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Nutmeg - Myristica Fragrans

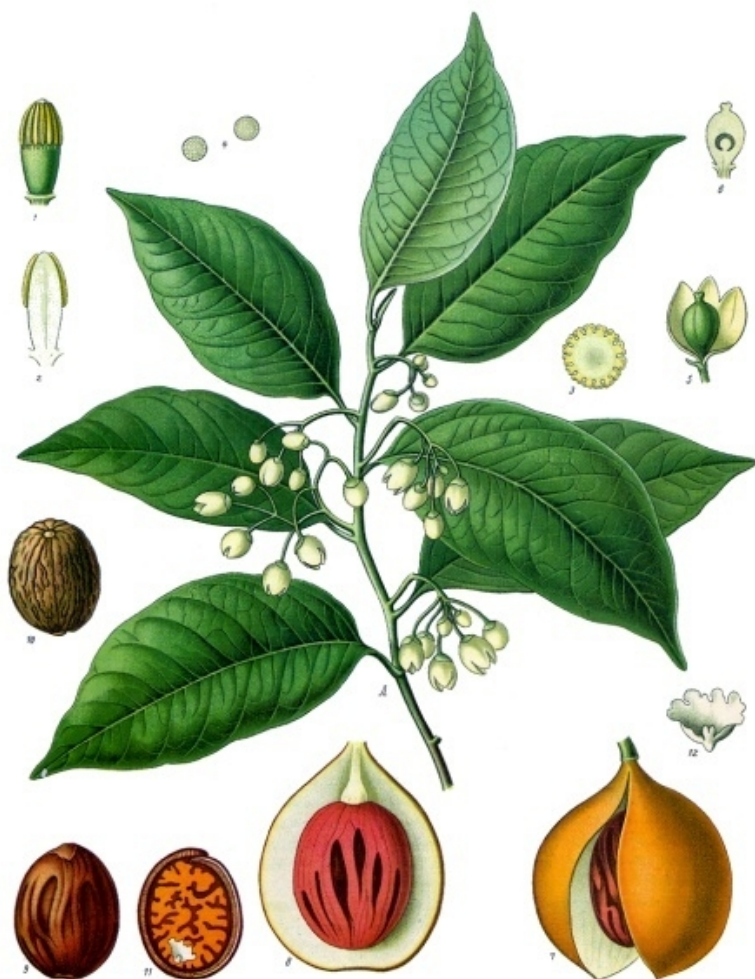
[Phytochemicals](#)

Author: [Andrea Demeco](#)

Date: 16/02/2013



Description



Common Name: [Nutmeg](#) .

Scientific Name: Myristica fragrans Houtt.

Botanical Family: Myristicaceae

Physical Description:

This aromatic evergreen tree grows 9-12 m (30-39 ft) high with spreading branches and a yellow fleshy fruit similar in appearance to an apricot or peach. The ripe fruit splits to expose a single glossy brown nut enclosed by a scarlet aril. The

tree produces fruit year round, but the harvest usually occurs in April and November.

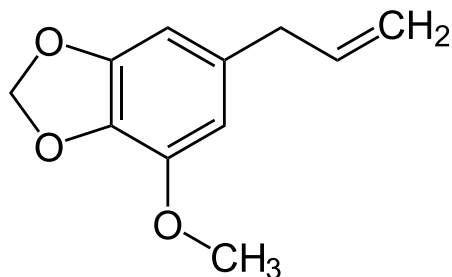
Distribution and Ecology: The nutmeg tree is indigenous to the Maluku Province of Indonesia, formerly known as the Spice Islands. The nutmeg tree is grown commercially on the Caribbean islands of Grenada and Trinidad as well as in Central and East Java.

h3. Structure and Properties

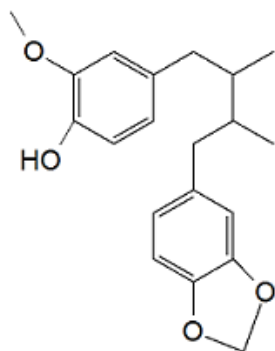
The concentration of active components depends on the botanical source, environmental conditions, storage, and analytical methods. The two oils of nutmeg are fixed oil (expressed oil, nutmeg butter) and essential oil. The fixed oil is an orange, butter-like material obtained by applying heat and hydraulic pressure to nutmeg. This oil contains primarily trimyristin, and the product has no culinary value. Essential oil of nutmeg is a steam distillate that appears as a pale-yellow, nearly colorless liquid with the characteristic odor of spice.

