

# Phyto-pharmacological potential of Jaiphal (*Myristica fragrans* Houtt): A spice of medicinal importance and its utilization in Unani Medicine

Mohd Akhtar Ali<sup>1</sup>, Hamiduddin<sup>2</sup>, Mohammad Zaigham<sup>2</sup>, Mohd Ikram<sup>2</sup>

<sup>1</sup>Department of Ilmul Saidla, Unani Pharmacy, Z.H. Unani Medical College & Hospital, Siwan, Bihar, India,

<sup>2</sup>Department of Ilmul Saidla, Unani Pharmacy, National Institute of Unani Medicine Kottigepalya, Bengaluru, India

## Abstract

Jaiphal is a common fruit of *Myristica fragrans* Houtt. plant used as spices as well as for medicinal purpose in Unani System of Medicine since antiquity. The *Saydalaneh* (pharmacist) in Arab introduce a large number of new drugs to clinical use including nutmeg. As a Unani concept of temperament, it is hot and dry. It is very common and popular drug used as digestive, carminative, appetizer, exhilarant and mood elevator, antitussive, antiemetic, demulcent, aphrodisiac, stomachic, liver, nervine, cardio, and uterine tonic in Unani System of Medicine. Extensive information is provided in Unani text by Greek physicians about this drug so it is used in many compound formulations and useful recipes. These importance and benefits lead to further review to explore its medicinal importance. Review reveals digestive, appetizer, exhilarant and mood elevator, antitussive, antiemetic, nervine tonic, aphrodisiac, antiarrheal, liver tonic, cardiotoxic, and uterine tonic. Recent researchers indicate antimicrobial, hypolipidemic, antioxidant, anticancer, sedative, analgesic, and anti-inflammatory activity. Further, scope of research can also be explored with the help of traditional knowledge exist in Unani and other traditional medicine.

**Key words:** Digestive, Greek physician, jaiphal, Jozbua, *Myristica fragrans* Houtt., Unani Medicine

## INTRODUCTION

*Jozbua* is a fruit/seed of plant origin drug *Myristica fragrans* Houtt. with bitter and pungent aromatic taste<sup>[1]</sup> and is brown in color.<sup>[2]</sup> It has fragrant property and is hot in nature. It is more friable, and its bark is thin.<sup>[3]</sup> The best quality of nutmeg is that which gives fragrance, it is compact with shallow covering and is easily breakable. It has *Qabziyat* (astringent) property.<sup>[4,5]</sup> Nutmeg tree (*M. fragrans* Houtt.) is a bushy evergreen tree about 10–20 m in height, indigenous to India, Indonesia, and Sri Lanka. The nutmeg is ovoid, 2.0–3.5 cm long × 1.5–2.8 cm diameter, grayish brown in color with minute reddish-brown spots and lines and is reticulately furrowed. The cut surface has a waxy luster and a mottled appearance. It has strong aromatic odor.<sup>[1]</sup> East Indian nutmeg is available in three grades Banda Nutmeg, consider to be the finest for use and containing up to 8% essential oil, Siau Nutmeg, almost as good as Banda, but

containing 6.5% essential oil, and Penang Nutmeg, which is usually wormy and moldy and suitable only for distillation purposes.<sup>[1]</sup>

## Historical Aspect

Arabs and Muslims from vast Arab empire from the farthest corners met each other during pilgrimage to Mecca provided the exchange of both ideas and goods between people from China and India as well as from Spain. Thus, a lot of new medicines were introduced including nutmeg. On another side, *Saydalaneh* (pharmacist) in Arabic, managed

### Address for correspondence:

Dr. Hamiduddin, Department of Ilmul Saidla, Unani Pharmacy, National Institute of Unani Medicine, Kottigepalya, Magadi Main Road, Bengaluru - 560 091, Karnataka, India. E-mail: drhamid2003@rediffmail.com

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to introduce a large number of new drugs to clinical use, including nutmeg.<sup>[6]</sup> Nutmeg was brought to Europe in the middle ages by the Arabs through the Venetians. Nutmeg was so expensive a few 100 years ago that a small bag of it would have brought enough money for the possessor to be financially independent for the rest of his life.<sup>[7,8]</sup> Europe's wealthy people well knew about nutmeg, in middle ages it was in demand for its medicinal uses. According to Humoral theory, nutmeg was considered a "hot food," taken from ancient Greek medicine, which still guided physicians of European at the time. It could balance cold foods. Nutmeg had the advantage of being light-weight compared with jewels, pottery, or even silk cloth, so camel caravans and trading ships could easily carry a fortune in nutmeg.<sup>[9]</sup>

