

Review

Traditional Unani uses with multiple pharmacological activities of aril of *Myristica fragrans* (Mace)

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ABSTRACT

Myristica fragrans Houtt is commonly known as “nutmeg”, it produces two spices: mace and nutmeg. Mace and nutmeg are strongly aromatic in nature and known as jowzabuwa and javetri/bisbasah respectively in the Unani system of medicine. *M. fragrans* was used as early as 700 BCE by Indian, however, ancient Greeks and Romans were not aware of it. Later Arab traders introduce *M. fragrans* into Europe followed by Portuguese and Dutch merchants. Mace is very useful medicine in the Unani system of medicine because of its therapeutic uses in salasal al-bawl (urinary incontinence), amrad-i-qalb (cardiac diseases), amrad-i-dimagh (central nervous system), zo'fe bah (sexual debility), amrad al-rahim (uterine diseases), and su-i-hazim (indigestion). The most important constituents of mace essential oil are α -pinene, sabinene, myrcene, limonene, 1,8-cineole, terpinen-4-ol, myristicin, γ -terpinene, and safrole. The seed and mace extract of nutmeg contain quite high tannins, flavonoids, and terpenoids. Mace has pharmacological functions such as antibacterial and antifungal, anti-inflammatory, analgesic, antidiarrhea, antioxidant, chemoprotective, neuropharmacologic, and antidiabetic properties. To explore the correlation between the traditional uses and the same proven by recent researches, a comprehensive review is highlighted in this paper. Further, pharmacological activities which are not reported in classical texts are also discussed

Keywords aril, Mace, *Myristica fragrans* Houtt, nutmeg, pharmacological activities, traditional uses

INTRODUCTION

Unani (Greco-Arabic) medicine is the one among ancient systems of medicines based on the teaching of the Greek physicians Hippocrates and Galen (that exists till date and still preserves its classical fundamental nature. “The name ‘Unani Tibb’ or ‘Unani Medicine’ has a medical tradition and a history, embraced and shaped by people of different cultures over a thousand years stretching from the Eastern Mediterranean, and West Asia to North Africa, Hispano-Arabia, and Western Europe in the west, to Central, South and South-East Asia to the east.” (Sultana et al., 2015) Unani classical literature consists of thousands of books. The description of *M. fragrans* plant is available in the authentic books of Traditional Unani medicine. Hence, thorough literature exploration was carried out to comprehend the description of *M. fragrans* plant discussed in ancient Unani literature. The classical Unani texts viz., Al Qanoon fit Tibb (Canon of Medicine), Khazainul Advia, Jamia ul Mufradat al Advia al Aghiza, Busthan al-Mufradat, Al Qarabdin, Makhzan al-Mufradat, Muhit-i-A'zam, Kitab al-Fath fi al-Tadawi, Hamdard Pharmacopoeia of Eastern Medicine, Unani Pharmacopoeia of India, Indian Medicinal plants, and

Wealth of India were referred. These classical texts were referred for Unani morphology, the temperament of the plant, Unani action, traditional Unani uses, corrective action, adverse effect, and compound formulation. Further, browsing of PubMed/Google Scholar and other websites was explored for ethno botanical description, phytoconstituents, traditional uses and pharmacological activities.

Introduction of the plant

Myristica fragrans is commonly known as “nutmeg”, it produces two spices: mace and nutmeg (Asgarpanah et al., 2012; Shafiei et al., 2012). The tree of *M. fragrans* usually grows to 5 to 13 metres high; it seldom reaches 20 metres high. It is an aromatic evergreen spreading tree. Seeds (nutmegs) are broadly ovoid (2 to 3 cm long), firm and fleshy. When fresh, the aril (mace) is bright scarlet becoming hornier, brittle and a yellowish-brown colour when dried (Kritikar and Basu, 2008). It requires a hot and moist climate with a rainfall of 150-300 cm per annum. It is also cultivated in hotter parts of India (Naikodi et al., 2011). It was not known by the ancient Greeks and Romans, but was used by Indians and Arabs as early as 700 BCE. It was later introduced into Europe by Arab traders and, subsequently, by Portuguese and Dutch merchants (Wiar, 2007). In the Unani system of medicine, it is well known drug since ancient times since, it has a great therapeutic value (Standardization of Single Drugs of Unani Medicine, 1997). Aril of *Myristica fragrans* Houtt (mace), strongly aromatic in nature is known as javetri/bisbasah in the Unani system of medicine. Mace plays the foremost role in the Unani system of medicine because of its therapeutic uses in salasal al-bawl

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(urinary incontinence), amrad-i-qalb (cardiac diseases), amrad-i-dimagh (central nervous system), zo'fe bah (sexual debility), amrad al-rahim (uterine diseases), and su-i-hazim (indigestion) (Magrahbi, 2007; Naikodi et al., 2011). Myristicaceae species is useful in mood disorders, anxiety, and other psychological disturbances. The active principle in nutmeg is myristicin, a catecholamine-like phenylpropanoid (Wiert, 2007).

