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MYRISTICA FRAGRANS HOUTT: AN OVERVIEW OF BIOLOGICAL CHARACTERISTICS AND APPLICATIONS

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ABSTRACT

The evergreen tree *Myristica fragrans (Houtt.)* is indigenous to Indonesia's Maluku Islands. The kernel of M. fragrans is widely used to cure a variety of illnesses in Indian traditional medicine. Numerous investigations endeavor to gather and analyze the therapeutic value of aqueous and different chemical extracts of *Myristica fragrans (Houtt.)*. Nutmeg essential oil's pharmacological potential has not, thus, been examined from a phytochemical and pharmacological perspective. Thus, the goal of this study was to offer relevant information on the chemical makeup of plant essential oils and the potential therapeutic benefits of *Myristica fragrans* essential oil.[1] Worldwide, MFEO of leaves, mace, kernels, and seeds was utilized as a possible Ayurvedic scent and medicine. Worldwide, MFEO of leaves, mace, kernels, and seeds was utilized as a possible Ayurvedic scent and medicine.[2] MFEO was extracted using a variety of techniques, and the oil yield in the leaf, mace, seed, and kernel was 0.7-3.2, 8.1-10.3, 0.3-12.5 and 6.2–7.6%. Myristicin, caryophyllene, β-myrcene, α-pinene, sabinene, and eugenol were the main chemical components of MFEO.[3] The anti-inflammatory, anti-cancer, anti-malarial, anticonvulsant, hepatoprotective, antiparasitic, nematocidal, antioxidant, and antibacterial properties of MFEO have been validated by clinical and experimental studies. Myristicin, caryophyllene, β-myrcene, α-pinene, sabinene, and eugenol were the main chemical components of MFEO.[4] The anti-inflammatory, anti-cancer, anti-malarial, anticonvulsant, hepatoprotective, nematocidal, antioxidant, and antibacterial properties of MFEO have been validated by clinical and experimental studies. This is the initial attempt to gather information on MFEO's oil output, composition, and biological activity. To comprehend the mode of action of MEFO and its bioactive components, more scientific research will be needed in the future.[5]

KEYWORDS: Nutmeg, *Myristica fragrans*, essential oil, Indian traditional medicine.

INTRODUCTION

The *Myristica fragrans*, or nutmeg, tree is a medium-sized, evergreen, aromatic member of the Myristicaceae familyIt can be found in North Australia, Southeast Asia, India, and the Pacific islands. The Banda islands of the moluccas in east indonesia are home to the nutmeg tree.[6] Mace, the fleshy aril of the nutmeg seed, is used as a spice. There is 4% myristicin in it. Since its usage as a fumigant and condiment in the 12th century, nutmeg has gained recognition in Europe. Tobacco, toothpaste, and perfumes all employ nutmeg butter, a fat made from the seed. It is used medicinally to cure rheumatism and aid with digestion. Additionally, *Myristica fragrans* seed is used to treat mouth sores, sleeplessness, and diarrhea. Malabaricon C, which is derived from the plant *Myristica fragrans*, has been shown to exhibit inhibitory effect against a variety of aerobic and anaerobic microbes.[7] Oil extracted from nutmeg seeds dramatically decreased the bacterial extracellular protein listeriolysin O, which is necessary for Listeria monocytogenes to successfully infect a host. Other from slight sedation, there were no psychedelic or hallucinatory effects. Myristicin is the primary aromatic ingredient in the volatile oil of nutmeg.[8] Nutmeg is still used as a spice today. Nutmeg (*Myristica fragrans*) is still used in many forms as stomachics, hypnotics, aphrodisiacs, analgesics, digestive aids, and amenorrheal agents. Highlighting the many pharmacological characteristics of *Myristica fragrans* is the aim of this review. Due mostly to myristicin oil and elemicin, which can induce cardiac arrest, vomiting, nausea, agitation, and hallucinations, high doses of nutmeg seeds have been found to be harmful.[9] These effects are not seen at typical low dosages, though, and are linked to the misuse of the spice. Nutmeg seeds' safety and effectiveness as a medicinal agent are contradicted in the literature currently under publication, which emphasizes the need for more research into their pharmacological action. Significant medicinal potential exists for nutmeg seeds, especially in the creation of new medications.[10] Notwithstanding its encouraging therapeutic potential, there are still some gaps that must be addressed by examining the most recent research on nutmeg's mode of action. Because nutmeg seed contains active chemicals and metabolites such myristicin, safrole, and elemicin, it has remarkable pharmacokinetic properties.[11] But a better grasp of nutmeg's pharmacokinetics and how its active ingredients interact with various bodily systems can close the knowledge gap and provide fresh perspectives on creating safe and efficient nutmeg-based medications. Furthermore, nutmeg's excretion and metabolism mechanisms, whether in vitro or in vivo, may open the door for future use in contemporary medications. Therefore, the purpose of this review is to thoroughly assess the body of research, pinpoint any knowledge gaps, and provide insight into the possible application of nutmeg as a supplemental or alternative medicine for a range of illnesses.[12] The impact of nutmeg seeds and their medicinal qualities such as their chemical makeup, antioxidant, antibacterial, anticancer, antiangiogenic, and use in the treatment of chronic illnesses were thoroughly examined. To comprehend its possible therapeutic approach, further information will be provided on nutmeg's bioavailability, pharmacokinetics, and current clinical trial applications. In general, nutmeg seed's medicinal potential can be unlocked, opening the door for its use in a variety of fields that will have a big influence on people's health and businesses.[13] Furthermore, the results of this research address a possible rise in interest in natural remedies, which may provide fresh perspectives on novel medicinal innovations for many medical ailments. The food, pharmaceutical, and nutraceutical sectors may benefit from this kind of innovation, which might result in the development of novel medications and goods derived from nutmeg.