Active Molecules Description:

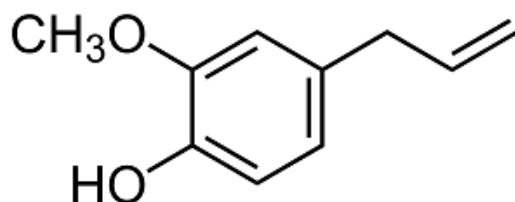
- **Myristicin**, which is the main psychoactive constituent of nutmeg. Myristicin is also the major component of the aromatic ether fraction of essential oil of mace. Fig 1 displays the chemical structure of myristicin.



- **Macelignan**. Lignans are a class of [phytoestrogens](#) having numerous potential pharmacological activities including anticancer, anti-inflammatory, antimicrobial, antioxidative, and immunosuppressive activities. Among the bioactive plant lignans ubiquitous in human diets, macelignan has been isolated from *Myristica fragrans*



- **Eugenol** (4-allyl-2-methoxyphenol), Eugenol has been used traditionally in Asian countries, mainly as a medicinal antiseptic, analgesic and antibacterial agent. Eugenol has been used as a flavoring agent in cosmetics and food products and also plays a role in dentistry as cavity filling cement.



It was found that *M. fragrans* is still used for both culinary and medicinal purposes in its area of origin. *M. fragrans* is used for diarrhea, mouth sores, and insomnia.

[Ethnobotany of nutmeg in the Spice Islands, 1994](#)

Medical Research:

New reserches describe several effect of *M. fragrans* such us:

- Antioxidant and Anti-inflammatory
- Improvement of memory
- Antiepileptic effect
- Anticaries effect
- Antimalarial activities

- Anticancer
- Treatment of Alzheimer's Disease

Antioxidant and Anti-inflammatory

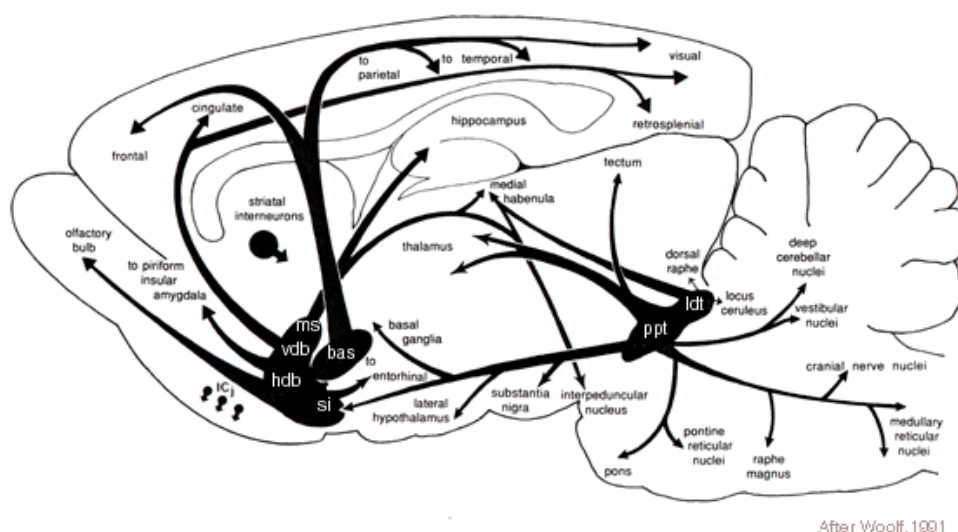
Exposure to ultraviolet (UV) light causes premature skin aging that is associated with upregulated matrix metalloproteinases (MMPs.) and decreased collagen synthesis. Macelignan, a natural [lignan](#) compound isolated from *Myristica fragrans* HOUTT. (nutmeg), has been reported to possess antioxidant and antiinflammatory activities. Macelignan attenuate [UV-induced MMP-1 expression](#) by suppressing phosphorylation of mitogen-activated protein kinases (MAPKs.) induced by [reactive oxygen species](#). Skin response to UV . Macelignan also increase type I procollagen expression and secretion through transforming growth factor β ([TGF- \$\beta\$ /Smad signaling](#)). These findings indicate that macelignan regulates the expression of MMP-1 and type I procollagen in UV-irradiated human skin fibroblasts by modulating MAPK and TGF- β /Smad signaling, suggesting its potential as an efficacious anti-photoaging agent. Moreover, evidences showed that nutmeg oil has high antioxidant activity. The nutmeg oil effectively inhibited the oxidation of [linoleic acid](#).