### Controversies

Papu nutmeg is derived not from *M. fragrance* but from the allied species *Myristica argentea* Warb.; it is sometimes classed as the fourth grade of East Indian nutmeg and can be disguised from the true nutmeg by its comparatively long size, peculiar shape, absence of external spots, poor aromatic odor, and acrid taste. Bombay nutmeg is obtained from *Myristica malabarica*; it is long and narrow in shape and destitute of aroma; it is used as an adulterant of true nutmeg. Fictitious nutmeg, the material is molded into shape and sometimes used as an adulterant of true nutmeg.<sup>[1]</sup>

## SCIENTIFIC/TAXONOMICAL CLASSIFICATION<sup>[10]</sup>

Kingdom: Plantae  
 Subkingdom: Viridiplantae  
 Infrakingdom: Streptophyta  
 Division: Tracheophyta  
 Subdivision: Spermatophytina  
 Class: Magnoliopsida  
 Superorder: Magnolianae  
 Order: Magnoliales  
 Family: Myristicaceae.  
 Genus: *Myristica* Gronov. nutmeg  
 Species: *Myristica fragrans* Houtt.  
 Botanical Name: *Myristica fragrans* Houtt.  
 Synonyms: *Myristica*, *Nux Moschata*.

### Habitat and Distribution

Native to the Moluccas Islands grown in the Nilgiris, Kerala, Karnataka, and West Bengal.<sup>[11]</sup> It is procured from India.<sup>[5,12]</sup> It is (fruit) from Jazayere Sumatra (Island of Sumatra in Indonesia) but now comes from India, grown in the Nilgiris,<sup>[13]</sup> Moluccas, Malayan peninsula, archipelago, Ceylon, Malabar, and part of tropical America.<sup>[14]</sup> It is found in area of Indian mountains, Asian islands.<sup>[15,16]</sup> Nutmeg tree is produced in the tropical areas indigenous of Indonesia and the West Indies,

tropical regions of Southeast Asia and Australasia. Nutmeg is inhabiting to the Banda islands of Indonesia's Moluccas or Spice Islands.<sup>[7,8]</sup>

Worldwide nutmeg production is estimated annually to average between 10,000 and 12,000 ton with annual world demand estimated at 9000 ton; Indonesia and Grenada lead production and exports, with a world market share of 75% and 20%, respectively. Other producers include India, Papua, Malaysia, Sri Lanka, New Guinea, and the Caribbean Islands. The main markets are the Europe, USA, India, and Japan. The Netherlands and Singapore they are major reexporters. Indonesia traditionally has been the main supplier of nutmeg to the US market, an average 65% of volume of total US imports of nutmeg per year.<sup>[3,17,18]</sup> The East Indian Islands of Siau, Ternate, Sangihe, Banda, and Ambon, produce highly aromatic nutmeg, traded as East Indian nutmeg.<sup>[18]</sup> In India, it is grown in Madras State (Nilgiris, Coimbatore, Salem, Ramanathapuram, Tirunelveli, Kanyakumari, and Madurai districts). A few trees are found in various localities of Kerala, Assam, and other states.