Morphological characteristics

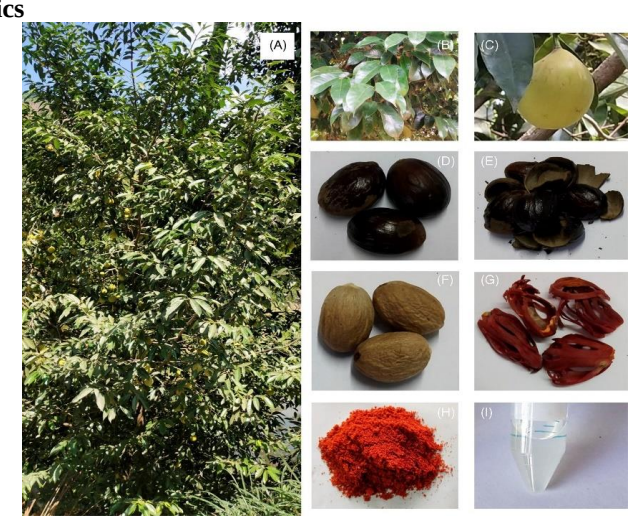

Figure 1: Morphological identification of *Myristica fragrans houtt.*

(a)Young tree; (b) Fresh plant leaves; (c) fruits; (d) dry seeds; (e) rind; (f) kernel(nutmeg), (g) mace(aril); (h) mace powder; (i) essential oil(mace)

Taxonomy

- Kingdom: Plantae
- Class: Eudicots
- Phylum: Angiosperms
- Family: Myristicaceae
- Order: Magnoliales
- Species: M. fragrans
- Genus: Myristica

Biological source

1. Scientific Name: *Myristica fragrans houtt*.
2. Common Name: Nutmeg
3. Family: Myristicaceae
4. Plant part used: Seed (Nutmeg), Aril (mace), Fruit pericarp (Flesh), Essential oil.
5. Plant type: A tropical ever green tree
6. Origin: Originating from Indonesia's Banda Island, also referred to as "spice land,"
7. Cultivation Areas: extensively grown in tropical areas of Southeast Asia, India, and Sri Lanka.

Morphological Features

Tree

- Height: Grows up to 33–66 feet (10–20 meters) in height.
- Canopy: Sprawling and dense, offering shade.

Leaves

- Type: Simple, evergreen, alternate.
- Shape: Ovalate-lanceolate with entire margins.

- Size: 2-7 cm wide and 5-15 cm long.
- Surface: Upper side is dark green and glossy; underside is pale.

Flowers

- Type: Small, dioecious, and unisexual.
- Color: Pale yellow.
- Arrangement: Axillary or terminal clusters.
- Male flowers: Contains stamens fused into coloum.
- Female Flowers: Contain a single ovary with a short style and stigma.