Taxonomy

Kingdom: *Plantae*

Family: *Myristicaceae*

Genus: *Myristica*

Species: *fragrans*

Common name: *Nutmeg*

Botanical name: *Myristica fragrans* Houtt (Kritikar and Basu, 2008; Standarisisation of Single Drugs of Unani Medicine, 1997)

Vernacular name

Unani Tibbi Name: **Urdu:** *Jaiphal* (Naikodi et al., 2011); *Jouzbuwwa* (Kritikar and Basu, 2008), *Maakhan valadin* (Baytar, 2000), **Arabic:** *Bisbasah* (Baytar, 2000), *Jouzul teeb*, *Jainsiban* (Naikodi et al., 2011); **English:** *Mace* (Baytar, 2000); **Persian:** *bizbaz*, *charkhun* (Baytar, 2000); **Hindi:** *Jaiphal*; **Kannada:** *Jadipattiri*; **Latin:** *Merisiniae* (Naikodi et al., 2011); **Malayalam:** *Jadi-patri* (Naikodi et al., 2011); **Persian:** *Bazabazah* (Nadkarni, 2009); **Sinhala:** *Vasavasi* (Nadkarni, 2009); **Sanskrit:** *Jatipatri* (Nadkarni, 2009); **Shami:** *Warkiyah* (Baytar, 2000); **Tamil:** *Jadi-pattiri* (Baytar 2000); **Telugu:** *Japatri*

Morphological Description in Unani Literature: According to Ibn Maaswaih mace is the peel of nutmeg. Masih holds that in potency it equal *naarmushk* (iron wood tree) but is a little more attenuated. The leaves of *bisbasah* intertwined, corrugated, dry, reddish or yellowish and look like bark. The wood and leaves are pungent like cubeb and are obtained from China (Sina, 1988). The fruit of this tree is just like apricot, which after ripening opens into two pieces, inner part is *jaiphal* and the outer part is *javithri* (Ghani, 2001). Hence, *Javithri* is the outer covering on the *jaiphal* and on drying it gets separated from *jaiphal*. Fresh *javithri* is greenish in colour on drying colour changes to reddish yellow, strongly aromatic in nature. It grows in Malabar area, Srilanka, and Malaysia (Khan, 2012; Said, 1997).

Ethno botanical description: The evergreen tree of the *myristicaceae* family, the tree grows to about 30m high with an undivided trunk. The leaves are alternate, dark green, entire margined, sharp edged, short petioled, ovate-elliptical, leathery and up to 8 cm long. The inflorescence of the female trees is composed of 1-3 flowers with a white, bell shaped perianth and a 1 celled ovary ending in a 2-lobed stigma. The ovary develops into a light yellow fleshy fruit, almost round, acuminate at the stem end, 3-6cm long and 2, 5-5cm thick. The fruit ripens 7-10 months after flowering. When ripened, the fleshy part bursts open and exposes the bright red aril, the aril loses its red colour as it dries, becoming brownish yellow and hardening to a horny consistency. The aril is used as a spice known as mace, which arises in the region of hilum before the flowers open and fertilization take place. The seed is dried to produce nutmeg. The mace is an orange coloured modification of nutmeg seed (Ross, 2003).

Pharmacognostical and Phytochemical Standardization

Macroscopic of Mace: The drug consists of reddish pieces, about 2–4 cm in size that is the blades of the arils. In transectional view, the aril is flat and isobilateral (Parimala and

Amerjothy, 2013). They are smooth, flat, slightly flexible, irregularly slit, or brittle and somewhat translucent (Naikodi et al., 2011) when fresh, the aril is bright red colour, and removed either by the finger or a knife. When removed entire, it forms “double blade” mace, but if in two pieces, it is known as “single blade” mace. The mace is slowly dried, after flattening by treading under the feet or pressing between boards (Evans, 2004). They are rich in oil and therefore exude a reddish or orange oily colour when pressed (Naikodi et al., 2011).

Microscopic of Mace: The cross-section of the mace shows leaf-like structures somewhat. “It is bounded by a single-layered epidermis on either side, while the rest of the area is occupied by simple, thick-walled cells with no intercellular space, and oil cavities are in abundance” (Naikodi et al, 2011). “The mace is 400µm thick in the middle and 150µm thick at the ends and epidermal cells are 10µm thick. “*The ground tissue of the aril is in admixture of small and larger cells*”. The larger cells are oil bearing idioblasts. “*They are angular in the outline and fairly thick walled. The idioblasts are 40µm wide; in between the idioblasts are smaller, angular or spindle-shaped parenchyma cells. In the median part of the aril there are prominent discrete vascular bundles arranged in a plate*”. The vascular bundles have small, strands of phloem and xylem elements (Parimala and Amerjothy, 2013).

Powder analysis: The powder is fine, homogeneous and yellowish-brown with a strong aroma and slightly bitter taste. The powder when seen under the microscope shows an abundance of thick-walled cells. Starch and aleuronic grains are absent (Naikodi et al., 2011).

Habitat: The plant has been successfully cultivated in :Madras and Southern India, Nilgiri hills, Coimbatore, Salem, Ramanathapuram, Tirunelveli, Kanya Kumari, and Madurai districts, Malabar coast, Assam and in other states (Naikodi et al, 2011).

Parts used: Dried seed, nutmeg, mace and wood (Nadkarni, 2009).

Odour: Strong and aromatic (Wallis, 2005)

Taste: Aromatic and bitter and Pungent (Naikodi et al., 2011).

