WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 8.084
Volume 10, Issue 8, 488-498. Review Article ISSN 2277– 7105

MYRISTICA FRAGRANS (HOUTT): A BRIEF REVIEW

Ihjas Habeeb M.*, Karunakar Hegde and Shabaraya A. R.

Department of Pharmacology, Srinivas College of Pharmacy, Valachil, Farangipete Post, Mangalore- 574 143, Karnataka, India.

Article Received on
12 May 2021,

Revised on 1 June 2021,
Accepted on 20 June 2021

DOI: 10.20959/wjpr20218-20895

***Corresponding Author**
Ihjas Habeeb M.
Department of Pharmacology, Srinivas College of Pharmacy, Valachil, Farangipete Post, Mangalore- 574 143, Karnataka, India.

ABSTRACT

Medicinal plants contain a variety of biologically active chemicals with therapeutic characteristics that have been used to cure a variety of diseases and conditions over time. It is used as a single drug as well as an aromatic spice in a variety of therapeutic formulations such as vati, syrups, lozenges, and avaleha. In addition to bringing flavour, colour, and odour to food, spices from India have a variety of therapeutic properties. It is in high demand as a spice, as well as a pharmaceutical and dietary supplement, both regionally and overseas. Diarrhoea, dysentery, sleeplessness, inflammation, heart disease, and impotency have all been treated with *Myristica fragrans* (Houtt) family (Myristicaceae) for generations. Essential oil, myristicin, fatty acids, alkaloids, and flavonoids are all said to be present. M. fragrans extract can be found in a variety of herbal treatments on the market today Essential oil, myristicin, fatty acids, alkaloids, and flavonoids are all said to be present in it. Spices have enormous culinary, medical, and other benefits, as well as commercial significance.

INTRODUCTION

The nutmeg tree, *Myristica fragrans* (Houtt), is a bushy, evergreen tree usually 9-12 m tall or more. When fully ripe, the fruit has the shape of an apricot, being yellow, smooth, and mushy. The rind rips open as the seed matures, exposing a bright crimson, fringed fleshy coating on the outside. This coating, when dried, is known in commerce as mace and used for culinary purposes throughout the world. Nutmeg is used not only as a spice and a medicine, but as a foodstuff from nutmeg rind.[1] *Myristica fragrans* (Houtt), is still widespread and abundant. Nutmeg can be used for medication, sweets, and jam, in addition to being a classic culinary spice. Past medicinal use of nutmeg to alleviate stomach disorders, rheumatism, nervousness, vomiting, sprains, and headaches are still practiced.[2]

Synonym[3]

Nutmeg, Semen myristicae, Myristica, Nux moschata, *Myristica aromata.*

Taxonomical Classification[4]

Kingdom – Plantae.

Phylum – Tracheophyta.

Division – Magnoliophyta.

Class – Magnoliopsida.

Order – Magnoliales.

Family – Myristicaceae.

Genus – Myristica.

Species – Fragrans.

Geographical distribution

The nutmeg tree requires a hot, humid climate, and is widely cultivated in the tropics, particularly on the Spice Islands (the Moluccas) Indonesia. Now it is widely cultivated in the West Indies, South Africa, India and other tropical areas.[5]

In India, it is grown in Nilgiri, Tirunelveli, Kanyakumari and Madurai districts of Tamilnadu a few trees are found in various localities of Kerala, Karnataka, Assam and some other states also.[6]

Botanical Description

Tree

The tropical evergreen tree Nutmeg, 20–25 feet high, which have brown-red bark which is soft, smooth and flakes off in thin layers or large plates. The branching pattern is such that horizontal branches radiate in whorls from the trunk.[7]

Fig. 1

Leaves

The leaves (5 to 15 cm × 2 to 7 cm) are simple, entire, 2 ranked and alternately arranged on branches. Leaf veins are pinnate and free. Leaf blades may be densely pubescent or totally glabrous, *Myristica fragrans* (Houtt) plants are usually dioecious, with the exception of a few monoecious.[8]

