

A systematic review on Nutmeg and its medical importance

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Abstract

Nutmeg and mace have a very important role in ayurvedic medicine and home remedies. It is a very important spice used as a flavouring agent as well as it is a good remedy for stomach and kidney disorders. Essential oils, triterpenes, and various types of phenolic compounds are helpful in treating various ailments. This review paper provides an overview of the medical importance of various chemical metabolites isolated from nutmeg kernel and mace. It includes the analysis of various extracts and compounds, as well as their role in various treatments.

Key words: Nut meg, *Myristica fragrans*, Myristic acid, medical importance of nutmeg

Introduction

The spice nutmeg (Jatiphala), which is made from the seed of the *Myristica fragrans* tree, has a long history of use in medicine. It has received recognition for its multiple health benefits, including anti-inflammatory, anti-cancer, anti-bacterial, anti-diabetic, pain-relieving, liver-protecting, and more. (Kumari et al., 2021) Native to Indonesia, nutmeg is frequently used in American classic baked products as well as Asian, European, Middle Eastern, and African cuisines. Due to pharmacological activities nutmeg essential oils and extracts are used in development of new drugs. (Abourashed EA, Khan IA, 2010). According to studies, nutmeg may provide health advantages like reduced pain and inflammation, better heart and brain health, improved digestion, and better sleep. The fibre in nutmeg can aid with bloating, cramps, and diarrhoea brought on by food allergies or intolerances. The carminative properties of the spice can also soothe an upset stomach and aid in the release of digestive enzymes that increase metabolism. Traditionally Indian spices, as part of the diet, have comprehensive effects on human health. (Sachan AK et al., 2018). The nutmeg extract can be used to the external treatment of skin infections, rheumatism and paralysis (Abourashed and Khan 2010). There are so many reports of traditional uses and activities of nutmeg and mace, its underlying mechanisms are still unclear. So there must be a proper pharmacological study to understand the medical importance of this super spice.

The world is currently dealing with the introduction and spread of new types of infectious diseases, which is a major issue and necessitates a sizable amount of time and effort to develop the treatments to treat them. The best way to lower the danger of these illnesses is to strengthen our immunity, which is a growing health problem. There is some evidence to suggest that by enhancing the immune response, numerous nutritional supplements made from different spices help lessen the risk or severity of a variety of microbial diseases. The harmful consequences caused by many infections can be lessened by using these spice

extracts.(Martins IJ,2018) Therefore, using natural substances may offer an alternative to traditional preventative and therapeutic support. In this article, we examine the medical importance of nutmeg.

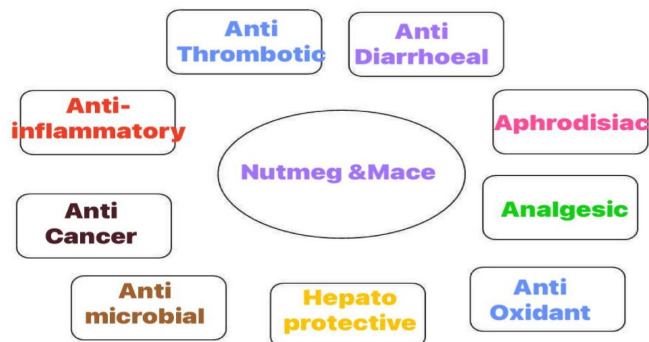


Fig1: Medical importance of Nutmeg

Botanical description of plant

Mace and nutmeg are two separate spices that are produced from the nutmeg tree, *Myristica fragrans*. This evergreen shrub, which may reach a height of more than 20 meters (Periasamy et al., 2016), is planted in India, Ceylon, Malaysia, and Granada. The leaves are alternating, oblong, glabrous, acuminate, fragrant, dark green, and glossy above (Periasamy et al., 2016). According to Haldankar et al. (2007), flowers are typically dioecious but occasionally monoecious with varied sex expression, tiny, axillary, sub-umbellate racemes, complex, or infrequently forked. The peduncles and pedicels appear to be glabrous. The spherical fruit contains a fleshy pericarp, and its yellowish fruit skin divides into two longitudinal valves. When wet, the mace (aril) is a fleshy, reddish-purple aril that is folded, lacinate, and encases the nut; when dry, it becomes much hornier, yellowish-brown in colour, and extremely brittle. The tree's fruit, known as a drupe or nutmeg apple, resembles an apricot or a peach in appearance. The nutmeg, which is a rocky endocarp or seed encircled by a scarlet, slightly squishy network or aril, is visible as the fruit matures and cracks open. While nutmeg is made by removing and drying the nut, mace is the name given to the dried aril alone. (Wallis, 1985).