Phyto-chemical constituents

Mace and nutmeg: The chief constituents are volatile oil, solid fat, amyloextrin, reducing sugar, pectin, resinous, coloring matter and starch. The volatile oil consists of myristicin, hexane, myristic acid, elemicin, saffrole, eugenol, palmitic, oleic, lauric and other acid, protein, fiber, mineral matter, calcium, phosphorus, iron starch, terpenoids, phenolics, lignin compounds, mucilage, flavonoids, saponins, anthraquinones, alkaloids, and phlobatanins. Bioactive compounds are camphene, isielemicin, isoeugenol and methoxyeugenol (Asgarpanah et al., 2012; Wealth of India, 1998). The volatile oil of mace resembles that of nutmeg, the major phenolic compounds isolated being dehydrodiisoeugenol and 5-methoxydehydrodiisoeugenol, both of which have a significant antibacterial action. In recent years a series of lignans and neolignans has been isolated from mace (Evans, 2004).

Mace has 7% to 14% essential oil and about 30% fixed oil. The aroma compound contents are same as nutmeg however, differs in amount, mainly 87.5% monoterpenes, 5.5% monoterpene alcohols and 7% other aromatics. Like nutmeg essential oil, the main constituents of mace essential oil are α -pinene, sabinene, limonene, myrcene, 1,8-cineole, terpinen-4-ol, myristicin, γ -terpinene, and saffrole (Pooja et al., 2012). Assa et

Table 1. Af'al (Actions) of Mace in Unani medicine and Ethnomedicine

Unani Medicine	Ethnomedicine
• <i>Da'fe'-i-ta'affun</i> (antiseptic) (Kabir al-Din, 2007) • <i>Hadm</i> (digestive) (Ghani, 2001; Hakim, 2002; Kabir al-Din, 2007; Khan, 2012) • <i>Islah</i> (reformation) (Ghani, 2001) • <i>Kasir-i-riyah</i> (carminative) (Baytar 2000; Ghani, 2001; Khan, 2012; Sina 1998) • <i>Mufarrih-i-hadm</i>; <i>Mufarrih</i> (exhilarant) (Hakim, 2002); • <i>Mufattih-i-sudad</i> (deobstruant) (Kabir al-Din, 2007; Khan 2012) • <i>Mufattih-i-hasah</i> (lithotriptic) (Ghani, 2001) • <i>Muhallil</i> (resolvent) (Ghani, 2001) • <i>Muhallil-i-waram</i> (anti-inflammatory) (Khan 2012; Ghani, 2001) • <i>Muharrrik</i> (stimulant) (Ghani, 2001) • <i>Mujaffif</i> (desiccant) (Kabir al-Din, 2007) • <i>Mujaffif-i-rutubut</i> (fluid absorbent) (Hakim, 2002) • <i>Mulattif</i> (Hakim, 2002; Khan 2012) • <i>Muqawwi</i> and <i>munaqqi al-rahim</i> (clean the uterus) (Hakim, 2002; Sina, 1998; Kabir al-Din, 2007) • <i>Muqawwi-i-bah</i> (aphrodisiac) (Ghani, 2001) • <i>Muqawwi-i-mi'da</i>, <i>muqawwi-i-kabid</i> and <i>muqawwi al-rahim</i> (Hakim, 2002; Ghani, 2001; Magrahbi, 2007; Kabir al-Din, 2007) • <i>Muqawwi-i-qalb</i> (Magrahbi, 2007; Kabir al-Din, 2007) • <i>Musakhkhin</i> (which produce heat) (Kabir al-Din, 2007) • <i>Nazf al-dam</i> (haemoptysis) (Hakim, 2002) • <i>Qabiz</i> (astringent) (Baytar 2000; Sina, 1998; Ghani, 2001) • Savior of <i>hararat-i-ghareezi</i>	• Analgesic (Asgarpanah et al, 2012) • Antibacterial (Evans, 2004) • Anti-inflammatory (Khare, 2007) • Antimuscarinic (Asgarpanah et al, 2012) • Aphrodisiac (Nadkarni, 2009; Wealth of India, 1998) • Astringent (Wealth of India 1998) • Carminative (Khare, 2007; Nadkarni, 2009; Wealth of India, 1998) • Digestive (Nadkarni, 2009) • Diuretic (Kritikar and Basu, 2008) • Hepatoprotective (Nadkarni, 2009) • Lactagogue (Kritikar and Basu, 2008) • Solvent of inflammation • Spasmolytic (Khare, 2007) • Stimulant (Khare, 2007; Nadkarni, 2009; Wealth of India 1998); • Stomachic • Uterine tonic

al., (2014) proved that the seed and mace extract of nutmeg contain quite high tannins, flavonoids and terpenoids. The quantity of total phenol was found to be high in Acetone mace extract (14.2 mg GAE/gm) when compared with other plant extracts. The total phenol content in aqueous seed extract, acetone seed extract and aqueous mace extract was found to be almost equal (Gayathri et al., 2015).

Mace is aromatic and its aroma is due to the presence of terpenes. Malabaricone-B and Malaabaricone-C are two resorcinol (Naikodi et al., 2011).

The colour of mace is an important factor, influencing its commercial value. The red pigment of mace was identified to be lycopene by thin layer chromatography and absorption studies. The neolignans, fragnasol C and D and myristicanol A and D have been isolated from mace. A neolignan, characterized as dihydro-di-isoeugenol was isolated from the hexane and chloroform extracts of *M. fragrans* arils. Five phenyl propanoids had been reported from the seed kernel of the plant. Dihydroguaiaretic acid has been isolated from the mace of nutmeg (Latha et al., 2005).