Fruits

- Type: A dehiscent drupe
- Size: 3-6 cm in length, resembling an apricot.
- Pericarp: Fleshly and splits upon ripening.
- Seed: The hard, brown seed (nutmeg) is enclosed in a red, lacy aril (mace)

Applications *Myristica fragrans houtt*

Seed (Nutmeg): Nutmeg seeds are widely used in cuisine as a spice to enhance the flavor of baked goods, curries, desserts, and beverages. Because of its mild sedative effects, it also has medical qualities that help with digestion, reduce bloating, and promote natural sleep. For pain in the muscles and joints, nutmeg oil is administered topically. Nutmeg powder is used in skincare products and exfoliating scrubs in the cosmetics sector, and its essential oil is utilized in fragrance and as a food and beverage preservative.

Mace (Aril): A prized spice, mace (Aril) is used in meat recipes, soups, sauces, and spice blends. Mace is used medicinally as a carminative to relieve gas and indigestion and to reduce inflammation. In the industrial setting, it contributes a distinct flavor profile to liqueurs like Vermouth and Chartreuse.

Essential oil: The mace and nutmeg fragrance oil is used in aromatherapy for a number of purposes, including promoting relaxation and reducing tension. It is used medicinally for its analgesic properties in treating muscle soreness and rheumatism. Because of its aromatic properties, it is also a crucial component of soaps, lotions, and fragrances.

Leaves: Traditional medicine uses *Myristica fragrans* leaves to cure infections and fevers. To extract essential oils for perfumery, they are occasionally treated. Although it is used less frequently, the bark is utilized in traditional medicine to treat digestive and respiratory conditions.

CHEMICAL CONSTITUENTS

In plants, the term "chemical composition" describes the range of chemical compounds that contribute to a plant's structure and function. Along with inorganic components like minerals, this also comprises organic substances like proteins, lipids, carbohydrates, and essential oils. Secondary metabolites including alkaloids, flavonoids, terpenes, and phenolic compounds are also included in the chemical composition; these substances are involved in plant defense, growth here some of the phytochemical present in *Myristica fragrans houtt*.

Table 1: Various Phytochemicals present in *Myristica fragrans houtt.*

S. No.	Phytochemical Name	Plant Part	Molecular Formula	Molecular Weight (g/mol)
1	Myristicin	Seed, Essential Oil	C11H12O3	192.21
2	Safrole	Seed, Essential Oil	C10H10O2	162.19
3	Eugenol	Aril, Essential Oil	C10H12O2	164.20
4	Elemicin	Seed, Essential Oil	C12H16O3	208.25
5	Camphene	Essential Oil	C10H16	136.23
6	Limonene	Essential Oil	C10H16	136.23
7	Linalool	Essential Oil	C10H18O	154.25
8	Alpha-Pinene	Essential Oil	C10H16	136.23
9	Beta-Pinene	Essential Oil	C10H16	136.23
10	Myristic Acid	Seed Oil	C14H28O2	228.37
11	Palmitic Acid	Seed Oil	C16H32O2	256.43
12	Oleic Acid	Seed Oil	C18H34O2	282.46
13	Isoeugenol	Essential Oil	C10H12O2	164.20
14	Terpinolene	Essential Oil	C10H16	136.23
15	Sabinene	Essential Oil	C10H16	136.23
16	Caryophyllene	Essential Oil	C15H24	204.35
17	Guaiene	Essential Oil	C15H24	204.35
18	Nerolidol	Essential Oil	C15H26O	222.37
19	Geraniol	Essential Oil	C10H18O	154.25
20	Vanillin	Seed	C8H8O3	152.15
21	Quercetin	Seed, Bark	C15H10O7	302.24
22	Kaempferol	Seed, Bark	C15H10O6	286.23
23	Tannins	Bark	Complex Polyphenols	Varies
24	Saponins	Bark, Leaves	Complex Glycosides	Varies
25	Flavonoids	Bark, Leaves	Various Polyphenols	Varies

MEDICINAL USES

Properties of *Myristica fragrans*

Nutmeg, or *Myristica fragrans*, has several medicinal benefits, such as anti-inflammatory and antioxidant qualities that shield cells from harm. It relieves pain from ailments like joint pain and headaches by acting as an analgesic. Additionally, the spice possesses antibacterial qualities that aid in the battle against illnesses. Nutmeg is a sedative that enhances sleep quality and encourages relaxation. It facilitates digestion, reducing bloating and indigestion. Furthermore, nutmeg contains chemicals that may help stop the growth of cancer cells, which may have anticancer properties.