Fig. 2

Flowers

Flowers are unisexual, inconspicuous, small in size <4mm composed of three sepals (rarely 4) that are fused to varying degrees and exude a strong fragrance. Female flowers (up to 1 cm long) are unicarpellate and uniovulate, and they show very little morphological differentiation within the family. Male flowers (5 to 7 mm long) are composed of 2-60 anthers which are

fused to various degrees to a central column. Flowers are borne on racemose or thrysoidal paniculate inflorescences, which themselves originate within leaf axils. Once fertilized, the uni carpellate ovary develops into an elliptical fruit called a follicle.[9]

Fig. 3

Fruit

The fruit is a fleshy pericarp with a fairly spherical form, about the size and shape of a small pear. The flesh is astringent, yellowish, and nearly white on the inside, with four or five lines thick and two longitudinal valves that are approximately equal in size.[10]

Fig. 4

Seed

The seed (kernel) is ovoid or ellipsoidal, 3 to 3.5 cm long and 2 cm thick. The seed is wrapped in a ribbon-like lacinated aril that is linked to the seed's base. The seed has shallow longitudinal furrow which represents the raphe. The seed consists of thick seed coat measuring 140 µm in thickness along the ridges. The seed coat comprises epicarp (epidermis) which includes tiny, squarish cells with prominent cuticle. The inner epidermis of the seed coat includes radially elongated palisade like compact, thin walled cells.[10]

Fig. 5

Aril

The arillus (mace) is thick, horny and fleshy, strongly laciniated, folded and anastomosing toward the end, nearly encircling the nut so tightly that inequalities occur on its surface. When fresh, it is brilliant scarlet, when dry, it is much more horny, of a yellowish-brown colour, and very brittle.[11]

Fig. 6

Phytochemical Constituents

Parts	Chemical constituents
Leaves	*Myristica fragrans* (Houtt) leaf contributes ~94% of compound that are monoterpenes (~91%) predominated. These contain major compounds: α-pinene (18.04%), sabinene (19.07%), 4-terpineol (11.83%), limonene (8.32%) and β-pinene (7.92%). Minor compounds include β-myrcene, α-phellandrene, δ-3-carene, α-terpinene, α-terpinolene, α-terpineol, t-2-menthen-1-ol andmyristicin.[8]
Fruits	The main chemical components existing in the essential oil derived from nutmeg fruit flesh include αpinene (14.2%), α-terpineol (13.6%), myristicin (13.1%), terpinene-4-ol (12.4%), limonene

	(10.9%), β-pinene (8.2%), α-terpinolene (7.5%), and δ-terpinene (7.3%).[12]
Seeds (kernel)	The major compounds in the oil were sabinene (21.38%), 4-terpineol (13.92%) and myristicin (13.57%). allylbenzene and propyl benzene derivatives (myristicin, safrole, eugenol, and derivatives thereof) were the predominant compounds in nutmeg seeds.[13]
Mace	51.2% monoterpenes, 30.3% oxygenated monoterpenes and 18.8% phenyl propanoid ether.[14]

Traditional Uses

Myristica fragrans Houtt. (Myristicaceae) has long been used as an herbal spice to treat various disorders. In general traditional medicine, it is mostly used two parts i.e. seed and aril. The seed (nutmeg) is widely used as carminative, astringent, hypolipidemic, antithrombotic, antiplatelet aggregation, antifungal, aphrodisiac, anti-flatulence, anti-nausea, and anti-dyspepsia agents. Mace (aril) is a flavouring agent, hair dye, and folk medicine that is extensively used. It also possesses antipapillomagenic, anticarcinogenic, anti-bacterial and anti-inflammatory activities.[15]

1. Antioxidant activity

Nutmeg possesses antioxidant activity due to the presence of various compounds including β-caryophyllene and eugenol, having hydrogen atoms in the allylic or benzylic positions. Eugenol in nutmeg favors the antioxidant property by promoting the activities of superoxide dismutase, catalase, glucose-6-phosphate dehydrogenase, glutathione peroxidase and glutamine transferase enzymes.[16]