Bioactive molecules

The seed contains about 10% essential oil (Verghese J.2001, Maya KM et al.,2004), which is mostly composed of terpene hydrocarbons (α-pinene, camphene, p-cymene, sabinene, β-phellandrene, γ-terpinene, limonene, myrcene (60% to 90%), terpene derivatives (linalool, geraniol, terpineol - 5% to 15%) and phenylpropanes (myristicin, elemicin, safrole-2% to 20%). One of the factors contributing to the intoxicating effects of *M. fragrans* seed is the presence of myristicin and elemicin. (Su L et al.,2005) Fats (30–40%) and essential oils (10%) are the two components present in nutmeg. GC-MS analysis is typically used to characterise essential oils (A.Y.Al-Maskri et al.,2011)(J.Widelski,et al.,2017) Phenylpropanoids include myristicin, elemicin, safrole, eugenol, and eugenol derivatives. (Kapoor IP et al.,2013)

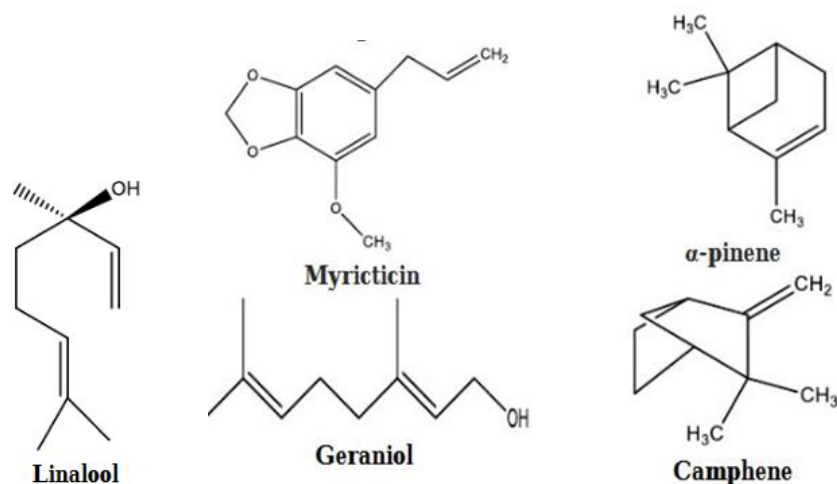


Figure 2: Important chemical molecule present in nutmeg oil

Table 1 : Active phytochemicals present in Nutmeg in various studies

Name of phytochemical	Method of isolation	Reference
essential oils(α -Thujene, α -Pinene, camphene, sabinene, β -Pinene, myrcene, α -Phellandrene, 3-Carene, α -Terpinene, p-Cymene, limonene, β -Phellandrene, γ -Terpinene, cis-Sabinene hydrate, terpinolene, trans-Sabinene hydrate, cis-p-Menth-2-en-1-ol, trans-p-Menth-2-en-1-ol, Terpinen-4-ol, p-Cymen-8-ol, α -Terpineol, cis-Piperitol, trans-Piperitol, citronellol, bornylacetate, safrole, α -Cubebene, terpenyl acetate, citronellyl acetate, α -Copaene, geranyl acetate, methyl eugenol, β -Caryophyllene, trans- α -Bergamotene, α -Humulene, myristicin, elemicin, docosane)	cleverger and soxhlet apparatus	Kapoor et al.(2013)
myristicin, elemicin, safrole, (Iso) eugenol	hydro-distillation method	Marzuki et al.,(2014)
Sabinene, myristicin, elemicin, α -pinene, β -pinene, limonene, terpinen-4-ol and myristic acid	absolute ethanol extraction method(1:4 of material) at room temperature	Morsy et al.,(2016)

Table 1: Bioactive molecules of nutmeg

Pharmacology

Antimicrobial effects

The oils of mace and nutmeg and their individual components (trimyristin, myristic acid, myristin, mace lignan) have been assessed for *in vitro* activity, which has been shown against some oral microorganisms. (Yanti, Rukayadi Y, 2008). The essential oils of spices have been reported to inhibit microorganism growth (Ashokkumar et al., 2020a, 2020b, 2021b) and are insoluble in water. *Helicobacter pylori* was found to be strongly inhibited by the crude extract of *M. fragrans* (aril or leaf), which had a minimum inhibitory concentration (MIC) of 12.5 mcg/mL for the aril extract and 50 mcg/mL for the leaf extract. As controls, MIC ranges of amoxicillin (0.0039 to 0.25 mcg/mL) and metronidazole (64 to 124 mcg/mL) were employed. (Bhamarapravati S et al., 2003)

Extract of *M. fragrans* has antibacterial efficacy against *Proteus vulgaris*, *Staphylococcus aureus*, and *Klebsiella pneumonia*, (Ibrahim et al. 2011) and ineffective against *Pseudomonas aeruginosa*, *Bacillus subtilis*, and *Salmonella typhirium*. *Aspergillus glaucus*, *Aspergillus niger*, *Collectotrichum gloeosporoides*, *Colletotrichum musae*, *Fusarium oxysporum*, and *Fusarium semitectum* are all inhibited by 0.1% nutmeg essential oil, according to the radial growth determination. When the *M. fragrans* concentration rose to 0.3%, this growth inhibition could have reached a maximum of 100% (Valente et al., 2011). In addition, mace and nutmeg have potent antibacterial properties against pathogens that affect plants and animals, such as *Escherichia coli*, *Saccharomyces cerevisiae*, and *Helicobacter pylori*. (Dorman & Deans, 2000; Rani & Khullar, 2004; De et al., 1999)

Antioxidant activities

Chemical assays such as DPPH (2,2-diphenyl-1-picrylhydrazyl), FRAP (ferric reducing/antioxidant power assay), suppression of lipid peroxidation, and bleaching of -carotene can be used to demonstrate the antioxidant activity of MFEO (*M. fragrans* Essential oil) (Gupta, Bansal, Babu, & Maithil, 2013). With an EC₅₀ dosage of 181.4 g/ml, the nutmeg essential oil demonstrated 88.7% suppression of linoleic acid oxidation (Piaru et al., 2012). According to Matulyte et al. (2020), the antioxidant activity of pure MFEO and MFEO with 1% magnesium aluminometasilicate was comparable at EO concentrations of 0.2-20%.