The amount of myristicin was found to be higher in the petroleum ether extract with 313.51 µg (0.03 %) with respect to the drug taken for the extract. Myristicin is the chief principle in the drug responsible for its pharmacological properties (Naikodi et al., 2011).

Mizaj (Temperament): Hot 2⁰ and Dry 3⁰ (Nadkarni, 2009; Sina, 1998); Hot 2⁰ and Dry 2⁰ (Khan, 2012; Sina, 1998)

Af'al (Action) mentioned in Unani medicine and ethnomedicine: The actions are summarized in table 1.

Therapeutic uses mentioned in Unani Medicine

Effect on central nervous system: It has been recommended in the treatment of *suda barid*, *falij* and *amrad-i-chashm* (Magrahbi, 2007). It is useful in treating *sehar* (insomnia) (Asgarpanah et al., 2012). Local application of paste of *bisbasah* relieves *shaqiqa* (migraine headaches) (Ghani, 2001; Hakim, 2002; Magrahbi, 2007). It is used as deodorant along with *barge morad* (Ghani, 2001). It is used with *roghan-i-banafsha* by producing snuff in headache due to retention of

ghaleez madah (Ghani, 2001; Magrahbi, 2007). The paste made from *javithri* with *roghan-i-banafsha* is also useful in epilepsy (Ghani, 2001)

Effect on respiratory system: It is very useful for lungs diseases (Khan, 2012; Kabir al-Din, 2007) and haemoptysis (Ghani, 2001).

Effect on gastrointestinal system: It is useful in indigestion (*su'i-hadm*) as it has *hadim* effect. It is tonic for the liver, spleen, lungs, stomach, and uterus (Khan, 2012). It strengthens the stomach and the liver (Baytar, 2000; Sina, 1998). It is useful in abrasions (of intestines and uterus) (Baytar, 2000; Khan, 2012; Hakim, 2002) and it is also useful for the treatment of diarrhoea, mouth sores and insomnia (Asgarpanah et al., 2012). It helps to reduce excessive gastric secretion (Baytar, 2000). It has astringent effect and control flatulence (Ghani, 2001; Naikodi et al, 2011; Sina, 1998).

Effect on cardio vascular system: It has *muqawwi-i-qalb* and *mufarrih* effect hence, useful in cardiac diseases (*amrad-i-qalb*) (Kabir al-Din, 2007; Magrahbi, 2007). It is useful in tachycardia (Magrahbi, 2007).

Effect on urogenital system: It is very useful in the urogenital system as it strengthens the uterus by its *muqawwi-i-rahim* property (Magrahbi, 2007). It is also used with saffron to expel the retained product of conception from the uterus. It helps to maintain the pregnancy (Ghani, 2001). It helps in treating abrasions of the uterus (Baytar, 2000). Owing to its *muqawwi-i-bah*, property it is useful in sexual debility (*Mud'if-i-Bah*) (Ghani, 2001). Mace is especially useful for treating urinary incontinence, and local application of paste on suprapubic area is more effective (Khan, 2012; Ghani, 2001; Hakim, 2002). It reduces the chances of abortion (Hakim, 2002). The paste of nutmeg with honey can be used in parturient women for backache. A tampon soaked in mace is used per vaginum after menses in infertility cases (Ghani, 2001; Hakim, 2002). It is useful in severe dysmenorrhea and uterine diseases (Magrahbi, 2007).

It is useful in *ihtibas al-bawl* (retention of urine) as it has

mudirr al-bawl (diuretic) property (Rafeequddin, 1985).

Effect on musculo-skeletal system: Essential oil of mace is useful in relieving sprains, *waja al-mafasil* (arthritis) and *fali* (paralysis) (Asgarpanah et al., 2012). Local application of *qurati* (an ointment) is useful in *waram sulb* (Inflammation due to black bile) (Magrahbi, 2007).

Miscellaneous: It is used with honey to cure hard swelling (Baytar, 2000; Khan 2012). When used in *qairuti* (an ointment), it dissolves hard and thick swellings (Sina, 1998). It is used externally with *barg-i-morad* to reduce bad odour caused by excessive sweating in the armpit (Hakim, 2002; Ghani, 2001).

Therapeutic indications and uses mentioned in ethnomedicine:

- Nutmegs, maces and their oils are used as carminatives and flavoring agent. An aqueous extract of nutmeg is used for the treatment of infantile diarrhea in traditional Indian medicine (Evans, 2004; Wealth of India, 1998).
- It is useful in cardiac diseases, indigestion and sexual debility (Naikodi et al., 2011).
- It useful in bronchitis, asthma, thirst, improves the appetite, choleraic diarrhea, disease of the liver and spleen, headache, palsy, eye troubles (Kritikar and Basu, 2008). Essential oil of mace is traditionally used to relief sprains, rheumatism and paralysis (Asgarpanah et al., 2012; Naikodi et al., 2011; Wealth of India, 1998).
- Oil of nutmeg or mace has been recommended for the treatment of inflammation of the bladder and urinary tract (Wealth of India, 1998). It also activates hepatic detoxification process (Khare, 2007).