Some spices' antioxidant activity was compared to that of food antioxidants such as Propyl gallate, butylated hydroxyanisole (BHA), and butylated hydroxytoluene (BHT). Anise, Liquorice and Nutmeg showed good performance in the deoxyribose assay. Propyl gallate, Liquorice, Ginger, and Nutmeg boosted the stability of several fixed oils such as olive, sunflower, and corn oil, as well as fats such as margarine and butter, and inhibited oxidation at 110 degrees Celsius. In the Trolox equivalent antioxidant capacity (TEAC) experiment, nutmeg was found to have better antioxidant activity than BHT(butylated hydroxytoluene).[17]

2. Antimicrobial activity

The essential oil and different extracts of aromatic plants have shown strong antimicrobial activity against variety of fungi as well as bacteria[18]. In a study involving 25 distinct bacterial strains, the antibacterial activity of the volatile oil derived from the seeds of *Myristica*

fragrans (Houtt) was examined, and it was discovered that it was equally efficient against the majority of gram positive and gram negative bacteria.[19]

3. Hypoglycemic and antidiabetic activities

It was observed, that when rats were given pre-treatment with petroleum ether (60-80º C) extract of Myristica fragrans(Houtt) seed, at dose of 200 mg/kg, a significant decrease in blood glucose level, ($P<0.05$), was obtained, i.e. blood glucose level reduced from 145.75±9.65 to 81.5±4.03 mg% in oral glucose tolerance test (OGTT) after 30 min compared to control group of glucose-fed rats. The nutmeg extract has significant peroxisome proliferator-activated receptor (PPAR) α/γ dual agonist activity, but its potency is less than PPAR α and PPAR γ full agonist. Therefore, nutmeg (*Myristica fragrans* (Houtt)) extract being a natural dual agonist PPAR α/γ can be developed as a potential anti-diabetic agent for the treatment of type 2 diabetes.[20]

4. Hypolipidaemic and platelets anti-aggregatory activity

In albino rats, it was shown that an oral dose of 500 mg/kg of ethanolic extract of Nutmeg for 60 days dramatically lowered total cholesterol in the heart and liver. The levels of low-density lipoproteins (LDL) and very low-density lipoproteins (VLDL) were also lowered dramatically. The toxicology analysis revealed that no harmful effects on major haematological and biochemical parameters were observed.[21]

5. Hepatoprotective activity

The key ingredient of *Myristica fragrans* (Houtt), myristicin, has been shown to prevent the lipopolysaccharide plus d-galactosamine-induced enhancement in serum TNF-alpha values in mice**.** Therefore, it was recommended that the hepatoprotective activity of Myristicin could be due to the inhibition of tumour necrosis factor (TNF)-alpha release from macrophages.[22]

Another modern study revealed that mace lignan isolated from *Myristica fragrans* (Houtt) had a hepatoprotective effect on cisplatin-induced hepatotoxicity in mice.[23]

6. Anti-inflammatory activity

By blocking the generation of inflammatory cytokines and nitric oxide, an ethanolic extract of nutmeg seed exhibited impressive anti-inflammatory effect. The active ingredient responsible for the anti-inflammatory properties was discovered to be quercetin.[24]

7. Anticancer activity

By down regulating SIRTI mRNA, the methanol extract of *Myristica fragrans* (Houtt) triggered cell death in Jurkat leukaemia T cells. At a dose of 100g/ml, an ethanolic extract of the plant showed anti-cancer activity against human cancer cell lines, inhibiting proliferation by more than 70%.[25]

8. Memory enhancing activity

Anticholinesterase inhibition is used to treat Alzheimer's disease by slowing cognitive deterioration caused by cholinergic deficiencies. In one study, it was discovered that a hydroalcoholic extract of Nutmeg showed considerable (50 percent) suppression of acetylcholinesterase for the treatment of Alzheimer's disease.[26]

9. Anti-diarrhoeal activity

The anti-diarrheal action of Nutmeg crude suspension and petroleum ether extract was tested, and it exhibited a decrease in the mean number of loose stools and an increase in the latency period. Nutmeg in a crude suspension had a strong anti-diarrheal effect.[27]

