



PHYTOPHARMACOLOGICAL REVIEW ON *MYRISTICA FRAGRANS* HOUTT (JAIPHAL)

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ABSTRACT:

Myristica fragrans Houtt, commonly known as nutmeg, is a very common spice, belonging to the family Myristicaceae, is the source of two spices, nutmeg (Jaiphal) and mace (Javitri), used around the world. It is described in almost each medicine system such as Ayurveda, Siddha, Unani and folk system. It has wide range of fixed oils and essential oils in it for example terpenes and phenylpropenes, sabinene, caryophyllene, β -myrcene, and α -pinene, myristicin, safrole, myristic acid, trimyristicin, eugenol, elimicin and meso-dihydroguaiaretic acid. *Myristica fragrans* Houtt is well considered medicinal plant for its extraordinary properties like aphrodisiac, hepatoprotective, antioxidant, antimicrobial, anti-inflammatory, anticancer, antimalarial, anticonvulsant, antiparasitic, insecticidal, and nematocidal, anti-diabetic, digestive, carminative, appetizer, exhilarant and mood elevator, antitussive, antiemetic, demulcent, nervine, cardio, and uterine tonic etc. The review aim is to provide data/information related to medicinal herbal plant called *Myristica fragrans* such as its phytomedicinal value in traditional medicine systems like Ayurveda and folk system, its therapeutic uses and associated toxicity.

Keywords: Jaiphal, Aphrodisiac, *Myristica fragrans*, nutmeg or mace, Myristicaceae.

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INTRODUCTION

Nature is served as primary source of numerous medicines for thousands of years [1,2]. Medicinal plants/herbs hold a great significant value. Medicinal plants/herbs possess phytochemical constituents that are medically important and are used for developing new drugs [3,4]. Kingdom plantae is also entitled with “the treasure house of many important drugs”. The use of plants for health benefits and other purposes is a very common tradition, which has been in practice since ancient times^[5]. In the old times plants were the only source of most of the medicinal preparations^[6]. Medicinal products/products derived from the plants are often named as herbal drugs, botanical drugs, botanicals, phytomedicines, traditional medicines, herbal medicines, traditional Chinese medicines (TCMs), traditional herbal medicinal products, natural health products, or plant food supplements. These herbal drugs have several advantages over the synthetic drugs such as their easy availability, safety, low cost, efficiency, negligible side effects^[7,8,9]. Most of the modern drugs in the present times have derived from plant sources. As per the data resources, in industrialized countries tropical plants are the direct or indirect sources where quarter of the medicines have been derived from^[10,11,12]. The practice of using plants for

the treatment of several human ailments is as old as origin of mankind^[13,14]. As per the WHO reports on the use of medicinal plants, it has observed that 80% of the total population in developed countries of the world depends primarily on herbal medicines to maintain their overall health and fulfill their day to day requirements^[15,16,17,18]. India is one of the countries, which are categorized under world biodiversity centers. India has a very rich history of utilizing medicinal plants. It is a home to more than 45000 various species of plant and this is the reason why India is called as the Botanical garden of the world^[19,20]. Many traditional systems of medicine such as Ayurveda, Siddha, Unani Folk system and as well as allopathy use medicinal plants in diseases treating practices^[21]. Ayurveda is the most ancient system of medicine known in India which uses almost 600 different medicinal herbs/plants and their parts such as leaves, roots, fruits and stem and their formulations in treating variety of diseases^[22,23]. Herbal medicines are used in almost each and every corner of the world. One such valuable medicinal plant is *M.fragrans* Houtt . It is a well-known spice in the world, which is commonly called as Jaiphal and Javitri in India, belonging Myristicaceae family, produces two spices named as mace and nutmeg respectively. The name ‘Myristica’ is derived