Miqdar (Dosage): 1 - 10 gram (Ghani, 2001; Khan, 2012); 3 to 10 g (Hakim, 2002); 10-20 grains (Waring, 2010)

Muzir (Adverse effect): Narcotic (large doses) (Waring, 2010; Wealth of India, 1998), hepatotoxic and headache in hot temperament person (Hakim, 2002; Ghani, 2001)

Musleh (Corrective): *Gond babool* (*Acacia arabica* gum) for hepatotoxicity (Ghani, 2001; Hakim, 2002) and *arq gulab* (Hakim, 2002), and sandalwood for headache (Ghani, 2001)

Badal (Substitute): *Jouzawwa* (Khan, 2012) *Bombay mace* from *M. malabarica* and *Macassar* or *Papua mace* from *M. argentea* (Wallis, 2005)

Important formulations: *Jawarish bisbasah* (Kabir al-Din, 2004); *Halwa salab*; *Halwa supari pak* (National Formulary of Unani Medicine, 2008); *Majoon pethapak* (Unani Pharmacopoeia of India, 2010)

Pharmacological activities

M. fragrans has pharmacological functions such as antibacterial and antifungal, anti-inflammatory, analgesic, antidiarrhoea, antioxidant, chemoprotective, neuropharmacologic, and antidiabetic properties.

- **Aphrodisiac effect:** Researchers have described that 50% ethanolic extracts of nutmeg has enhanced the male sexual activity (Tajuddin et al., 2009). In Traditional Unani medicine, mace is used as in male sexual dysfunction, Tajuddin et al., (2009) proved aphrodisiac effect of mace in experimental animals.

- **Anti-microbial properties:** Seeds and seed kernels, mace of nutmeg is known to exhibit strong antimicrobial activity against animal and plant pathogens. The mace of *M. fragrans* showed antimicrobial properties against *Staphylococcus aureus* and *Candida albicans*. Dehydrodi-isoeugenol and 5-methoxy eugenol from mace prevented *Streptococcus mutans* induced dental caries. Methanolic extract of *M. fragrans* mace was reported to inhibit the growth of the *Helicobacter pylori* (Jaiswal et al., 2009; Latha et al., 2005). The resorcinols, malabaricones B and C, isolated from the mace exhibited strong antibacterial and antifungal activities (Khare, 2007).
- **Antibacterial properties:** The extract of *M. fragrans* has antibacterial activity against *Staphylococcus aureus*, *Proteus vulgaris* and *Klebsiella pneumonia* (Asgarpanah et al., 2012; Wealth of India, 1998). Methanol extract and phenolic fraction of the aril were active on *Streptococcus mutans*. The aril essential oil, on agar plate, was active on *Bacillus subtilis*, *Escherichia coli* and *staphylococcus aureus* (Ross, 2003).
- **Anticholinergic activity:** The acetone extract of *Myristica fragrans* (seeds) on sheep tracheal ring showed anticholinergic activity. Hence, it may be useful in treating upper respiratory infections including bronchial asthma (Swamy et al., 2013). In Unani traditional medicine, mace is useful in respiratory system for cough, asthma and lung affections as it as anticholinergic effect.
- **Anticonvulsant effect:** Nutmeg essential oil extract possesses anticonvulsant activity against the animal model of grandmal, petitmal and status epilepticus (Asgarpanah et al., 2012) Ghani (2001) discussed that mace with roghan-i-banafsha is useful in epilepsy, same has been proven by Asgarpanah et al. (2012).
- **Antifungal activities:** Methanol extract of *M. fragrans* showed activity against fungal strains such as *Alternaria alternata*, *Colletotrichum coccodes*, *Colletotrichum gloeosporioids*, *Magnaporthe grisea*, *Agrobacterium tumefaciens*, *Acidovorex konjaci* and *Burkholderia glumae* (Asgarpanah et al., 2012). Pooja et al., (2011) reported that Methanol and Hexane extracts obtained from mace were most effective against the filamentous (*Candida albicans*) and non-filamentous fungus (*Aspergillus niger*). The dried aril on an agar plate was active on various fungi (Ross, 2003).
- **Antidiabetic properties:** Mace lignan enhances the insulin sensitivity and improved lipid metabolic disorders by activating peroxisome proliferator receptor (PPAR, α/β) and attenuating endoplasmic reticulum stress, suggesting that it is an antidiabetic agent for the treatment of type 2 diabetes (Jaiswal et al., 2009). Ethanolic extract of *M. fragrans* fruits (Which part) decreased blood glucose level in streptozotocin (STZ) induced diabetic rats, thus *Myristica fragrans* possesses potent anti diabetic activity (Asgarpanah et al., 2012).
- **Antidiarrhoeal activity:** Hot water extract of the aril, administered orally for prevention of diarrhoea (Ross, 2003). Unani scholars surmised that mace is useful in indigestion (*su'i-hadm*) as it has *hadim* effect and it is also useful in abrasions (of intestines and uterus) (Baytar, 2000; Khan, 2012; Hakim, 2002) As per Unani concept mace has astringent effect and control flatulence (Ghani, 2001; Naikodi et al, 2011; Sina, 1998) hence useful for the treatment of infantile diarrhea in traditional Indian medicine (Evans, 2004; Wealth of India, 1998).