Table 2: Medicinal Properties of *Myristica fragrans.*

S. No.	Medicinal Benefit	Biological Activity	Parts Used	Extraction Method	Solvent Used
1	Antioxidant	Neutralizes free radicals, preventing oxidative stress	Seed, Aril, Essential Oil	Steam distillation	Water, Alcohol
2	Anti-inflammatory	Reduces inflammation, helps in conditions like arthritis	Seed, Aril	Steam distillation, Cold pressing	Alcohol, Hexane
3	Analgesic	Provides pain relief, reduces headaches and muscle pain	Seed, Essential Oil	Steam distillation	Ethanol, Hexane
4	Antimicrobial	Inhibits growth of bacteria and fungi, boosts immunity	Seed, Aril, Essential Oil	Steam distillation, Solvent extraction	Methanol, Ethanol
5	Sedative	Promotes relaxation, reduces anxiety and improves sleep	Seed, Essential Oil	Steam distillation, Cold pressing	Ethanol, Hexane
6	Digestive Aid	Enhances digestion, alleviates indigestion and bloating	Seed, Aril	Cold pressing, Solvent extraction	Ethanol, Water
7	Anticancer	May inhibit cancer cell growth, has potential anti-cancer properties	Seed, Essential Oil	Steam distillation, Solvent extraction	Methanol, Ethanol

Antioxidant

Polyphenolic components like eugenol, myristicin, and quercetin are the main source of *Myristica fragrans*' (nutmeg) antioxidant qualities. These compounds scavenge free radicals, which are unstable molecules that cause oxidative stress and damage to cells and tissues. Free radicals are linked to chronic diseases like diabetes, heart disease, and cancer. Nutmeg helps prevent cellular aging, DNA damage, and inflammatory reactions that may accelerate the course of disease by scavenging free radicals. According to studies, nutmeg can increase the body's antioxidant enzyme activity, which helps to maintain a healthy oxidative equilibrium. Nutmeg is therefore advantageous for preserving general health and maybe postponing the onset of age-related illnesses.

Anti-inflammatory

The bioactive components in nutmeg, such as myristicin, eugenol, and elemicin, are thought to have anti-inflammatory properties because they prevent the body from producing inflammatory mediators. The cyclooxygenase-2 (COX-2) and lipoxygenase (LOX) enzymes, which produce pro-inflammatory prostaglandins and leukotrienes, are inhibited by these substances. Chronic inflammation is a major contributing factor to several illnesses, including inflammatory bowel diseases, osteoarthritis, and rheumatoid arthritis. The anti-inflammatory qualities of nutmeg can help lessen redness, discomfort, and swelling in afflicted areas, making it a useful natural treatment for inflammation management and joint function enhancement. By reducing inflammatory reactions, it also enhances general immunological health.

Analgesic

The well-established analgesic (pain-relieving) properties of nutmeg are ascribed to its constituents, specifically myristicin and eugenol. These substances work by preventing the brain and nervous system's pain receptors from being blocked and by preventing the production of chemicals that cause pain. It has been shown that nutmeg essential oils can reduce sensitivity to pain and aid in the relief of chronic pain disorders such headaches, joint pain, and muscle soreness. Because of its capacity to relieve localized pain, it is frequently found in topical oils and balms. It has also been utilized in massage therapy to ease discomfort and stress. Because of its modest analgesic properties, nutmeg can be used as a supplement or as an alternative to over-the-counter pain relievers without the potential negative effects of prescription pharmaceuticals.

Antimicrobial

The main source of nutmeg's antibacterial qualities are its volatile oils, which have been demonstrated to have fungicidal and bactericidal effects. These oils include safrole, myristicin, and eugenol. These substances prevent the growth of dangerous microbes such as yeasts, fungus, and bacteria. For example, research has shown that nutmeg oil can successfully fight off fungal diseases like Candida albicans and harmful bacteria like Escherichia coli and Staphylococcus aureus. Because of its antibacterial qualities, nutmeg is useful for strengthening the immune system and avoiding infections. Because of its capacity to lessen oral bacteria, stop foul breath, and cure gingivitis, it has also been included in oral care products. Additionally, by inhibiting the growth of bacteria in small cuts and abrasions, nutmeg's antibacterial properties aid in the promotion of wound healing.