### Vernacular Name

Hindi: Jaiphal,<sup>[19]</sup> multi phal.<sup>[20]</sup> Urdu: Jauzbuwa, jaiphal.<sup>[19]</sup> Arabic: Jowz buwwa, jouza atteeb, (due to its smell), josat attib,<sup>[19]</sup> zanza-ba wawa.<sup>[21]</sup> English: Nutmeg.<sup>[19]</sup> Persian: Djus hendi, jous hendi,<sup>[22]</sup> jozbaweh.<sup>[5]</sup> Unani: Fuqlaj,<sup>[5]</sup> moschokarido.<sup>[22]</sup> Ayurvedic: Jaatiphala, jaatishasya, maalatiphala.<sup>[11]</sup> Assamese: Jayphal, kanivish,<sup>[19]</sup> jaiphal.<sup>[19]</sup> Bengali: Jayphala, jaepatri,<sup>[19]</sup> jaepatri.<sup>[21]</sup> Burma: Zadi-phu.<sup>[21]</sup> Chinese: Dauh kau syuh, yuhk dauh kau.<sup>[22]</sup> Dutch: Nootmuskaat, muskaatnoot.<sup>[22]</sup> French: Muscadier, musque.<sup>[21]</sup> German: Achter muscatnussbaum.<sup>[21]</sup> Gujarati: Jaiphala, javantri.<sup>[19]</sup> Hebrew: Egos muskat, egoz musqat.<sup>[22]</sup> Indonesian: Pala.<sup>[22]</sup> Kannada: Jadikai, jaykar, jajakai.<sup>[19]</sup> Kashmiri: Jafal,<sup>[19]</sup> zafal.<sup>[21]</sup> Korean: Neotumek, notumek, yuktugu.<sup>[22]</sup> Latin: Muscata.<sup>[22]</sup> Malayalam: Jatika,<sup>[19]</sup> bush.<sup>[21]</sup> Marathi: Jaiphal.<sup>[19]</sup> Nepali: Jaiphal.<sup>[22]</sup> Oriya: Jaiphola.<sup>[19]</sup> Punjabi: Jaiphal.<sup>[19]</sup> Russian: Opex muskatnyj orekh.<sup>[22]</sup> Sanskrit: Jati-phalam,<sup>[19]</sup> malathi-phalam.<sup>[19]</sup> Sindhi: Jafar,<sup>[23]</sup> jadika.<sup>[21]</sup> Spanish: Moscada,<sup>[22]</sup> nuez moscada.<sup>[22]</sup> Tamil: Sathkhai, jathikkai, jadikkay,<sup>[19]</sup> jadhikai, jadhikkai, jatikkai.<sup>[24]</sup> Telegu: Jajikaya.<sup>[19,21]</sup> Armenian: Meshgengouz, Mshkenkoyz, Mekenkouz, Greek: Moschokarido, Indonesian: Pala, Italian: Noce moscata, Portuguese: Noz-moscada, Romanian: Nucșoară, Turkish: Hindistancevizi, Uzbek: Musqat<sup>[25]</sup> Latin: *M. fragrans* Houtt.<sup>[3]</sup>

Morphology (*mahiyat*) mentioned in Unani text: Fruit kernel is oval or nearly round in shape, with length about one inch, and is marked externally with reticulated furrows and is internally grayish-red with dark brownish vein its odor is strong and peculiar and its taste is bitter and aromatic.<sup>[2,13,26]</sup> The outer covering of Jaiphal is known as Jawetri.<sup>[23]</sup> It has fragrant property and is hot in nature.<sup>[4,27]</sup> The best quality of

nut mug is that which have fragrance, compact with shallow covering, and easily breakable. It has *Qabziyat* (astringent) property.<sup>[4,5,28,29]</sup> According to 'Ali ibn al-'Abbas al-Majusi (died 994 AD), also known as *Masoudi*, or Latinized as *Haly Abbas*, the best quality of *Jaiphal* is heavy and its outer covering should be black.<sup>[30]</sup> It has *Quwwate Qabiza* (astringent activity) and *Rubate Fazlia* (excessive moisture).<sup>[31]</sup> Two types of oil are extracted from *Jaiphal*, one is white which is *Charpara* (Pungent) having fragrans of *Jaiphal* and other one is yellowish and thick oil which is also called butter of *Jaiphal*.<sup>[13]</sup> Its shelf life/life span is 3 years.<sup>[15,23,26]</sup> Color: Reddish<sup>[31]</sup>-brown in color,<sup>[2]</sup> grayish-brown in color.<sup>[1]</sup> Smell: Pleasant smell,<sup>[31]</sup> strong aromatic odor.<sup>[1]</sup> Taste: *Tez charpara* (more pungent), *Khush zaiqa* (Aromatic),<sup>[23,31]</sup> *Talkhi Mael* (Slightly bitter),<sup>[2]</sup> and pungent aromatic taste [Figure 1].<sup>[1]</sup>

*Mizaj* (temperament): hot 2° dry 3°,<sup>[2,15,21]</sup> HOT AND DRY 3°,<sup>[4,28,32]</sup> hot and dry 2°,<sup>[5,12,26]</sup> hot and dry 2° (from last of second to third degree),<sup>[29]</sup> hot in the last of second degree and dry in the third degree,<sup>[13,31]</sup> hot and dry,<sup>[27,30]</sup> *Motadil Mail Ba Rutoobat* (near normality with moisture).<sup>[33]</sup>

