagation units of this fungus in the medium[64,82]. Also, Enabulele *et al.*[12] reported that the aqueous and ethanolic extracts of *M. myristica* seeds, were active against both gram negative and gram positive organisms-*Staphylococcus aureus*, *Klebsiella pneumonia*, *Escherichia coli* and *Salmonella typhi*. Its methanol and dichloromethane extract was active against mites and traditionally used against scabies[83].

Ethanolic extracts of the leaves of the plant was tested against *Escherichia coli*, *Staphylococcus aureus*, *Streptococcus pneumoniae*, *Proteus mirabilis*, *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* by the agar diffusion method[84]. They reported that this extract had the ability to inhibit the growth of the test pathogenic microorganisms and observed a corresponding increase in the rate of inhibition of the growth of the pathogens as the concentration of the extracts increased. Adewole *et al.*[61] reported that the oil of *Monodora myristica* had strong antimicrobial properties and was very active against *Escherichia coli*, *Bacillus substlus* and *Staphylococcus aureus*.

Ukaegbu-Obi *et al.*[85] reported that the seed extracts of *M. myristica* possess some antimicrobial activities which can be employed in the development of novel therapeutic agents against the test organisms. They assessed the antimicrobial activity of *Monodora myristica* seeds on four selected human pathogens, *Escherichia coli*, *Staphylococcus aureus*, *Salmonella typhi* and *Pseudomonas aeruginosa* using Disc diffusion technique for *in vitro* antibacterial screening. They observed that the most susceptible bacterium were *E. coli*, while the most resistant bacterium was *P. aeruginosa* and the minimum inhibitory concentration result showed that the seed extracts of *M. myristica* was bacteriostatic.

Antispasmodic, antiulcer and hepatoprotective activities: Lekana-Douki *et al.*[86] tested dichloromethane and methanolic extracts of *M. myristica* plant for their antiplasmodial activity on two chloroquine-resistant strains of *Plasmodium falciparum* based on lactate dehydrogenase activity. Cytotoxicity was assessed with the MTT test on MRC-5 human diploid embryonic lung cells. They observed that the methanolic extract of *Monodora myristica* showed promising activity and low cytotoxicity and its dichloromethane extracts showed moderate activity against *Plasmodium falciparum*. In a similar experiment, crude extracts from the bark of *M. myristica* were assayed for *in vitro* antiplasmodial activity against the chloroquine-resistant strain of *Plasmodium falciparum*. It showed a good antiplasmodial activity with inhibition of 42.1% at 10 μg mL^{-1} [87].

Oyinloye *et al.*[88] investigated the protective effect of *Monodora myristica* (MM) on cadmium-induced liver damage in male Wistar albino rats. MM exhibited reversal potential on cadmium-toxicity at the tested doses. These results demonstrates that aqueous extracts of MM is effective in the amelioration of hepatic damages arising from

cadmium-induced toxicity, indicating that the antioxidant bio-constituents of MM play an important role in the prevention of liver toxicity possibly by inhibiting bioaccumulation of free radicals in animal models. Also, *M. myristica* extracts exhibited anti-clastogenic, hepatoprotective activities and maintained semen viability in Wister rats[89].

The aqueous seed extract of *Monodora myristica* was investigated for its antiulcer properties using the aspirin and alcohol-induced ulcer models in Wistar rats. The extract was seen to have a high percentage protective index, which compared favourably with the known anti-ulcer drugs in ulcer models. But it had a higher percentage protective index in the alcohol-induced model than the aspirin-induced model, which suggests that its mechanism of action may be coating and protecting the mucosal surface of the stomach[90].

Anti-inflammatory and anticancer activities: *Monodora myristica* seeds are a natural source of anti-inflammatory agent. Flavonoid rich fraction of *M. myristica* seeds exhibited significant *in vitro* anti-inflammatory potentials by stabilizing red blood cell membrane exposed to hypotonic and heat induced lyses with maximum percentage stability of 88% in a biphasic mode of response that is comparable with Ibuprofen a standard anti-inflammatory drug. It also inhibited heat induced albumin denaturation with maximum inhibition of 75.38% in a concentration dependent manner that is comparable with aspirin and showed an anti-lipoxygenase activity range from 19-71% which is comparable to that produced by indomethacin[70].

Ishola *et al.*[91] carried out a study to investigate the antinociceptive and anti-inflammatory effects of the hydroethanolic seeds extract of *Monodora myristca* (HMM) in male albino rats. They reported that HMM possesses antinociceptive effect mediated through interaction with opioidergic, serotonergic and dopaminergic systems and an anti-inflammatory action through inhibition of inflammatory mediator's release. Their study established the scientific basis for its use in the management of pain and inflammatory conditions in traditional medicine.