Sedative

Traditional medicine has long recognized nutmeg's sedative properties, particularly its capacity to quiet the mind and encourage deeper sleep. By interacting with the brain and spinal cord, the bioactive substances myristicin and elemicin, which are present in nutmeg, help people feel relaxed and at ease. Nutmeg increases the production of serotonin

hormone a neurotransmitter that controls mood, relaxation, and sleep, which helps alleviate signs of anxiety, stress, and sleeplessness. Due to its calming qualities, nutmeg is a useful natural treatment for people who suffer from anxiety disorders or insomnia. For soothing effects, it has been utilized in herbal formulations. It is also frequently added to warm liquids, like as milk or tea, to encourage relaxation before bed. Nutmeg enhances general mental health and wellbeing by lowering anxiety and promoting better sleep.

Digestive Aid

Due to its potential to relieve digestive discomforts including gas, bloating, and indigestion, for many years, nutmeg has been utilized as a digestive aid. The substances in nutmeg promote the synthesis of bile and digestive enzymes, which improve nutritional absorption and aid in the more effective breakdown of food. Additionally, nutmeg possesses carminative qualities, which prevent gas from forming in the intestinal tract and ease bloating. It also calms the lining of the stomach, avoiding acid reflux and facilitating easy digestion. The gentle antispasmodic properties of nutmeg aid to calm the gastrointestinal tract's muscles, which can lessen discomfort and cramping. Traditional medicine frequently uses it to treat digestive disorders like dyspepsia and nausea.

Anticancer

Nutmeg's abundance of bioactive substances, including myristicin, eugenol, and flavonoids, is drawing attention to its anticancer qualities. In lab experiments, these substances have demonstrated the ability to stop the development of malignant cells and stop tumors from spreading. In particular, myristicin has been demonstrated to induce programmed cell death, or apoptosis, in cancer cells, while preserving healthy cells, indicating that it may have use as a chemopreventive drug. Nutmeg's capacity to alter important signaling pathways implicated in inflammation, metastasis, and cancer cell proliferation may possibly contribute to its anticancer properties. Additionally, the antioxidant qualities of nutmeg aid in preventing DNA damage, which can result in cancer.

PHARMACOKINETICS

Myristica fragrans (nutmeg) pharmacokinetics is the study of how its bioactive components are absorbed, distributed, metabolized, and eliminated after ingestion. The following information summarizes the general pharmacokinetic behavior of nutmeg based on its main ingredients, despite the fact that detailed pharmacokinetic data on the spice is scarce:

Absorption

Mostly found in nutmeg essential oil, bioactive substances like myristicin, elemicin, and safrole are lipophilic and absorbed in the digestive system. The solubility of these chemicals in dietary fats and their interaction with gastrointestinal enzymes determine how well they are absorbed. Due to their weak solubility, certain flavonoids and polyphenols found in nutmeg may have a limited bioavailability.

Distribution

The active ingredients and volatile oils in nutmeg are transported to different tissues via the circulation after absorption. Myristicin is one example of a lipophilic substance that effectively crosses lipid membranes to reach the liver, brain, and other fatty tissues. Since myristicin and related chemicals affect the central nervous system, this distribution explains why nutmeg has a sedative and psychedelic effect.

Metabolism

The cytochrome P450 enzyme system biotransforms the active ingredients of nutmeg in the liver. Some of the compounds produced by the metabolism of myristicin and safrole show bioactivity. For instance, 5-allyl-1-methoxy-2,3-dihydroxybenzene is produced during the metabolism of myristicin, which could be a factor in its pharmacological actions. Longer half-lives and sustained bodily activity are possible for some metabolites.

Excretion

A portion of the metabolites of nutmeg compounds are eliminated through bile into feces, while the majority are eliminated by the kidneys in the urine. Dosage, metabolic rate, and personal health are some of the variables that affect the precise elimination half-life of nutmeg's active ingredients.

Bioavailability

The bioactive components in nutmeg have different levels of bioavailability. Myristicin and other lipophilic components are more easily absorbed than hydrophilic ones. Nevertheless, the liver's first-pass metabolism may lessen these substances' total systemic availability. Absorption may be improved by formulation techniques like adding fat or emulsifiers.