Pharmacological action (Afal) as per Unani literature: *Dafe' fasade balgham* (remover of abnormal phlegm)<sup>[15,34]</sup> *dafe' kalaf* (remover of melasma/cholasma),<sup>[4]</sup> *dafe' sua'l* (antitussive),<sup>[20,23]</sup> *dafe' ta'ffun* (antiseptic),<sup>[23]</sup> *dafe' wajul mafasil* (antilyartheritic),<sup>[23]</sup> *dafe' qai* (antiemetic),<sup>[20]</sup> *habisi-dam* (hemostyptic),<sup>[5]</sup> *hazim* (digestive),<sup>[5,15,20,26]</sup> *jadhibe rutubat* (desiccant),<sup>[5]</sup> *kasire riyah* (carminative),<sup>[2,23,31]</sup> *mudir* (diuretic),<sup>[4,11]</sup> *mufarrih* (exhilarant and mood elevator),<sup>[26,28,31]</sup> *mufatteh* (deobstruent),<sup>[20]</sup> *muhafize hararate ghareezi* (preserver of innate heat),<sup>[13,15,26]</sup> *muharrik* (stimulants),<sup>[13]</sup> *muharrike bah* (sexual stimulants),<sup>[23]</sup> *mujaffif* (desiccant),<sup>[23]</sup> *mukhaddir* (anesthetic) in large dose,<sup>[2,13]</sup> *mulattif* (demulcent),<sup>[26,28,31]</sup> *mumsik* (Retentive of semen),<sup>[13,20]</sup> *muqawwi-i-a'sab* (nervine tonic),<sup>[23]</sup> *muqawwi-i-baah* (aphrodisiac),<sup>[13,20,21]</sup> *muqawwi-i-basar* (tonic for eye),<sup>[4,12,32]</sup> *muqawwi-i-mi'da wa jigar* (stomachic and liver tonic),<sup>[28,30,32]</sup> *muqawwi-i-qalb* (cardio tonic),<sup>[20,28,34]</sup> *muqawwi-i-raham* (uterine tonic),<sup>[21]</sup> *musaffi-i-dam* (blood

purifier),<sup>[34]</sup> *musakkhin meda wa kabid* (calorific of stomach and liver),<sup>[28]</sup> *musakkin-i-alam* (analgesic),<sup>[4,28]</sup> *musammin-i-badan* (adipogenous),<sup>[23]</sup> *mushtahi* (appetizer),<sup>[20,27,34]</sup> *musaffie halaq* (throat cleanser),<sup>[20]</sup> *muskir* (narcotic),<sup>[26,31]</sup> *mutayyibe dehan* (mouth freshner),<sup>[4,5,12]</sup> *nafe ishal* (antidiarrheal),<sup>[31]</sup> *nafe tihal* (beneficial for spleen),<sup>[5,12]</sup> *qabiz* (astringent),<sup>[4,28,30]</sup> *qatil kirme shikam* (antihelmentic).<sup>[20,34]</sup>

Nafae Khas (specific action): *Dafe' sual* (antitussive),<sup>[2,23,33]</sup> *mufarrihe qalb wa dimagh* (exhilarant and mood elevator),<sup>[2,23]</sup> *muqawwie meda* (stomachic).<sup>[2,23]</sup>