Essential oils obtained by hydrodistillation of fruits of *Monodora myristica* exerted cytotoxic activity against cancer and normal cell lines with more pronounced effect on neoplastic cells in the majority of cases[58].

Antihypertensive and cholesterol lowering activities: To evaluate the cholesterol lowering potential and protective ability of aqueous extract of *Monodora myristica* on experimental hypercholesterolemic rats, Onyenibe *et al.*[7] induced hypercholesterolemia in the rats by administering cholesterol through the mouth. Results they obtained shows that treatment with *M. myristica* elicited a significant reduction ($p = 0.05$) in serum total cholesterol, triglycerides and low-density lipoprotein cholesterol levels while there was concomitant increase in high-density lipoprotein cholesterol of hypercholesterolemic rats. Elevations in serum aminotransferases activities and lipid peroxidation level were reversed and a significant amelioration was noticed in enzymatic and non-enzymatic antioxidants status in the liver and heart of hypercholesterolemic rats. Their study suggests that *M. myristica* possess cholesterol lowering potentials and protective ability in experimental hypercholesterolemia rat model.

Agomuo *et al.*[92] reported that there was a significant ($p<0.05$) cholesterol reduction in male and female rats placed on 5% ground *Monodora myristica* seed and portable water; when compared with their control group placed on normal rat feed and portable water after 1 week. Furthermore, essential oil from *M. myristica* seed reduced Guinea pig blood pressure in a dose dependent manner[66].

Antioxidant activities: Ogunmoyole *et al.*[59] reported that ethanolic and water extract of *M. myristica* seed exhibited potent dose-dependent antioxidant properties such as ferric reducing, metal chelating, free radical scavenging and inhibition of both lipid and deoxyribose oxidation. In a similar experiment, Moukette *et al.*[93] reported that the different extracts from *M. myristica* specifically the aqueous ethanol extract revealed several properties such as higher free radical scavenging properties, significant antioxidant capacities and protective potential effects on liver enzymes. Its dichloromethane and ethanol extracts exhibited free radical scavenging activity against 2,2-Diphenyl-1-Picrylhydrazyl (DPPH)[94] and its antioxidant properties have been reported and attributed mainly to its phenolic and flavonoids composition[23].

Womeni *et al.*[95] investigated the efficacy of methanolic extracts and powders of *M. myristica* seed in stabilizing crude soyabean oil during accelerated storage and found them to be potent antioxidants for stabilization of crude soyabean oil.

Diabetes is known to involve oxidative stress and changes in lipid metabolism. Nwankwo[96] evaluated the antihyperlipidaemic effect of methanolic extracts of *M. myristica* in comparison with vitamin E (a known antioxidant) in streptozotocin-induced diabetic rats and reported that oral administration of plant extracts of 200 mg kg^{-1} of the body weight daily for 3 weeks to both normal and diabetic rats resulted in significant ($p<0.05$) reduction in plasma and liver levels of total protein, total cholesterol, triacylglycerol, low density lipoprotein cholesterol

and increase in the level of high density lipoprotein cholesterol and attributed it to the high level of flavonoids in *M. myristica*. The results of Nwankwo[96] results clearly showed that the methanolic extracts of *M. myristica* may enhance protection against dyslipidaemia in streptozotocin-induced diabetic rats without possible damage to hepatic tissues. Aqueous extracts of *M. myristca* have equally been reported to possess anti-amylase activities which may be potentially useful in the treatment and management of diabetes mellitus and obesity[97,98] due to the presence of phenolic compounds[99].

Antioxidants protect the body against adverse effects of free radical or reactive oxygen species (ROS) generation[100], which are characterized by their ability to cause oxidative damage to the body. Study by Erukainure *et al*.[35] has shown that ROS are involved in various related physiological processes and diseases such as aging, cancer and atherosclerosis. Feyisayo and Oluokun[11] evaluated the antioxidant activity of the flavonoid fraction of the seed extract of *Monodora myristica*. The flavonoid fraction exhibited potent and appreciable anti-oxidant potentials with maximum DPPH-radical scavenging activity (41.20%), hydroxyl radical scavenging activity (46.34%). It also exhibited a significant $p<0.05$ reduction of Fe^{3+} to Fe^{2+} (64.64%). It exhibited a dose dependent protective effect against free radical induced haemolysis of red blood cells with maximum protection and inhibition of lipid peroxidation and free radical generation in liver homogenate. They concluded that *M. myristica* seeds contained secondary metabolites with antioxidant activity which appeared to be significant in the reduction of free radicals in a dose dependent manner. Its phenolic compounds content could be a plausible explanation for the antioxidant activities exhibited by this spice. Therefore, its consumption could possibly boost the antioxidant defense system, thereby reducing the free radical status in humans[101]. *Monodora myristica* has been proven to have anti-sickling properties[102].