[Effects of macelignan isolated from *Myristica fragrans* \(Nutmeg\) on expression of matrix metalloproteinase-1 and type I procollagen in UVB-irradiated human skin fibroblasts,2012](#)

Improvement of Memory

Memory is one of the most complex functions of the brain and involves multiple neural pathways and neurotransmitter systems. *Myristica fragrans* (MF) extract at the lowest dose of 5 mg/kg p.o. administered for 3 successive days significantly improves learning and memory of young and aged mice. This extract also reversed [scopolamine-](#) and [diazepam-](#) induced impairment in learning and memory of young mice. MF extract enhanced learning and retention capacities of both young and aged mice. The exact mechanism of the memory-improving effect of MF extract was not explored . But, the observed memory-enhancing effect may be attributed to a variety of properties (individually or in combination) the plant is reported to possess, such as antioxidant, anti-inflammatory, or perhaps procholinergic activity, on [brain cholinergic pathways](#).

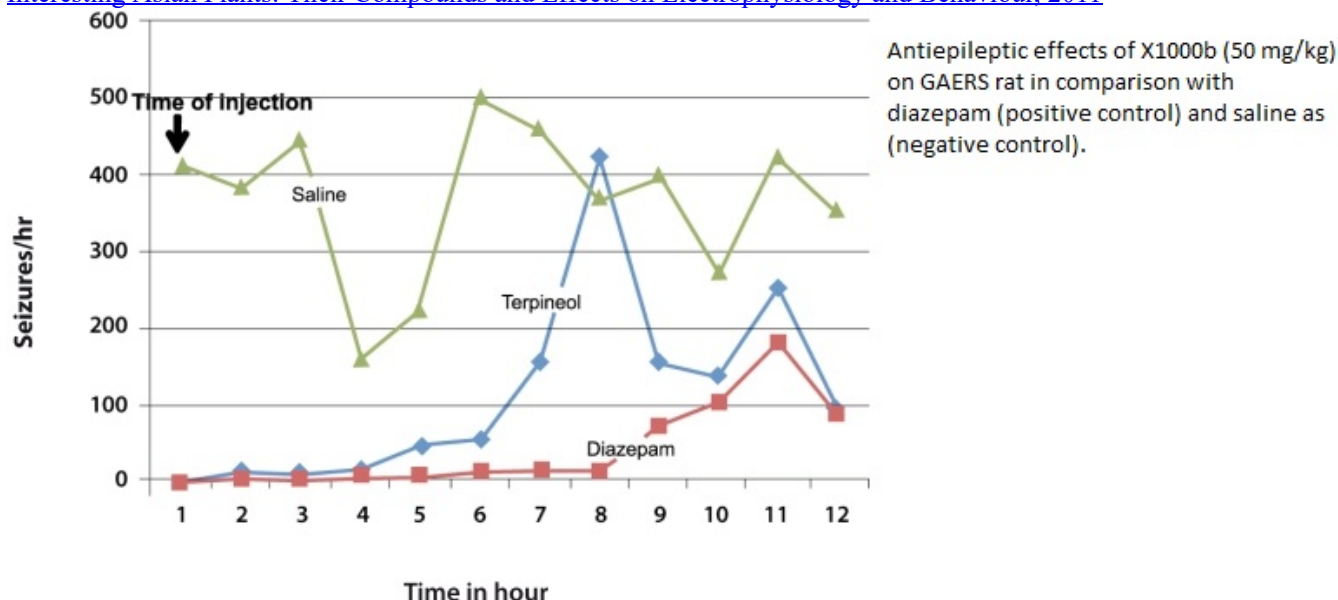
[Improvement of mouse memory by *Myristica fragrans* seeds,2004](#)