Important Points to Remember

- Myristicin, one of the bioactive chemicals found in nutmeg, interacts with the central nervous system to produce psychedelic effects at high dosages.
- Because some chemicals (like safrole) are converted into potentially hazardous intermediates, prolonged or excessive use may result in toxicity.
- Pharmacokinetic characteristics, such as half-life, maximum concentration (Cmax), and time to achieve maximum concentration (Tmax), are influenced by human variability, including metabolic enzyme activity and health status.

PHARMACODYNAMICS

Table 3: Pharmacodynamics of *Myristica fragrans.*

Biological Activity	Mechanism of Action	Key Compounds	Effects
Antioxidant	Scavenges free radicals, enhances antioxidant enzymes like superoxide dismutase and catalase.	Myristicin, quercetin, eugenol	Reduces oxidative stress and protects cells from damage.
Anti-inflammatory	Inhibits COX-2 and LOX enzymes, reducing the synthesis of pro-inflammatory mediators.	Myristicin, elemicin, eugenol	Decreases inflammation and swelling.
Analgesic	Modulates pain signaling pathways by blocking pain receptors and reducing inflammatory cytokines.	Eugenol, myristicin	Relieves headaches, muscle aches, and joint pain.
Antimicrobial	Disrupts microbial membranes and inhibits the growth of bacteria and fungi.	Eugenol, safrole, myristicin	Prevents infections and supports immune defense.
Sedative	Modulates neurotransmitters such as serotonin to induce relaxation and calmness.	Myristicin, elemicin	Promotes relaxation and improves sleep quality.
Digestive Aid	Stimulates digestive enzyme secretion, reduces gastrointestinal spasms.	Terpenoids, eugenol	Alleviates bloating, indigestion, and gas.
Anticancer	Induces apoptosis in cancer cells, inhibits cell proliferation, and modulates signaling pathways.	Myristicin, lignans	Potentially reduces tumor growth and spread.

Future Prospects of *Myristica fragrans*

Advanced Pharmacological studies

The medicinal potential of nutmeg's bioactive components can be better understood with more thorough research on its pharmacological activity. For example, investigating its anti-inflammatory and antioxidant pathways may result in the creation of new medications.

Clinical trails

Myristica fragrans has shown promise in preclinical research, but further clinical trials are required to verify its safety and effectiveness in people. Research into how it affects the treatment of long-term illnesses like diabetes, arthritis, and neurodegenerative disorders may be very helpful.

Formulation development

Attempts to increase the bioavailability of nutmeg's active ingredients by novel formulations (such as emulsions or nanoencapsulation) may increase its medicinal efficacy and get around pharmacokinetic restrictions.

Synergistic Effects

Studies on the combination of nutmeg with pharmaceutical medications or other medicinal plants may show synergistic effects that improve therapeutic results and lower dosage requirements.

Toxicology Studies

In order to determine acceptable dosages, thorough toxicology studies are essential, particularly in light of the possible toxicity of substances like myristicin and safrole at greater quantities.

Sustainable cultivation & Extraction

The sustained use of nutmeg without diminishing natural resources might be ensured by concentrating on environmentally friendly farming and effective extraction methods. Utilizing cutting-edge biotechnology techniques could help improve quality and yield.

Novel Applications

Its potential use in beauty products, anti-aging products, and as a natural preservation agent in the food industry might all be expanded by research into other areas.

Genomic and Metabolomic Studies

Myristica fragrans genomic and metabolomic profiling may reveal pathways for the creation of its active chemicals, supporting the plant's genetic improvement and biotechnological production.

CONCLUSION

There are several medical uses for extracts from different fractions of *Myristica fragrans*. Among the many medicinal properties of nutmeg's phytochemical constituents include antimicrobial, anticancer, antioxidant, antifungal, antidiabetic, antidepressant, hepatoprotective, anti-obesity, and anti-inflammatory properties, cardioprotective, and many more, are the subject of most research. Myristicin is one of the most potent substances responsible for numerous health advantages, according to the literature. More work is needed to update the traditional applications of nutmeg, as well as its therapeutic properties and mode of action. More research is required to assess this plant's effectiveness on

the human body because it has been extensively studied in rat models but has very little clinical evidence. Nonetheless, nutmeg contains a wealth of medicinally active ingredients that contribute to its various beneficial properties. As a result, this plant encourages scientists to learn more about its special medicinal qualities. This study demonstrates M. fragrans' potential for use in therapeutic drugs and offers a theoretical framework for further investigation into the pharmacological characteristics of nutmeg.

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