- **Antidepressant activity:** N-Hexane extracts of nutmeg seeds in mice has shown significant antidepressant activity (Dhingra et al., 2006).
- **Anti-inflammatory and analgesic effect:** Ozaki et al., (1989) found that Methanol extract obtained from mace and its active principles (myristicin) showed anti-inflammatory “effect on carrageen in induced edema in rats and acetic acid-induced vascular permeability in mice”. The anti-inflammatory effect was similar to indomethacin and this is due to presence of myristicin. Myristicin may also exert an analgesic effect. Methanol extract of the dried aril, administered intragastrically to mice at a dose of 0.3gm/kg showed analgesic effect vs acetic acid-induced writhing (Ross, 2003). The methanol extract of mace has been proven for its anti-inflammatory activity as myristicin inhibits prostaglandin synthesis mace showed anti-inflammatory effects, similar to indomethacin (Tomás-Rodríguez et al., 2015). In traditional uses oil of nutmeg or mace has been recommended for the treatment of inflammation of the bladder and urinary tract (Wealth of India, 1998). Unani scholars opined it is useful in urogenital infection. (Baytar, 2000; Magrahbi, 2007)
- **Antioxidant activity:** Antioxidants chemical compounds present in spices and herbs include vitamins, carotenoids, terpenoids, alkaloids, flavonoids, lignin, simple phenols, phenolic acids etc (Assa et al., 2014). Monomeric and dimorphic phenyl propanoids from mace, on p.o. administration in mice, produced suppression of lipid peroxidation in liver (Khare, 2007). Antioxidant in flesh, seeds and mace extracts showed strong scavenging capability of free radicals on linoleic peroxidation. Peroxyl and alkoxy radicals are had major influence on propagation stage of linoleic peroxidation (Assa et al., 2014). Ethanol (95%) extract of the aril essential oil, at a concentration of 0.02% was effective on lard as antioxidant (Ross, 2003). Methanol extract of nutmeg seed has the best ability to scavenge free radicals. Flesh seeds and mace extracts are very effective in inhibiting linoleic peroxidation, especially nutmegs seed and mace has the potential to be a source of natural antioxidants (Assa et al., 2014).
- **Antitoxic activity:** Ether extract of the dried aril essential oil, administered intra peritoneal to mice at a dose of 100.0 mg/kg was effective vs strychnine toxicity (Ross, 2003).
- **Antithrombolytic effect:** *M. fragrans* seeds are reported to inhibit platelet aggregation and hence showed anti thrombolytic effect (Ross, 2003).
- **Anxiolytic effect:** *Myristica fragrans* at dose of 25mg/kg possess anxiolytic activity (Sahar et al., 2013).
- **Barbiturate potential:** Ether and Methanol extracts of the dried aril, administered intra peritoneal to mice at a dose of 200.0 mg/kg were effective. Ether extract of the dried aril essential oil, prolonged the sleeping time induced by hexobarbital (Ross, 2003).
- **Behavioral effects:** Nutmeg and mace are called pshychotropic spices (Latha et al., 2005).
- **Cytotoxic, anticancer and chemoprotective effects:** The essential oil of the leaves of *Myristica fragrans* in the MCF-7 breast cancer line and A-357 epidermal skin cancer cell line showed cytotoxic activity (Helen et al., 2012). The dihydroguaiaretic acid from *M. fragrans* mace s^uppressed leukaemic cells, colon cancer and lung cancer cells in vitro (Latha et al., 2005). Administration of dried aril intra gastrically, decrease incidence of carcinogenesis.

Jannu et al., (1991) reported that mace had chemo preventive property on “DMBA-induced papillomagenesis in the skin of male Swiss albino mice”. They concluded that 50% reduction was noted in the skin papilloma incidence and only 1.75 was the average tumor per tumor-bearing mouse. The incidence of carcinogenesis was decreased by 52% with dried aril vs methylocholanthrene-induced carcinogenesis (Ross, 2003).

Effects of mace lignan on “UVB-induced matrix metalloproteinase-9 and cyclooxygenase-2” in immortalized human keratinocytes (HaCaT) cells: Anggakusuma et al., (2010) found that mace lignan protects skin keratinocytes from UVB-induced damage and inhibits MMP-9 and COX-2 expression by attenuating the activation of MAPKs and PI3K/Akt.

- **Depressive effect:** Fundaro and Cassone (1980) reported that the oils of Chamomile, Cinnamon, Absinthium, Mace, Origanum essential oils at the highest doses caused a depressive effect whereas at the lowest doses they caused weak or doubtful effects on rat's operant conditioning behavior.
- **Glutathione-s-transferase induction:** Powdered dried aril, administered intra gastrically to mice at a dose of 0.5% of the diet for 10 days showed glutathione-s-transferase induction (Ross, 2003).
- **Hypolipidaemic effect:** The ethanolic extract of *M. fragrans* seeds shows hypolipidaemic effect on experimentally induced hyperlipidaemia in albino rats (Latha et al., 2005).
- **Hepatoprotective effects:** The mace is reported to modulate glutathione-S-transferase activity in mouse liver. The active principles found in the aqueous extract of mace were effectual in “transmammary modulation of hepatic xenobiotic metabolizing enzymes in the liver of mouse pups”. These active principles from mace also influenced the hepatic detoxification systems in adult mice (Latha et al., 2005). *M. fragrans* showed evidence that it had strong hepatoprotective activity to rats with liver damage induced by lipopolysaccharides and this effect was linked to “activation of the mitogen activated protein kinase (MAPK) signaling pathway”. This active principle from mace also influenced the hepatic detoxification systems in adult mice (Jaiswal et al., 2009). Unani scholars surmised that mace has tonic property for liver, spleen, brain, heart and uterus. (Baytar, 2000; Sina, 1998).
- **Immunomodulatory and radioprotective effects:** The authors reported the antioxidant, radioprotective and immunomodulatory effects of lignans present in the aqueous extract of fresh nutmeg mace in mammalian splenocytes (Checker et al., 2008).
- **Liver regeneration stimulation:** The aril essential oil, administered subcutaneously to partially hepatectomized male rats at dose of 100.0 mg/animal daily for 7 days showed liver regeneration stimulation property (Ross, 2003).
- **Memory enhancing activity:** Nutmeg has been investigated on learning capabilities and memory level in mice which showed significant inhibition of acetylcholinesterase for the treatment of Alzheimer's disease (Nagja et al., 2015).