Uses as per Unani literature: *Amraze barida* (phlegmatic ailments),<sup>[13,15,30]</sup> *amraze qalb* (cardiac diseases),<sup>[27]</sup> *aurame barida* (cold swelling),<sup>[15,26]</sup> *bukhar* (fever),<sup>[5,15]</sup> *busoore labania* (acne),<sup>[13]</sup> *dakar* (belch),<sup>[28]</sup> *dared shaqeeqa* (migraine),<sup>[2,13,15]</sup> *dast* (diarrhea),<sup>[13,21]</sup> *du'f al-bah* (anaphrodisia/loss of libido),<sup>[2,27]</sup> *du'f al-basar* (asthenopia/amblyopia),<sup>[4,5,29]</sup> *du'fe hararte garizi* (innate heat insufficiency),<sup>[2]</sup> *du'fe jigar* (hepatic insufficiency),<sup>[4,5,29]</sup> *du'fe jigar wa tihal* (hepatosplenic insufficiency),<sup>[4,12]</sup> *du'fe mari* (esophageal insufficiency),<sup>[13]</sup> *du'fe me'da*, (delayed digestion),<sup>[4,5,29]</sup> *du'fe qalb* (cardiac insufficiency),<sup>[2]</sup> *du'fe tihal* (splenic insufficiency),<sup>[4,29]</sup> *falij* (paralysis),<sup>[13,15,26]</sup> *ganda dehni* (insanitary mouth),<sup>[5,26,28]</sup> *ishale shikam* (stomachy diarrhea),<sup>[5,26,28]</sup> *istirakha* (atony/flaccidity),<sup>[5]</sup> *istisqaye lahmi* (anasarca),<sup>[5,15,34]</sup> *kalaf or jhaen* (melasma/cholasma),<sup>[4,15,34]</sup> *khadar* (narcotic effect),<sup>[15]</sup> *kharish* (pruritis),<sup>[5,13,15]</sup> *kharishe palak* (pruritis of eye lids),<sup>[31]</sup> *kuzaz* (tetanus),<sup>[13,15,28]</sup> *laqwa* (facial paralysis),<sup>[13,15,28]</sup> *nafakhe shikam* (flatulence),<sup>[2]</sup> *namsh (lahsan)* (naevus),<sup>[13,26,29]</sup> *nazla* (coryza),<sup>[13]</sup> *qai* (vomiting),<sup>[5,15,31]</sup> *ra'sha* (tremor),<sup>[15,26]</sup> *ratqe ama'* (intestinal atresia),<sup>[26]</sup> *riyahi amraz* (flatus diseases),<sup>[26,27]</sup> *rutoobat fasida* (putrid humor),<sup>[5]</sup> *salabate tihal* (chronic splenitis),<sup>[15]</sup> *salabte jigar* (cirrhosis of liver),<sup>[5,15,26]</sup> *salsul baul* (dribbling of urine),<sup>[13]</sup> *siqle sama't* (hearing impairment),<sup>[31]</sup> *subul (jala)* (vascular keratitis),<sup>[15,28,29]</sup> *sue hazm* (indigestion),<sup>[28]</sup> *surate inzal* (premature ejaculation),<sup>[5,27]</sup> *tanqiye riyah* (elimination of morbid material from lungs),<sup>[4]</sup> *taskheen* (calorification),<sup>[3]</sup> *usrul baul* (dysuria),<sup>[5,29,31]</sup> *wajul mafasil* (polyarthritis),<sup>[2,13,15]</sup> *warme jigar* (hepatitis),<sup>[13]</sup> *warme tihal* (splenitis),<sup>[2,13,28,]</sup> *yarqan* (jaundice),<sup>[13,15,26]</sup> *zalq al-Am'a'* (lenteric diarrhea),<sup>[5]</sup> *zukam* (catarrh).<sup>[27]</sup>



Figure 1: Jaiphal (*Myristica fragrans* Houtt.)

## PHARMACOLOGICAL ACTION AND USES AS PER OTHER LITERATURE

### Ayurveda

Digestive, deobstruent, liver tonic, cardiogenic, appetizer.<sup>[13]</sup> In Ayurveda used for Thrust, hoarseness of voice, diarrhea, worms infestation,<sup>[13]</sup> asthenopia/amblyopia, delayed digestion, hemiplegia, flatulence, vomiting, epilepsy, headache, intestinal spasm, toothache, polyarthritis, general weakness, catarrh,<sup>[13]</sup> insomnia, eczema, diarrhea, hiccups, dehydration, running nose, rheumatism,<sup>[35]</sup> *atisara* (diarrhea), *svasa* (dyspnea), *chardi* (vomiting), *kasa* (cough), *pinasa*



(rhinitis), *grahani* (ulcers), *mukharoga* (oral cavity disorders), *âukrameha*.<sup>[24]</sup>

### Ethnomedicine (Tribal Medicine) and other Traditional Medicine

Aphrodisiac, astringent,<sup>[21]</sup> carminative,<sup>[14,21]</sup> digestive tonic,<sup>[21]</sup> narcotic (in larger dose),<sup>[14,21]</sup> rubefacient,<sup>[21]</sup> stimulant.<sup>[14,21]</sup> Used for atonic diarrhea, dyspepsia, flatulence, flatulence colic.<sup>[14]</sup> The Chinese consider it to be an aphrodisiac. Conventionally, it is used in digestive disorders such as nausea and diarrhea and for kidney ailments (in Southeast Asia), fevers, headaches, and bronchial problems.<sup>[3]</sup>