Inhibitory effects on [GABA A receptor](#) and [Antiepileptic](#) effects

The essential oil of *M. fragrans* was tested in *Xenopus* oocytes that were injected with GABAA receptor comprising of $2\alpha 1$, $2\beta 2$, and $\gamma 2s$ subunits by using automated fast perfusion system during 2-microelectrode voltage-clamp measurement. At 1.0% essential oil and 5 μ M GABA, the percentage of current stimulation was more than 100%. Two compounds from *M. fragrans*, X1000a and X1000b, also exhibited a significant increase in current flow at 100 μ M. These findings showed that the compounds acted at the GABAA receptor as positive modulators or agonists. The compounds also showed interesting antiepileptic effects, as observed in the improvement of the number and the type of seizures in rats monitored with intracranial implants using video wireless telemetry methods.

[Interesting Asian Plants: Their Compounds and Effects on Electrophysiology and Behaviour, 2011](#)



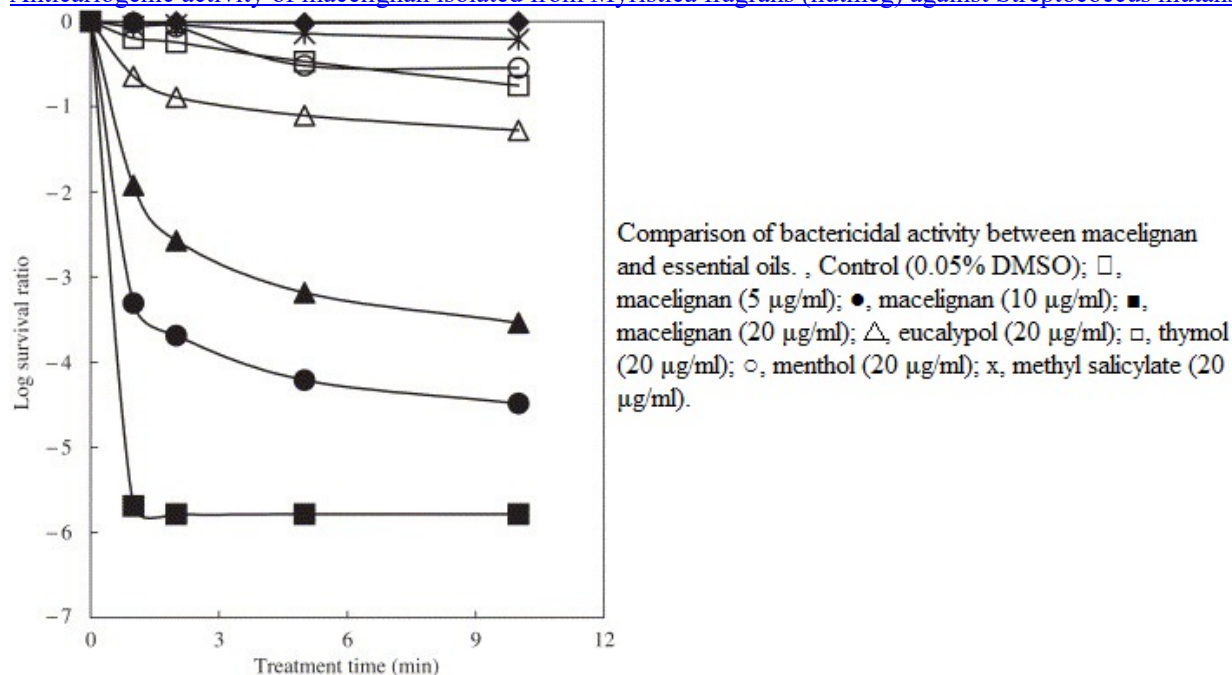
[Anticaries](#) effect

The extract of nutmeg, widely used as a spice, possesses strong inhibitory activity against [Streptococcus mutans](#). The anticariogenic compound was identified as macelignan ((8R, 8'S)-7-(3,4-methylenedioxyphenyl)-7'-(4-hydroxy-3-methoxyphenyl)-8,8'-dimethylbutane) with a MIC of 3.9 µg/ml, which is much lower than that of [thymol](#) (500 µg/ml). Twenty µg/ml macelignan concentration completely inactivated Streptococcus mutans in 1 min. Macelignan is active also against [lactobacilli](#) at the 2–31.3 µg/ml MIC range. Macelignan in particular conditions reduces biofilm formation by more than 50%.