10. Osteoblast proliferation stimulation activity

Components from M. fragrans have been shown to induce osteoblast differentiation. The p38 mitogen-activated protein (MAP) kinase was activated by Machilin A from *Myristica fragrans* (Houtt), which accelerated osteoblast differentiation. Other lignans found in *M. fragrans*, such as safrole, myristargenol, mace lignan, nectandrin B, mesodihydroguaiaretic acid, machilin F, licarin B, and licarin A, have similar anabolic effects in bone metabolism.[28]

11. Anti-obesity activity

In one study, it was found that tetrahydrofuran (THF) type lignans isolated from *Myristica fragrans* (Houtt) showed an anti-obesity effect in high fed diet (HFD) induced mice due to Adenosine Monophosphate (AMP)-activated protein kinase activation mechanism. The THF prevented the increase in adipose tissue mass, body weight, LDL levels and glucose in THF treated mice as compared to HFD group of mice.[29]

CONCLUSION

Nutmeg is an important element in a wide range of industrial applications, which include food and cosmetics. Because of its antioxidant and antibacterial characteristics, its medicinal

products are remarkably significant. Experimental and clinical research has also proven the medicinal efficacy of these distinct spices for distinct pharmacological activities. Modern pharmacological and experimental approaches have substantiated the traditional medical properties linked to Indian spices, providing a scientific justification for their traditional therapeutic use.

REFERENCES

1. Anonymous. Wealth of India: Raw materials. Vol. VI. Council of Scientific and Industrial Research, New Delhi, 1962; 474-6.
2. Van Gils C, Cox PA. Ethnobotany of nutmeg in the Spice Islands. Journal of Ethnopharmacology, 1994 Apr; 42(2): 117-124.
3. Prof. Lucas DS. Dravya Guna Vigyana Study of Dravya Materia Medica, 1 st ed. Varanasi; Chaukhambha Vishwabharati, 2008; II: 369.
4. *Myristica fragrans* Houtt. in GBIF Secretariat GBIF Backbone Taxonomy. Checklist dataset https://doi.org/10.15468/39omei accessed via GBIF.org on, 2021; 2021-06-09.
5. Peter KV. Handbook of herbs and spices. Woodhead Publishing Ltd., Cambridge, 2001; 2: 238-48.
6. Sharma PC, Yeine MB, Dennis TJ. Data Base on Medicinal Plants Used in Ayurveda. New Delhi; Central Council for Research in Ayurveda and Siddha Dept. of ISM and H Ministry of Health and Welfare, Govt. of India, 2002; IV: 213.
7. Sharma PC, Yeine MB, Dennis TJ. Data Base on Medicinal Plants Used in Ayurveda. New Delhi; Central Council for Research in Ayurveda and Siddha Dept. of ISM and H Ministry of Health and Welfare, Govt. of India, 2002; IV: 213.
8. T John Zachariah, N K Leela, K M Maya, J Rema, P A Mathew, T M Vipin et al.. Chemical composition of leaf oils of *Myristica beddomeii* (King), *Myristica fragrans* (Houtt.) and *Myristica malabarica* (Lamk.), JOSAC 2008; 17(1): 11.
9. Thangaselvabai, Thadiyankudisai & K R, Sudha & Selvakumar, T. & Ramachandran, Balakumbahan. Nutmeg (*Myristica fragrans* Houtt) – the twin spice – a review. Agri. Review, 2011; 32: 283 - 293.
10. N.Parimalaa, S.Amerjothyb. Histological and Histochemical investigations of Myristica fragrans Houtt. (Myristicaceae). J Pharmacogn Phytochem., 2013; 1(5): 106-111.
11. Periasamy, Gomathi & Karim, Aman & Gebrelibanos, Mebrahtom & Gebremedhin, Gereziher & Gilani, Anwar-ul. Nutmeg (*Myristica fragrans* Houtt.) Oils, 2016; 10.1016/B978-0-12-416641-7.00069-9.