from the Greek word 'Myron', a sweet liquid distilled from the plant ^[24]. *M. fragrans* is one of the aromatic plants that are endowed with alluring properties of fragrance and flavours and produces odoriferous secondary metabolites in their fruits. (N.Parimala and S.Amerjothy 2013). The seed kernel inside the fruit is termed as nutmeg whereas the red lacy covering (aril) present on the kernel is called as mace. Dried kernel is the most important part of *M. fragrans* in terms of pharmacological activity ^[25,26]. The name nutmeg has come from a Latin word *nux muscatus*, which means "musky nut". It is believed that Portuguese discovered nutmeg in 1512. Arabs introduced nutmeg to Europe in the middle ages through the Venetians. It was used as a remedy to plague by Italians whereas Indians and Egyptians used it to treat problems related to intestine and embalming. In 19th century, its effect on Central Nervous System was observed for the very first time. Nutmeg was in the list of the expensive spices of the world in the earlier times. It was known as the hot-food ^[27]. It is commonly used as spice, which is found in almost every kitchen to add flavor in many dishes especially in North India where it is used as an ingredient of garam masala. Its oil is used in jam, chutney and juices, soft drinks, tea and also mixed with milk and alcohol ^[28,29,30]. It is used in bakery and

confectionary products, pudding, meats, sausages, sauces ^[31]. In traditional systems of medicine such as Ayurveda and folk system this plant is used in treating variety of human ailments due to the presence of different kind of phytochemical constituents in it such as alkyl benzene derivatives (myristicin, elemicin, safrole etc.), terpenes, alpha-pinene, beta-pinene, myristic acid and triacylglycerols like trimyristin, phenolic compounds, flavonoids, tocopherol, ascorbic acid, essential oils and many more ^[32,33]. Its essential oil is useful against sprains, muscle pulls etc. ^[34]. The seeds as well as fruits both of these plant parts are used in traditional practices for the treating conditions like dysentery, sexual disorders, weakness, and darkness of complexion ^[35]. The most common uses of *M. fragrans* is used as a carminative, anti-inflammatory, analgesic, diuretic, anti-pyretic, hypolipidemic, aphrodisiac, antiulcerogenic, anti-oxidant, hypnotic, hallucinogenic, antispasmodic, and as a stimulant agent. It enhances the digestion. It is used as remedy for nausea, stomachache, headache, vomiting, diarrhoea associated with cholera. It is helpful in treating the problems related to spleen, liver, and eyes. It significantly enhances the blood circulation, boosts up the brain functioning ^[36,37,38,39].

MATERIALS AND METHODS

Comprehensive review of the literature on *M. fragrans*, chemical composition, pharmacology, and biological studies was conducted, with data compiled using a variety of search engines and publishing houses, including PubMed, Google Scholar, Frontiers, and NCBI. Other literature sources, such as Wikipedia, ethnobotanical publications, and various online domains, were also examined to obtain information. *Myristica fragrans*, nutmeg, mace, therapeutic uses, phytochemicals, pharmacological activities, botany and numerous synonyms were also utilized in the literature search.

Table 1: Taxonomy of *Myristica Fragrans*

Taxonomic Rank	Taxon
Kingdom	Plantae
Subkingdom	Viridiplantae
Division	Tracheophyta
Subdivision	Spermatophytina
Class	Magnoliopsida
Order	Magnoliales
Family	Myristicaceae
Genus	Myristica
Species	fragrans

Vernacular Names of *Myristica Fragrans*

English –Nutmeg; Sanskrit -Jati-phalam, malathi-phalam; Hindi- Jaiphal, malti phal ;Assamese- Jayphal, kanivish, jaiphal ;Bengali- Jayphala, jaepatri, jaepatri ;Burma- Zadi-phu;