The specific activity and fast-effectiveness of macelignan ascribes it as a potent natural anti-biofilm agent.

[Food components with anticaries activity, 2012](#)

[Anticariogenic activity of macelignan isolated from Myristica fragrans \(nutmeg\) against Streptococcus mutans, 2006](#)



[Antimalarial](#) activities

The extracts from Myristica fragrans used in Thai traditional medicine showed potent antimalarial activity with median range IC₅₀ values of less than 10 µg/ml against chloroquine-resistant (K1) and chloroquine-sensitive (3D7) [P. falciparum](#) clones or both.

[Antimalarial activities of medicinal plants and herbal formulations used in Thai traditional medicine, 2013](#)

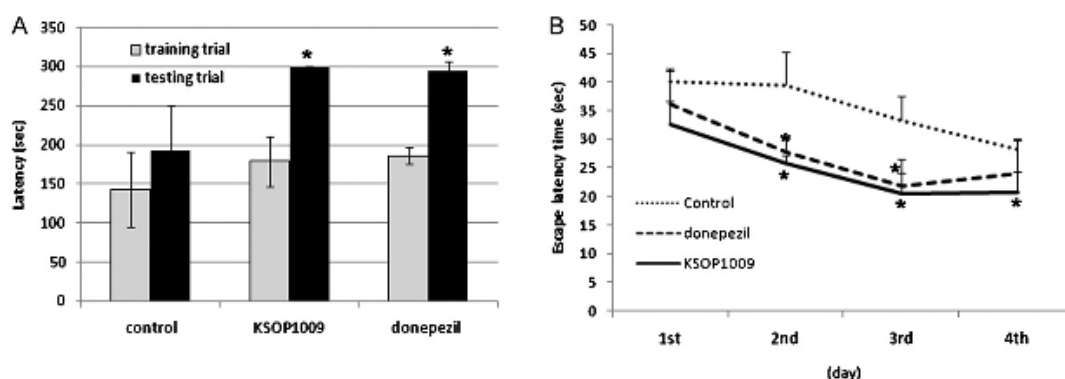
Anticancer effects

[Phenolic phytochemicals](#) are a broad class of [nutraceuticals](#) found in plants which have been extensively researched by scientists for their health-promoting potential. One such a compound which has been comprehensively used is [eugenol](#) (4-allyl-2-methoxyphenol), which is the active component on nutmeg and aromatic plants like cloves, basil, cinnamon. Increasing volumes of literature showed eugenol possesses anticancer properties. Molecular mechanism of eugenol-induced apoptosis in melanoma, skin tumors, osteosarcoma, leukemia, gastric and mast cells has been well documented. [Antiproliferative and molecular mechanism of eugenol-induced apoptosis in cancer cells, 2012](#)