Anti-inflammatory activities

Nutmeg's oil and anti-inflammatory properties have been noted by several authors (*M. Mueller* et al., 2010). (Das et al., 2020; Hiranrat & Hiranrat, 2019; Kholibrina & Aswandi, 2021; Nikolic et al., 2021; Özkan et al., 2018; Purkait, Bhattacharya, Bag, & Chattopadhyay, 2018; Thileepan, Thevanesam, & Kathirgamanathar, 2018; Valente, Jham, Jardim, Dhingra, & Ghiviriga, 2015). Nutmeg oil exhibits pharmacological actions that are comparable to those of non-steroidal anti-inflammatory medications (O.A. Olajide et al., 2000). But only petroleum ether extracts have been found to have anti-inflammatory action. The entire nutmeg extract stimulated the AMP-activated protein kinase enzyme, which is a possible therapeutic target for treating the metabolic syndrome, which includes type 2 diabetes and obesity. From this extract, seven active ingredients were identified,

including tetrahydrofuroguaiacin B, 2,5-bis-aryl-3,4-dimethyltetrahydrofuranlignans, fragransin C1, saucernetindiol, nectandrin B, verrucosin, galbacin, and nectandrin . The M. fragrance petroleum ether extract resembles non-steroidal anti-inflammatory medicines in terms of its characteristics.(Olajide et al.,2000)

Other medicinal importance

Some of the main advantages of nutmeg essential oil include reducing mood swings and depression, removing toxins from the liver, enhancing cognition, treating respiratory issues, alleviating insomnia, promoting digestive and bone health, aiding in kidney stone dissolution, maintaining optimal brain health, reducing skin inflammation and irritation, and boosting digestive and bone health. (Dhaslin YF et al., 2019) The Myristicaceae plant family has been tested by the National Cancer Institute for efficacy against certain leukaemia strains. Apoptosis was raised and leukaemia and neuroblastoma cell growth was lowered in in vitro tests using methanol extract and myristicin. Of the studied extracts, 18.8% had antileukemia activity.(Cragg GM et al.,2006) (Lee BK et al.,2005), 20) A few of older studies show some activity on the enzymes responsible for the activation and detoxification of carcinogens. (Chirathaworn C et al.,2007)

Table 2 : Recent studies of Nutmeg for medicinal importance on various extracts

Name of extract	Medicinal use	Reference
Ethanollic extract	Aphrodisiac	Ahmad, S., Latif,(2005)
n-hexane extract	Effect on memory	Parle, M., et al.,(2004)
Hexane soluble fraction	Anti-diarrhoeal	Gupta, S. et al.,(1992)
eugenol and iso-eugenol	Antithrombotic	Janssens, J.et al.,(1990)
Alcoholic extract	Hepatoprotective	Zhao, W., Song, F et al.,(2020)
Ethanollic extract	Anti-cancer	Prakash E, et al.,(2013)
Essential oil	Anti-oxidant	Dorman, H. D(2000)
a)Malabaricon B [1] and malabaricon C	Anti-microbial	Orabi, K. Y.et al.,(1991) and Hattori M et al.,(1986)
b)Dehydro-di-isoeugenol 5-methoxydehydrodiisogenol	Anti-microbial	Orabi, K. Y.et al.,(1991) and Hattori M et al.,(1986)
Ethanollic extract	Hypolipidemic effect	Ram, A., et al.,(1996)
Macelignan	Anti-diabetic	Han, K. L. et al.,(2008)
Nutmeg oil	Anti convulsant	Wahab, A. et al.,(2009)

Conclusions

The current study emphasises the potential use of *Myristica fragrance* as an antibacterial, antifungal, hepatoprotective activity, anti-inflammatory and analgesic property, memory-enhancing activity, anticonvulsant activity, anti-diabetic properties, neuropharmacologic properties, hypolipidemic, and hypocholesterolemic property due to its valuable bioactive compounds, which may have potential for the development of drugs against pathogenic microorganisms. Since nutmeg contains a complex mixture of different compounds, it can occasionally be beneficial when used in moderation but can also be quite hazardous when used improperly or in large doses. The pharmacological actions of MFEOs and their active components in humans should be the focus of future research. Future studies should investigate the toxicity, and pharmacokinetics of nutmeg to identify the chemical elements causing its effects and broaden the use of *M. fragrans* in medicine. We think that the details offered or covered here will raise people's awareness of nutmeg and mace and be useful for further studies.

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