Kannada- Jadikai, jaykar, jajakai;Kashmiri - Jafal, zafal;Malayalam- Jatika, bush; Marathi- Jaiphal;Oriya- Jaipholo ;Punjabi- Jaiphal; Tamil- Sathkhai, jathikkai, jadikkay, jadhikai, jadhikkai, jatikkai;Telugu- Jajikaya ,Gujarati- Jaiphala, javantri;Urdu- Jauzbuwa, jaiphal ;Arabic- Jowz buwwa, jouza atteeb, josat attib ;Sindhi- Jafar, jadika;Chinese- Dauh kau syuh, yuhk dauh kau ;Dutch- Nootmuskaat, muskaatnoot; French- Muscadier, musque;German -Achter muscatnussbaum Hebrew Egos muskat, egoz musqat ;Russian- Opex muskatnyj orekh. ;Armenian - Meshgengouz, Mshkenkoyz, Mekenkouz;Greek- Moschokarido ;Indonesian- Pala ;Italian- Noce moscata ;Portuguese - Nozmoscada ;Romanian- Nucşoară ;Turkish- Hindistancevizi;Uzbek Musqat;Persian- Djus hendi, jous hendi, jozbaweh ;Unani- Fuqlaj, moschokarido ;Spanish -Moscada, nuez moscada

Demography

For cultivation, a hot humid climate without dry season is key requirement but usually grows in warmer environment. It also grows well in the areas with sandy loam, clay loam and red laterite soils. It is broadly cultivated in China, Indonesia, Taiwan, Malaysia, India, Grenada, South America and Sri Lanka [40]. The actual production of nutmeg is difficult to obtained, World production of nutmeg on an

average is approximated between the ranges of 10,000 to 12,000 tons per year but annual world requirement is approximately 9,000 tons [41]. Grenada and Indonesia govern production and transport of nutmeg by sharing 20% and 75% of world market respectively [42].

BOTANY, MORPHOLOGY, ECOLOGY

Average nutmeg trees can grow up to 10-20m in height; they can be male or female trees. Nutmeg trees do not give flowers until they are 9 years old and after that, they continue to give flowers for 75 years [43]. Male and female trees have different characteristics. The flowering of female trees can continue upto 7 months and the whole development took

place in 154 days whereas male trees do it throughout the year and they just take 77days for the complete development. The best time for their flowering is from July to October and trees bear 2-3 crops in a year [44]. The tree has strong, delightful and peculiar smell and a strong sharp aromatic flavor. Nutmeg requires a warm and humid tropical climate. Annual daytime temperature requirements are within the range of 22 - 34°C is considered optimum for its growth, but it can also tolerate 12 - 38°C. Nutmeg requires well drained, fertile soil with high content of organic matter. It grows well in soils with pH 6.5-7.5. Its optimum growth has been observed 2000-3500 mm rainfall.

Table 2: Pharmacognosy of *Myristica Fragrans*

S.No.	Plant Part	Features
1.	Leaves	alternate and glabrous, obtuse at base, elliptical, aromatic, acuminate, glossy and dark green above, paler underside and 4-6 inches long
2.	branches	scattered in whorls
3.	Petioles	about 30 cm long
4.	Flowers	dioecious and small auxiliary racemes, waxy and fleshy, bell-shaped and of pale yellow in color
5.	Fruit	round drupe, fleshy and smooth, pendulous and composed of a succulent pericarp- Exocarp is a shiny outer coat, whereas mesocarp is fleshy and is divided into 2 parts nutmeg and mace. Nutmeg is shiny purplish-brown in color and it is 2 to 3 cm long, firm, fleshy surrounded by redbrown veins.

		Mace is 6 to 9 cm long with a longitudinal ridge ^[45]
6.	Seed	fleshy, firm, whitish and transverse by red-brown veins, rich in oil. 2–3 cm long with broad ovoid structure. usually hard and stony which are wrinkled in a longitudinal direction presence of small embryo and ruminant endosperm in the kernel ^[46]

PHYTOCHEMICAL CONSTITUENTS OF *MYRISTICA FRAGRANS*

Myristica fragrans is known for presence of different phytochemical constituents in it such as fixed oils, volatile oils, starch, cellulose, pentosans, resin, and mineral elements and many more ^[47,48,49].