Clinical trial

Anti-inflammatory activity: The dried aril, taken orally by human adults at variable dosage levels, was effective for anti-inflammatory activity (Ross, 2003).

CONCLUSION

The assets of information preserved as a traditional medicinal knowledge among the racial and cultural communities appears to be slowly disappearing. Further, the oral folklore of passing on knowledge to descend is also waning. Therefore, credentials and conservation of the traditional knowledge are the huge challenges of the hour, so that the enormous information that exists in the traditional texts can still be preserved for future research in pharmaceuticals and drug discovery. However, many modern, unreliable reports combined with centuries of traditional use would indicate that natural remedies like herbal medicine have been effective in reducing various diseases. Hence, literary review of mace was explored. This review makes apparent that traditionally *M. fragrans* mace and kernel are useful in central nervous system, respiratory, gastrointestinal, cardio vascular, urogenital, musculo-skeletal system and swellings. In aforementioned ailments this herb has been pharmacologically and clinically proven as analgesic, anti-inflammatory, anti-oxidant, antibacterial, anticholinergic, anticonvulsant, antidepressive, antithrombotic, antidiabetic, antifungal, antimuscarinic, aphrodisiac, diuretic, hepatoprotective, lactagogue, and spasmolytic. These effects are attributed to its phyto-chemical constituent's myristicin. Thus, this narrative review significantly acclaims that the traditional herb, *M. fragrans* has multipurpose pharmacological properties. Further, enormous randomized controlled clinical trials are recommended in large scales to prove the aforementioned pharmacological activities in various diseases.

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CONFLICT OF INTEREST

None.

REFERENCES

- Anggakusuma, Yanti, Hwang JK. Effects of mace lignan isolated from *Myristicafragrans*Houtt. on UVB-induced matrix metalloproteinase-9 and cyclooxygenase-2 in HaCaT cells. *J Dermatol Sci*. 2010;57:114-122.
- Anonymous. National Formulary of Unani Medicine. Part V. (India, New Delhi: Dept. of Ayurveda, Yoga, Unani, Sidda and Homeopathy), pp.68-69, 2008.
- Anonymous. The Wealth of India. Vol 6. (India, New Delhi: Council of Scientific and Industrial Research), pp. 477-478, 1988.
- Asgarpanah J, Kazemivash N. Phytochemistry and Pharmacologic Properties of *Myristicafragrans*Houtt.: A review. *Afr J Biotechnol*. 2012;11:12787-12793.
- Assa JR, Widjanarko SB, Kusnadi J, Berhimpon S. Antioxidant potential of Flesh, seed, Mace of Nutmeg (*Myristica fragrans* Houtt). *Int J Chem Tech Research*. 2014;6:2460-2468.
- Bayter I. *Jamia ul Mufradat al Advia al Aghiza*. (India, New Delhi: Central Council of Research in Unani Medicine), pp. 233, 2000.
- Checker R, Chatterjee S, Sharma D, Gupta S, Variyar P, Sharma A, Poduval TB. Immunomodulatory and radioprotective effects of lignans derived from fresh nutmeg mace (*Myristica fragrans*) in mammalian splenocytes. *Int Immunopharmacol*. 2008;8:661-669.
- Dhingra D, Sharma A. Antidepressant- like activity of n-hexane extract of nutmeg (*Myristica fragrans*) seeds in mice. *J Med Food*. 2006;9:84-89.
- Evans WC. Trease and Evans Pharmacognosy. 15th ed. (Australia, Sydney: Saunders), pp. 269-270, 2004.
- Fundarò A, Cassone MC. Action of essential oils of chamomile, cinnamon, absinthium, mace and origanum on operant conditioning behavior of the rat. [Article in Italian]. *Boll Soc Ital Biol Sper*. 1980;56:2375-2380.
- Gayathri R, AnuradhaV. Phytochemical screening and total phenolic content of aqueous and acetone extracts of seed, butter, mace of nutmeg (*Myristica fragrans* Houtt). *Int J Pharm Sci Rev Res*. 2015;33: 236-239.
- Ghani N. *KhazainulAdvia*. (India, New Delhi: IdaraeKitabusShifa), pp.572, 2001.
- Hakim MA. *Busthan al-Mufradat*. (India, New Delhi: IdaraeKitabusShifa), pp .219-220, 2002.
- Helen PA, Vargheese T A, Kumari JJJ, Abiramy MR, Sajina N, Sree SJ. Phytochemical analysis and anticancer activity of essential oil from *Myristica fragrans*. *Int J Curr Pharm Rev Res*. 2011-2012;2;188-198.
- Jaiswal P, Kumar P, Singh VK, Singh DK. Biological effects of *Myristica fragrans*. *Annu Rev Biomed Sci*. 2009;11:21-29.
- Jannu LN, Hussain SP, Rao AR. Chemopreventive action of mace (*Myristica fragrans* Houtt) on DMBA-induced papillomagenesis in the skin of mice. *Cancer Lett*. 1991;56:59-63.
- Kabir al-Din M. Al Qarabdin. (India, New Delhi: Central Council of Research in Unani Medicine), pp.49, 2004.
- Kabir al-Din M. Makhzan al-Mufradat. (India, New Delhi: Idarae Kitabus.Shifa), pp.171-172, 2007.
- Khan A. Muhit-i-A'zam, (India, New Delhi: Central Council of Research in Unani Medicine), pp. 665, 2012.
- Khare CP. *Indian Medicinal Plants: An Illustrated Dictionary*. (India, New Delhi: Springer India (p) Ltd), pp.428-429, 2007.
- Kritikar KR, Basu BD. *Indian Medicinal Plants*. 2nd ed. (India, Dehradun: International Book Distributors), pp.2141, 2008.
- Latha PG, Sindhu G, Suja S R, Geetha BS, Pushpangadan P, Rajasekharan S. Pharmacology and chemistry of *Myristica fragrans*.Houtt. – A review. *J Spices Aromatic Crops*. 2005; 14: 94-101.