Treatment of [Alzheimer's Disease](#)

Intake of KSOP1009 (consisting of a ethanol extract of 8 herbs, including seed of *Myristica fragrans* Houtt.) improved the A β -induced memory impairment and suppressed A β levels and plaque deposition in the brain of Tg-APPswe/PS1dE9 mice as much as that of [donepezil](#) treatment. KSOP1009 prevented the down-regulation of phospho-CREB and increased AKT phosphorylation in the AD-like brains. Moreover, KSOP1009 suppresses A β -induced apoptosis and ROS production in SH-SY5Y cells. KSOP1009 may develop as a therapeutic drug for treatment of AD patients.

[A modified formulation of Chinese traditional medicine improves memory impairment and reduces A \$\beta\$ level in the Tg-APPswe/PS1dE9 mouse model of Alzheimer's disease, 2011](#)



Overdose and toxicity

Mechanism of Toxicity

Structural similarities of myristicin to classical [hallucinogenic compounds](#) (eg, [mescaline](#)) suggest that myristicin may act as a [serotonin receptor](#) agonist and hallucinogenic compound. However, the acute toxicity of myristicin is relatively low. Although myristicin comprises the largest fraction (ie, about 4-8%) of compounds in the aromatic fraction of nutmeg, human studies with myristicin have not duplicated the effects of nutmeg intoxication on the central nervous system. In rodent studies, myristicin and elemicin impair coordination and decreased motor activity. Saffrole, eugenol, and isoeugenol do not have similar behavioral effects in these animal studies. However, there is a dose response mechanism with symptoms which go from mild obtundation (with 18 g dose) to tachycardia, palpitations, drowsiness, nausea, dry mouth, anxiety, restlessness, and agitation (with a 37g dose).

[Nutmeg \(*Myristica fragrans* Houtt.\), 2009](#)

Therefore, the data and informations that are available indicate that at the current level of intake, food flavoring use of myristic acid does not pose a health risk to humans. In conclusion, based on the data presented above, consumption of myristic acid as an added food-flavoring ingredient is safe at present use levels.

[Safety assessment of myristic acid as a food ingredient, 2007](#)

Conclusion

Although the earliest evidence of the use of spice by humans was around 5,000 B.C., their biological activities have been investigated last several decades. Today, considerable data regarding the beneficial effect of spice nutraceuticals on prevention and treatment of diseases in preclinical settings are available. Spices should be viewed as a part of an everyday lifestyle rather than as pharmaceuticals. In addition, although over 100 pilot clinical trials have been done with spices and their components in human subjects, more evidence is still needed to demonstrate their potential in prevention and treatment of chronic inflammatory disease, including cancer. The possibility for spice-derived nutraceuticals to exhibit multiple effects and for ability to counteract treatment regimens exists, just as the potential of a once-unknown world was first shown by the explorers Christopher Columbus and Vasco da Gama in their search for valuable spices several centuries before.

[Cancer cell signaling pathways targeted by spice-derived nutraceuticals. 2012](#)

Pathways

[AMPK \(AMP-activated protein kinase\)](#), [Acetylcholine](#), [Akt/PKB](#), [CREBH](#), [Transforming Growth Factor \(TGF\)](#)

MeSH

[Antioxidants](#), [Dental Caries](#), [Alzheimer Disease](#), [Epilepsy](#), [GABA Agonists](#), [Acetylcholine](#), [Anti-Inflammatory Agents](#), [Transforming Growth Factor beta](#), [Food Additives](#)

Attachments

file	user	date
Antiepileptic_effects_of_X1000.jpg	Andrea.demeco	16/02/2013
CholinergicFigure.gif	Andrea.demeco	16/02/2013
Eugenol_acsv.png	Andrea.demeco	16/02/2013
KSOP1009.png	Andrea.demeco	16/02/2013
Macelignan.png	Andrea.demeco	16/02/2013
macelignan_effect_on_dental_caries.jpg	Andrea.demeco	16/02/2013



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