Table 3. Phytochemical Constituents of *Myristica Fragrans*

Chemical constituents	Experiments and Examples	References
Lipids	These are the main fixed oils, which are present in <i>Myristica fragrans</i> for eg. myristic, petroselinic, and palmitic acids. Myristic acid constituent 74.9% of the total lipid content of nutmeg. Trimyristin is the major fixed oil of this plant. Nutmeg butter (expressed/extracted fixed oil) is composed of saturated fats (90%) with 10% unsaturated fats. Other compound of fixed oils are Monoterpene hydrocarbons, oxygenated monoterpenes, sesquiterpenes, alkenes, aromatic ethers, aromatic monoterpenes, organic acids	[50,51,52,53,54].
Essential oils	As per the reports of experimental study conducted by Kapoor et al., by using cleveger and soxhlet apparatus, it was revealed that there is vast variety of essential oils present in this medicinal plant such as α -Thujene, α -Pinene, camphene, sabinene, β -Pinene, myrcene, α -Phellandrene, 3-Carene, α -	[55,56,57]

	<p>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. Marzuki et al., extracted myristicin, elemicin, safrole, (Iso) eugenol by using hydro-distillation method. Sabinene, myristicin, elemicin, α-pinene, β-pinene, limonene, terpinen-4-ol and myristic acid were reported by Morsy et al., by using 1:4 of material and absolute ethanol ratio at room temperature. Myristicin, elemicin, safrole, eugenol and eugenol derivatives are categorized under phenylpropanoids.</p>	
Ligans	<p>The presence of ligans like 8-O-4' neolignans, for example, erythroΔ8'-4,7-dihydroxy-3,3',5'-trimethoxy-8-O-4'neolignan and Δ8'-4-hydroxy-3,3',5'-trimethoxy-8-O-4'-neolignan, have been reported . Sterols As per the report of study conducted by Khatib et al., sitosterol is the predominant sterol found in <i>M. fragrans</i>. Other sterols which are present in this medicinal plant are campesterol, desmosterol, and lanosterol . Others It contains minerals like potassium, phosphorus, and magnesium, calcium, iron. <i>M. fragrans</i> contains fair amount of vitamins like riboflavin, thiamine, niacin. It also contains fibers, carbohydrates and starch, flavonoid like epicatechin, phenyl propanoid ethers.</p>	[58,59,60,61,62,63]

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Traditional and Folk View of *Myristica Fragrans*

Ayurvedic View

Myristica fragrans Houtt is commonly known as “Jatiphala” in Ayurveda. It is a valuable medicinal plant. It is used in many Ayurvedic practices for the treatment of numerous diseases. It significantly works on vitiated *vatta* (air and space components of the body) and *kapha* (earth and water components of the body) [64]. *Myristica fragrans* Houtt is a single herbal remedy which is used to treat “*Vyanga*”

(melasma). Its use against *vyanga* has also been considered by Acharya Bhavamishra [65]. In Ayurveda it is used a stomachic, astringent, heart tonic, carminative, stimulant, aphrodisiac, appetizer, blood purifier, anti-thirst, intestinal trouble [66,67].

Rasapanchak of *Myristica fragrans* as per Ayurveda [68,69]

Veerya- Ushna, Vipak- Katu, Guna- Laghu, Teekshna, Rasa- Tikta , Katu

Properties and uses of *Myristica fragrans* [70,71]

Table 4 Properties and uses of *Myristica fragrans*

<i>Sansthanik karm-wahaya</i>	Its topical applications include its use as an anti-inflammatory and analgesic agent. It is beneficial for skin disorders, acts as an air freshener. It is used in treating cold and headache. It is used against joint inflammation in lepa form. It is useful in removing the foul smell of wound.
<i>Abhyantar-nadi sansthan</i>	It is an analgesic and antiepileptic agent. It is used in treating insomnia, epilepsy and pain.
<i>Paachan sansthan</i>	It is used as an appetizer and anti-helminthic agent. It enhances digestion and increases the liver metabolism. It is used in the treatment of diarrhoea, dysentery, irritable bowel syndrome, constipation, loose motion, cholera. It reduces thirst.
<i>Rakatwah sansthan</i>	It is helpful in treating cardiac problems.
<i>Swasan sansthan</i>	It is used as an anti-mucolytic agent. It is helpful against cold, cough, asthma and hiccups.
<i>Prajannan</i>	It is an aphrodisiac. It is helpful in inducing menstruation and ovulation. It is