- Magrabhi IB. Kitab al-Fath fi al-Tadawi. (India, New Delhi: Dept. of AYUSH), pp.68, 2007.
- Nadkarni KM. Indian Materia Medica. (India, Mumbai: Popular Prakashan PVT.LTD), pp.830-831, 2009.
- Nagja T, Vimal K, Sanjeev A. *Myristica fragrans*: A Comprehensive Review. Int J Pharm Pharm Sci. 2015;8:27-30.
- Naikodi MA, Waheed MA, Shareef MA, Ahmad M, Nagaiah K. Standardization of the Unani drug-*Myristica fragrans* Houtt. (Javetri) with modern analytical techniques. Pharma Methods. 2011;2:76-82.
- Ozaki Y, Soedigdo S, Wattimena YR, Suganda AG. Antiinflammatory effect of mace, aril of *Myristica fragrans* Houtt., and its active principles. Jpn J Pharmacol. 1989;49:155-163.
- Parimala N and Amerjothy S. Histological and Histochemical Investigations of *Myristica fragrans* Houtt. (Myristicaceae). J Pharmacognosy Phytochemistry. 2013;1:106-111.
- Pooja V, Sanwal H, Goyal A, Bhatnagar S, Srivastava AK. Activity of *Myristica fragrans* and its effect against Filamentous and Non-Filamentous Fungus. Int J Pharm Pharm Sci. 2012;4:538-540.
- Ross IA. Medicinal Plants of the World. Vol. II. (USA, New Jersey: Humana Press), pp.338-343, 2003.
- Sahar SH, Nagaraju B, Bolouri A, Zothanmawia C, Nemati H, Kushnoor N Z, Zahra A, Surendranatha A. Anxiolytic effect of *Myristica fragrans*. Jour Harmo Res Pharm. 2013;2:17-23.
- Said HM, the editor. Hamdard Pharmacopoeia of Eastern Medicine. 2nd ed. (India, New Delhi: Sri Satguru Publications), pp.404-451, 1997.
- Shafiei Z, Shuhairi NN, Yap NFS, Sibungkil CAH, Latip J. Antibacterial Activity of *Myristica fragrans* against oral pathogens. Evidence-Based Complementary Altern Med. 2012;2012:1-7.
- Sina I. Al-Qanun Fi'l-Tibb. (Trans: English). Book II. (India, New Delhi: Jamia Hamdard), pp.95, 1998.
- Sultana A, Rahman K, Padmaja AR Urinary Incontinence (Salasal Bawl) in Greco-Arabic Medicine: A Review. Acta Medico-Historica Adriatica; 2015;13:1-132.
- Swamy PL, Prasad VG, Krishna BV, Rao TS, Kumar LC, Rao GS et al. *In-vitro* anticholinergic activity of selected culinary spices on sheep airway smooth muscle. Int J Recent Sci Res. 2013;4:649-653.
- Tajuddin, Ahmad S, Latif A, Qasmi I A. Aphrodisiac activity of 50% ethanolic extracts of *Myristica fragrans* Houtt. (Nutmeg) and *Syzygium aromaticum* (L) Merr. & Perry. (Clove) in male mice: BMC Complement Altern Med. 2003;3:6.
- Tomás-Rodríguez MI, Palazón-Bru A, Martínez-St John DR, Toledo-Marhuenda JV, Asensio-García Mdel R, Gil-Guillén VF. Effectiveness of medical taping concept in primary dysmenorrhoea: a two-armed randomized trial. Sci Rep. 2015;5:16671.
- Unani Pharmacopoeia of India. Part II, Vol-II. 1st ed. (India, New Delhi: Dept. of Dept. of Ayurveda, Yoga, Unani, Sidda and Homeopathy), pp.116, 2010.
- Wallis TE. Text Book of Pharmacognosy. 5th ed. (India, New Delhi: CBS Publishers & Distributors), pp.230-231, 2005.
- Waring EJ. Pharmacopoeia of India. (India, Delhi: Asiatic Publishing House), pp.189, 2010.
- Wiat C, the Editor. Ch. 2. Plants affecting the central nervous system. In. Ethnopharmacology of Medicinal Plants: Asia and the Pacific. (USA, Totowa: Humana Press Inc), pp.57-58, 2007.