12. Sipahelut SG, Kastanja AY, Patty Z Antioxidant activity of nutmeg fruit flesh-derived essential oil obtained through multiple drying methods. Eurasia J Biosci., 2020; 14: 21-26.
13. Muchtaridi, Subarnas A, Apriyantono A, Mustarichie R. Identification of compounds in the essential oil of nutmeg seeds (*Myristica fragrans* Houtt.) that inhibit locomotor activity in mice. International Journal of Molecular Sciences, 2010 Nov; 11(11): 4771-4781.
14. G.R. Mallavarapu, S. Ramesh J. Med. Aromat. Plant Sci., 1998; 20: 746-748
15. Champasuri S, Itharat A. Bioactivities of ethanolic extracts of three parts (Wood, nutmeg and mace) from *Myristica fragrans* Houtt. J Med Assoc Thai., 2016; 99(4): S124-S30.
16. A.D. Gupta, D. Rajpurohit, Antioxidant and Antimicrobial Activity of Nutmeg (*Myristica fragrans*). In Nuts and Seeds in Health and Disease Prevention, Elsevier, 2011; 831-839.
17. Murcia MA, Egea I, Romojaro F, Parras P, Jiménez AM, Martínez-Tomé M. Antioxidant evaluation in dessert spices compared with common food additives. Influence of irradiation procedure. J Agric Food Chem., 2004; 52: 1872-81.
18. M.A. Hanif, H.N. Bhatti, M.S. Jamil, R.S. Anjum, A. Jamil, M.M. Khan. Antibacterial and antifungal activities of essential oils extracted from medicinal plants using CO_2 supercritical fluid extraction technology. Asian Journal of Chemistry, 2010; 22(10): 7787.
19. Dorman HJ, Deans SG. Antimicrobial agents from plants: antibacterial activity of volatile plant oils. J Appl Microbiol., 2000; 88: 308-16.
20. Lestari K, Hwang JK, Kariadi SH, Wijaya A, Ahmad T, Subarnas A, et al. Screening for PPAR γ agonist from *Myristica fragrans* Houtt seeds for the treatment of Type 2 diabetes by in vitro and in vivo. Med Heal Sci., J 2012; 12: 7-15.
21. Ram A, Lauria P, Gupta R, Sharma VN. Hypolipidaemic effect of *Myristica fragrans* fruit extract in rabbits. J Ethnopharmacol., 1996; 55: 49-53.
22. Morita T, Jinno K, Kawagishi H. Hepatoprotective effect of myristicin from nutmeg (*Myristica fragrans*) on lipopolysaccharide/d-galactosamine-induced liver injury. J Agric Food Chem., 2003; 51: 1560-5.
23. Morita T, Jinno K, Kawagishi H. Hepatoprotective effect of myristicin from nutmeg (*Myristica fragrans*) on lipopolysaccharide/d-galactosamine-induced liver injury. J Agric Food Chem., 2003; 51: 1560-5.

24. Dewi K, Widyarto B, Erawijantari PP, Widowati W. In vitro study of *Myristica fragrans* seed (Nutmeg) ethanolic extract and quercetin compound as an anti-inflammatory agent. Int J Res Med Sci., 2015; 3: 2303-10.
25. Prakash E, Gupta DK. Cytotoxic activity of ethanolic extract of *Myristica fragrans* (Houtt) against seven human cancer cell lines. Universal J Food Nutrition Sci., 2013; 1: 1-3.
26. Mukherjee PK, Kumar V, Houghton PJ. Screening of Indian medicinal plants for acetylcholinesterase inhibitory activity. Phytother Res., 2007; 21: 1142-5.
27. Grover JK, Khandkar S, Vats V, Dhunnoo Y, Das D. Pharmacological studies on *Myristica fragrans*- antidiarrhoeal, hypnotic, analgesic and hemodynamic (blood pressure) parameters. Methods Find Exp Clin Pharmacol., 2002; 24: 675-80.
28. Lee SU, Shim KS, Ryu SY, Min YK, Kim SH. Machilin, an isolated from *Myristica fragrans*, stimulates osteoblast differentiation. Planta Med., 2009; 75: 152-7.
29. Nguyen PH. AMP-activated protein kinase (AMPK) activators from *Myristica fragrans* (nutmeg) and their anti-obesity effect. Bioorg Med Chem Lett., 2010; 20: 4128-31.