<i>sansthan</i>	used in treating erectile dysfunctioning, amenorrhea, dysmenorrhea.
<i>Twacha</i>	It is useful against various skin related disorders
<i>Taapkram</i>	It is used as an anti-pyretic.
<i>Satmikaran</i> (Assimilation)	It is used in treating malnutrition caused by diarrhoea and lose motion.

Due to its extra-ordinary therapeutic properties *M. fragrans* is used in many herbal formulations [72].

Eg-Jatiphaladi churna: It is the most commonly used Ayurvedic polyherbal formulation in which *M. fragrans* is one of the main ingredients. It is used in treatment of diarrhoea, dysmenorrhea and cough, anorexia, nasal congestion, dyspnea, rhinitis. The description

of Jatiphaladi choorna lepa is mentioned in Bhavaprakash [73,74].

Folk View

Myristica fragrans is an important and most commonly used medicinal plant around the world. It is used in many folk cultures for its numerous therapeutic properties and food enhancing properties. It is used as a medicinal drug as well as cooking spice in many cuisines around the world [75-107]

Table no. 5: Uses of *M. fragrans*

S.No.	Places	Uses
1.	Maluku Province of Indonesia and Central and East Java	in <i>M. fragrans</i> is used for the treatment of diarrhea, mouth sores, and insomnia. people use <i>M. fragrans</i> oil to keep their body temperature warm
2.	Enugu State of Nigeria	fruits of <i>M. fragrans</i> are used as anti-parasitic
3.	Kaduna State, Nigeria,	used as a spice use seed powder or decoction of the seeds against diarrhea, rheumatism and also use it as carminative, rubefacient.
4.	South Aceh, Indonesia	used as a spice people use this plant as a remedy for headache
5.	China	used as a spice Chinese people use seed powder in the treatment of dysentery
6.	Tanane Province of Southwest Morocco	people use seed powder in the treatment of problems related to respiratory system, digestive system, skeleton, genital

	Region of Middle Oum Rbia (Morocco)	Seeds are used for the treatment of neurological disorders
7.	Myanmar	use seeds of <i>M. fragrans</i> for treating piles and leucorrhoea
8.	Bhutan	the seeds are used as anticephalagic and adaptogen. They are used to treat vertigo, dysphoria, insomnia, giddiness, headache and heart related problems
9.	North Sumatra, Indonesia	use the fruits of <i>M. fragrans</i> plant as steam-bathing material. They also use this plant in the treatment of rheumatism, syphilis and toothache . use <i>M. fragrans</i> seeds against cancer, virility, child immunity
10.	North Moluccas Indonesia	Fruits and seeds of <i>M. fragrans</i> are used in the preparation of oke sou which is an herbal drink
11.	Brazil	use seeds in tea for soothing effect
12.	Bangladesh	use fruit powder of <i>M. fragrans</i> as a remedy for burning, general weakness, headache and insomnia use seed and fruit of <i>M. fragrans</i> against paralysis, malaria, rheumatoid arthritis, leprosy and colic, also used as aphrodisiac agents
13.	India	used a sedative
14.	Kurumba ,Tamil Nadu	use fruits of <i>M. fragrans</i> to heal mouth wounds and stomach wounds use fruits in pickle form to cure problems related to digestion while the seeds are used along with the breast milk to provide immunity to the infants
15.	Karimnagar district, Telangana	use <i>M. fragrans</i> leaves and fruits to treat nervous disorders
16.	Deogarh district, Odisha,	use <i>M. fragrans</i> fruits in many home remedies
17.	Karnataka	decoction of fruit is administered orally against dysentery use boiled seeds of <i>M. fragrans</i> along with with <i>P. nigrum</i> , <i>P. longum</i> and <i>O. tenuiflorum</i> to treat malaria
18.	Paliyan tribes of Sirumalai Hills of Southern India	people use seeds along with milk to enhance their digestion
19.	Rangamanti district,	medicinal plant is used against fever