INDUSTRIAL APPLICATIONS OF SOME OF THE ACTIVE COMPONENTS OF *MONODORA MYRISTICA*

Stearic acid (n-octadecanoic acid) can be used as a binding agent in food products, such as butter flavoring, vanilla flavoring, chewing gum, fruit waxes and butter[61]. O-cymene is used as a flavouring agent in the food industries[60]. Antioxidants play a major role in food quality preservation due to their ability to prevent oxidative deterioration of lipids[103]. Essential oils add flavour and aroma to baked products and also acts as food preservative[61,104,105].

The α-phellandrene is a flavouring agent with a pleasant, fresh-citrusy and peppery-woody odor (No. 1328) and no safety concern-its estimated daily intake is below the threshold of concern (i.e., 1800 μg/person/day)[106] and can be used to flavour food products such as yoghurt, baked foods etc. Because it is inexpensive, palmitic acid (n-Hexadecanoic acid) is used to add texture to processed convenience foods[107].

The 1,3,3-Trimethyl-2-Oxabicyclo [2,2,2] octan-6- ol or eucalyptol a natural, organic compound which is a colorless liquid is used as an ingredient in many brands of mouthwash and cough suppressant[60]. Eucalyptol was found to control airway mucus hyper secretion and asthma, because it can suppress arachidonic acid metabolism and cytokine production in human monocytes[108-109]. Also, because of its pleasant spicy aroma and taste, eucalyptol is used in flavorings, fragrances and cosmetics[110]. This compound is also used as an insecticide and insect repellent[111-112]. The 1,3,3-Trimethyl-2-Oxabicyclo[2,2,2] oct-6-yl acetate and 4-(2,2-Dimethyl-6-methylenecyclohexylidene)-3-methyl-2-butanon are used as flavoring, fragrances and cosmetics[110]. Furthermore, n-Octadecanoic acid (stearic acid) can be used as a binding agent for products like lotions, soaps, deodorants and candles[60]. 9-Octadecenoic acid ethyl ester (oleic acid) inhibits collagen-stimulated platelet aggregation by approximately 90% when used at a concentration of 10 Aμg mL^{-1} [113].

O-cymene is used as a fragrance in the fragrance industries[61]. Myrcene is an important intermediate used in the perfumery industry. It has a pleasant odor and analgesic, anti-inflammatory, antibiotic and antimutagenic properties. Thymol is used as an antiseptic, a herbal supplement and for the treatment of bronchitis. Pinene, camphene and dipentene in the essential oil are used to scent soaps and perfumes[59]. Alkaloids are widely used as cancer chemotherapeutic agents[114]. Limonene is common in cosmetic products[115].

The seed oils can be used to scent soaps and perfumes[116-117]. They can be incorporated into cream as antimicrobial agent and as a perfume[76]. They can also be used in dental preparation[32]. Eicosanoic acid is used for the production of detergents, photographic materials and lubricants[118].

FUTURE PROSPECTS

So far numerous studies have been conducted on different parts of *M. myristica*, but there is a dire need to isolate and identify new compounds from different parts of the tree, which have possible antitumor promoters as well as

inhibitory properties. Further studies on the active components of its seeds should be conducted so as to maximize its medicinal and nutritional potential. The identified compounds could serve as important lead compounds in the synthesis of potent drugs and chemicals which can find use in the pharmaceutical and flavouring industries. Further purification of its crude extracts could produce activities comparable to that of standard antibiotics or even better as observed in most isolated active compounds from such sources. Its use in traditional medicine to treat various diseases deserves more in depth studies.

Many studies have found *M. myristica* to be a better candidate for treatment of both bacterial and fungal infections[78,80,84]. It can therefore be formulated in creams and ointments for the treatment of superficial infections and capsules for the treatment of gastrointestinal tract infections. It can also be exploited as an alternative antimicrobial drug for the treatment of diseases caused by these pathogens.