20.	Gujrat	use <i>M. fragrans</i> fruit against hemorrhoid
21.	Rajasthan	the fruit of this plant is used in cooking as a spice and to enhance the flavor
22.	Kangra district of Himachal Pradesh	use jaiphal along with ajwain seeds and choti elaichi to treat diarrhoea among infants
23.	Assam	Jaiphal is used in treating dysmenorrhea common home remedy for cough and cold

Pharmacological Actions

Antioxidant activity:

Anti-oxidant Dorman et al., conducted an in-vitro study to check the anti-oxidant potential of many medicinal herbs against synthetic antioxidants like BHA (butylated hydroxyanisole), BHT (butylated hydroxytoluene), alpha tocopherol and pyrogellol. It was found from the study that essential oil extracted from nutmeg is an effective anti-oxidant agent [108].

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. Because of the comparatively simple abstraction of atomic hydrogen from these functional groups, these compounds have high antioxidant activity. The abstraction of atomic hydrogen is done by peroxy radicals that produced under oxidative stress. In another view, role of 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 [109]. The compounds having catechol like structure as in caffeic acid are considered to be good antioxidants as they easily donate electrons or phenolic hydrogen to the acceptors, such as lipid peroxy groups or reactive oxygen species. Calliste et al., (2010) stated that lignan derivatives are considered as a class of compounds that shows the antioxidant potential of nutmeg seeds [110]. After absorption of lignans and their glycosides into the body, they are metabolized to produce biologically active compounds having catechol structures that are responsible of high antioxidant property of nutmeg seeds.

Immuno-modulatory and radio-protective activities -

The lignans present in fresh nutmeg and mace show radio modifying and immune modulatory properties, present in the aqueous extract of fresh nutmeg mace. These properties found in cell free systems and protected PUC18 plasmid against radiation that induced DNA damage. The mammalian splenocytes in response to polyclonal T cell mitogen concanavalin A (Con A) proliferate. This process is inhibited by

these mace lignans which was due to G1 phase of cell cycle and augmentation of apoptosis as presented by increase in pre G1 cells. The increase in activation of induced cell death by mace lignans was depending on the dosage. Splenocytes are protected by mace lignans against radiations. These radiations induced by producing intracellular reactive oxygen species depending on the dose. Mace lignans was not cytotoxic for lymphocytes. On the other hand, in splenocytes the radiation-induced DNA damage is inhibited by decreasing DNA fragmentation [111].

Antimicrobial activity –

Anti-microbial Orabi et al., conducted an experimental study in 1991 to check the antimicrobial potential of mace of *M. fragrans* against *Staphylococcus aureus* and *Candida albicans*. It was revealed that resorcinols malabaricon B [1] and malabaricon C [2] both showed significant anti-microbial potential against *Staphylococcus aureus* and *Candida albicans* [112]. As per the results of study conducted by Hattori et al., dehydro-diisoeugenol and 5-methoxydehydrodiisogenol were found to be effective against *Streptococcus mutans*. They significantly helped in the inhibition of *Streptococcus mutans* growth [113].

The essential oil and different extracts of aromatic plants have shown strong antimicrobial activity against variety of fungi as well as bacteria [114]. Narasimhan et al

(2006) demonstrated the antibacterial activity by preparing chloroform extract of nutmeg against both gram negative and gram positive bacteria. They found myristic acid and trimyristin are the main antibacterial compounds extracted from nutmeg seeds. Researchers isolated three lignans (mesodihydroguaiaretic acid, nectandrin-B and erythroaustrobailignan-6) showing antifungal activity, from the methanolic extract of nutmeg seeds [115]. The development of wheat leaf rust and rice blast was suppressed by these three lignans. Some compounds like carvacrol, γ -cymene, α -pinene, β -pinene, and β caryophyllene are reported to be antimicrobial present in essential oil of nutmeg seeds [116]. Some plant phenolics are also reported for antimicrobial activity.

Antifungal and anti-inflammatory activities-

Antifungal and anti-inflammatory activities of plant essential oil are due to the presence of β -caryophyllene [117]. α -Pinene and β -pinene which are monoterpene hydrocarbons are also antimicrobial agents. They are considered to be involved in membrane disruption [118]. Carvacol is another significant compound for antimicrobial activity. Carvacol works in the same way as the other phenolic compounds, which work through membrane destruction, resulting in an increase in permeability of membrane to potassium ions and protons, proton-motive force disruption and

intracellular ATP pool depletion. γ Cymene (a precursor of carvacrol) could also be an important component. It has been demonstrated that γ cymene works synergistically with carvacrol in membrane enlarging, which results weakening of the membrane while alone shows weak antibacterial activity [119]. It has been proposed that antimicrobial activity is due to the minor and major both compounds; while it is feasible that the major compound controlled by other minor compounds [120].

Anti-inflammatory activity - Several authors reported anti-inflammatory activity of nutmeg as well as its oil [121]. Similar to nonsteroidal anti-inflammatory drugs, pharmacological activities also exhibited by nutmeg oil [122]. But antiinflammatory activity is shown only by petroleum ether extracts. The total extract of nutmeg activated an enzyme that is AMP-activated protein kinase enzyme (potential therapeutic target) for curing the metabolic syndrome including type-2 diabetes and obesity. Seven compounds like tetrahydrofuroguaiacin B, 2,5-bis-aryl- 3,4-dimethyltetrahydrofuranlignans, fragransin C1, saucernetindiol, nectandrin B, verrucosin, galbacin and nectandrin A were isolated from this extract as an active constituents. Some of the isolated compounds produced strong AMPK stimulation in differentiated C2C12 cells, at 5 μ M concentration. Nutmeg and its active components not only used to treat type-2 diabetes and obesity but also for the

development of agents other metabolic disorders [123-125].

Anti-carcinogenic and hepatoprotective activity-

Anti-cancer Prakash et al, studied the anti-cancerous behavior of *Myristica fragrans* in an in-vitro study on human cell lines Colon cell (Colon502713, Colo205), Liver (Hep-2), Lung (A-549), Ovary OVCAR-5 and Prostrate (PC-5) and central nervous system. Ethanolic extract of seed of *Myristica fragrans* (Houtt) was found to be effective against these cell lines. Ethanolic extract exhibited highest anti-cancerous activity against OVCAR-5. The results of this study demonstrated that *Myristica fragrans* is a potent anti-cancer agent [126].

Nutmeg shows resistance against carcinogenic elements. Hussain and Rao, (1991) reported that, in Swiss albino mice uterine cervix, 3-methylcholanthrene -induced carcinogenesis could be prohibited by mace oral administration [127]. Nutmeg also shows hepatoprotective activity. This property observed in rats with damaged liver, by giving nutmeg in their diets. Kyriakis et al., (1994) studied on the activities of hepatic carcinogen-metabolizing enzymes, like aryl hydrocarbon hydroxylase, cytochrome P450, and acid soluble sulphhydryl and glutathione-Stransferase level in albino mice and checked the influence of essential oil from nutmeg [128]. They found that the essential oil hinders the

activities of the host enzymes related with detoxication and activation of xenobiotic components, as well as mutagens and chemical carcinogens.

Hepatoprotective Zhao et al., conducted an experimental study to check the effects of AEN (alcohol extract of nutmeg, the seed of *Myristica fragrans* on obesity and inflammation which are associated with Nonalcoholic fatty liver disease (NAFLD). They use mice models for the study. Models were fed with high-fat-diet. It was revealed from the study, alcohol extract of nutmeg significantly reduced the body weight and levels of inflammation, cholesterol and lipid accumulation, blood glucose which supports its use as an hepatoprotective agent [129]. Dkhil et al., also studied hepatoprotective activity of *Myristica fragrans*. The study was carried out on rat models. Models were administered with paracetamol (acetaminophen; N-acetyl-p-amino-phenol (APAP) for the artificial induction of hepatotoxicity.