Anyika and Uwaegbute[119] identified an increasing tendency among children and adults to move away from traditional eating pattern of three meals a day to eating snacks instead of meal. Snacks could be an excellent means to improve nutritional quality[120]. Therefore, addition of *M. myristica*-a natural food additive into snacks such as cookies could be an excellent means to improve nutritional quality, sensory properties and shelf life of snacks. Whereas, many synthetic additives can serve the same purpose, most consumers are allergic to them and they have too many side effects. Also, most of them are imported raising the need for a preservative that is cheap, inexpensive and readily available.

The antimicrobial activity of *M. myristica* can be tested on bread-a convenience baked food. Bread is an important stable food[121]. One of the main problems encountered by bread producers is its short shelf life. There is a need of innovation in bread making for attracting more people who are more reluctant for traditional products[122]. Anti-microbial activity of *M. myristica* against bacteria (*Lactobacillus casei*, *Bacillus subtilis*), yeast (*Pichia burtonii*) and moulds (*Aspergillus flavus*, *Penicillium*, *Eurotium*, *Fusarium*) responsible for spoilage of bread and other baked products[123] has not been investigated.

Dietary fibre components can be incorporated into commercial food products to enrich their fibre content and/or serve as functional ingredients[124]. The term "Dietary fibre" is widely accepted to include the complex mixture of indigestible polysaccharides (e.g., cellulose, hemicelluloses, oligosaccharides, pectins, gums), waxes and lignin found in plants, mainly as plant cell wall material[124]. Dietary fibres promote beneficial physiological effects including laxation and/or blood cholesterol attenuation and/or blood glucose attenuation[125]. Although, data on crude fibre content of *M. myristica* exist in scientific literature, there is no published data on its dietary fibre characterisation. This data could be of great practical importance in developing dietary interventions aiming to achieve certain positive health effects, both in healthy individuals and patients with certain health problems. It is therefore important to characterise the dietary fibre content of *M. myristica*.

Information on the nutritive value and phytochemical profiles of this medicinal plant should be disseminated to pharmaceutical firms, which have been depending on the wild sources of medicinal plants for drug formulation. This plant offer wide-scope for utilization as raw material for food and pharmaceutical industries. The different parts especially the seeds should be processed and packaged in a convenient form for home and industrial use as other internationally recognised spices such as curry, rosemary, thyme etc.

The amino acid composition of protein cannot completely account for its nutritional quality. The measurement of the digestibility of the protein and its amino acids must be taken into account. The digestibility of proteins and individual amino acids in *M. myristica* should be determined by an *in vitro* assay. Furthermore, dietary anti-nutritional factors have been reported to adversely affect the digestibility of protein, bioavailability of amino acids and protein quality of foods[126]. Although, Nkafamiya *et al.*[127] reported that the levels of anti-nutrients in *M. myristica* seeds are below the established toxic levels. High levels of antinutritional factors can significantly interfere with nutrient utilization and relationships between antinutritional factors and protein digestibility have been observed in *Phaseolus vulgaris*[128]. Therefore, it is imperative to investigate this relationship in *M. myristica*.

Further research is required to identify and isolate the bioactive component of *M. myristica* responsible for its hepatoprotective property and hence the exploration of the plant active substance in drug and nutraceutical formulation for liver toxicity. Although the antiplasmodial activities of the stem bark are promising, not much is known about the compounds responsible for this action. Additional research is warranted. In view of its multiple uses, *M. myristica* plant needs to be widely cultivated in most of the areas where climatic conditions favour its optimum growth. In this way, a maximum yield of its different useable parts could be achieved to derive the maximal amount of commodities of a multifarious nature for the welfare of human kind.

CONCLUSION

The antimicrobial strength, phytochemical compounds and the various organic compounds found in this plant is an eye opener for the discovery of novel bioactive compounds if the plant can be subjected to intensive research making use of various spectroscopic techniques like nuclear magnetic resonance (NMR), infra-red spectroscopy (IR), gas spectroscopy (GS) and mass spectroscopy (MS) to characterise the compounds to be isolated in order to discover known and new antibiotics and anti-parasitic agents. Extracts from *Monodora myristica* should be standardized and used in food processing industries to replace some of the artificial agents. Also, if it's essential oil is isolated using various types of chromatographic techniques, well purified and modified, it will be of high value in pharmaceutical, food component and agrochemical industries. The plant could contribute significantly to the nutrition security, health and well-being of indigenous population groups in sub-Saharan Africa.

SIGNIFICANCE STATEMENTS

This review discovered the multipurpose nature of various parts of *Monodora myristica* and provided prospects that will help the researcher to maximise its medicinal and nutritional potential. Thus, new bio-actives, medicines and nutritional substances may be discovered from the plant.

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