Myristica fragrans Kernel extract showed some significant effect against APAP induced toxication [130].

Aphrodisiac Activity-

Ahmed et al., conducted a study on male rat models to evaluate the activity of *Myristica fragrans* Hoult. (nutmeg) on sexual behavior. It was observed that 50% ethanolic extract of the plant exhibited aphrodisiac activity [131].

Effect on memory-

Parle et al., conducted a study on mouse models for evaluating the effect of *Myristica fragrans* seeds on the learning capacity and memory of the models used. The memory impairment was induced by scopolamine and diazepam. It was found that n-hexane extract significantly worked on learning capacity and memory [132].

Anti-stress activity-

was examined by Dhingra et al., on mice models. Stress was induced in the models by using two methods that are the forced swim test (FST) and the tail suspension test (TST) method. It was observed that *M. fragrans* extract significantly reduced the immobility periods of mice in both the FST and the TST methods [133].

Anti-diarrhoeal -

A study was conducted by Gupta et al., on ileal loops of rabbit and guinea pig. *E. coli* heat labile (LT) and heat stable (ST) enterotoxins were used in this experimental study. The result revealed that hexane-soluble fraction was associated with inhibition of secretory responses which were induced by *E. coli* heat labile (LT) and heat stable (ST) enterotoxins [134].

Antithrombotic-

As per the data report of an in-vitro study carried out by Janssens et al., it was revealed that eugenol and iso-eugenol were associated with inhibition of platelet aggregation, this attributes to its antithrombotic activity [135].

Hypolipidemic effect-

In-vivo study conducted on rabbit models by Ram et al., suggested that the oral administration of ethanolic extract of nutmeg at the dosage of 500 mg/kg at the regular interval of 60 days in artificially induced hypolipidemic rabbits significantly lowered the lipoprotein lipids levels which supports its use as an hypolipidemic agent [136]. Sharma et al., carried out an in-vivo study on hypercholestrolemic rabbit models which revealed that administration of seed extract of *M. fragrans* exhibited properties like reduction in serum cholesterol and LDL cholesterol by 69.1 and 76.3%. It also lowered down the ratio of cholesterol/phospholipid by 31.2% and it significantly elevated the ratio of decreased HDL [137].

Anti-diabetic -

As per the study report of Han et al., macelignan extracted from *M. fragrans* is associated with anti-diabetic potential. It activates the peroxisome proliferator receptor (PPAR, α/β) which helps in improving the insulin sensitivity and lipid metabolic disorders [138].

Anti-convulsant-

Wahab et al., studied anti-convulsant potential of *M. fragran* in well-established animal seizure models. It was observed that nutmeg oil exhibits anti-convulsant properties. During the study nutmeg oil showed anti-convulsant activity against tonic seizures induced by

pentylentetrazole which supports its use as an anticonvulsant agent. [139]

Toxicity study -

A case study on the toxicity of *M. fragrans* reported by Green et al., revealed that myristicin extracted from the volatile oil of plant has toxicity associated with it. It was observed that nutmeg at higher dose i.e. above 4 gm exhibits depressive actions on Central Nervous System. [140]

CONCLUSION -

M. fragrans is a promising herb which is most commonly used in traditional systems of medicine for treating numerous human ailments. It is widely used for its extra-ordinary property of enhancing overall reproductive health. Apart from its therapeutic uses, it is well known spice used in almost all type of cooking. In Ayurveda it is used to treat insomnia, pain, epilepsy, vomiting, stress, IBS, cardiac disorders, erectile dysfunctioning etc. *Myristica fragrans* is a resource of medicinally active compounds and has diverse pharmacological effects; hence, this drug encourages researchers to explore its various novel therapeutic uses for the benefit of mankind.

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