### Non-medicinal Use

Nutmeg, especially in the ground form, is used mainly in the food processing industry as a spice, cooking, or baking. Used as an ingredient in the pungent garam masalas (Spice) of North India.<sup>[3]</sup> The oleoresin of nutmeg finds use in the preparation of vegetables, meat, and to flavor milk dishes, soft drink, punches, and canned food.<sup>[3,36]</sup> Camphene presents in the oil of nutmeg is used in the manufacture of camphor and related compounds. Pinene one of the essential oils of nutmeg is used to make camphor, plasticizers, solvents, perfume bases, and synthetic pine oil. Myristic acid is used as a flavor ingredient in the food industry and also finds use in the preparation of soap, liquid detergents, shaving creams, shampoos, plastics, and perfumes, also used in compounding rubber, paints, and greases, in the synthesis of esters for flavors and perfumes and as a part of good-grade additives. The constituents of nutmeg myristicin, elemicin, and isoelemicin when presented in aroma form, they act as stress relievers.<sup>[3]</sup>

### Mazarrat (Toxicity)

Unani: For lungs<sup>[15,26,32]</sup> produce headache,<sup>[13,26,31]</sup> for *jigar* (liver)<sup>[13,28,33]</sup> for *mahrureen* (hot temperament people),<sup>[13,31]</sup> for *tihal* (spleen).<sup>[34]</sup>

### Toxicity as Per Conventional Literature

Nutmeg poisoning is very rare but probably under reported and should be considered in recreational substance users with acute psychotic symptoms and central nervous system neuromodulatory signs that may mimic in part an anticholinergic hyperstimulation.<sup>[37]</sup> Myristicin, 1-allyl-3, 4-methylenedioxy-5-methoxybenzene, a naturally occurring alkenylbenzene found in nutmeg, produced neurotoxicity. Myristicin at  $> - 0.5$  mM concentration showed cytotoxic effects in human neuroblastoma cells.<sup>[38]</sup> Nutmeg contains the active ingredient myristicin, which produced narcotic properties. Nutmeg butter contains elemicin and myristicin, which cause psychotropic effects. Taking in large quantities produces narcosis, drowsiness, delirium, epileptic convulsions,

and even death. It also may cause temporary constipation and difficulty in urination and excessive fat deposition in the liver. Nutmeg in powdered form is used occasionally as a hallucinogenic drug.<sup>[3]</sup> Toxicological detection of nutmeg abuse is possible by identification of the described metabolites myristicin, elemicin, and safrole in urine.<sup>[39]</sup>

A case of acute nutmeg poisoning was reported with numerous neurological symptoms and signs along with non-specific electrocardiographic changes and anticholinergic-type symptoms.<sup>[40]</sup> Despite antioxidant properties prolonged use at high doses (400–500 mg/kg) can cause low sperm count.<sup>[41]</sup> Several allylbenzene derivatives have been identified as psychotropic constituents. It suggests that the intensity of the hallucinogenic action of these compounds may be due to the possibility of simulation of LSD-like structural elements.<sup>[42]</sup> Alkaloid extract at a dose of 1 g/kg significantly reduced the number of writhing responses in female, but not in male mice; 0.5 g/kg of alkaloid extract had no effect in either sex. The LD<sub>50</sub> was 5.1 g/kg. Signs of abnormal behavior including hypoactivity, unstable gait, and dizziness were seen in animals given a dose of 4 g/kg or higher, lasted for several hours after administration of the alkaloids. Loomis and Hayes classified *M. fragrans* seed alkaloids as analgesic and slightly toxic.<sup>[43]</sup> The anti-inflammatory property of the seed also suggests that it may have damaging effects on hemopoiesis at high doses.<sup>[44]</sup>

### Musleh (Corrective)

*Kishneez* (*Coriandrum sativum* Linn.)<sup>[2,23,29]</sup> for *suda*<sup>[13,26]</sup> *bnafsha* (*Viola odorata* L.)<sup>[13,26]</sup> *shahad* (honey)<sup>[13,15,32]</sup> *sandal* (*Santalum album* L.) for *jigar haar* (hot liver)<sup>[13,28]</sup> *mastagi roomi* (*Pistacia lentiscus* Linn.)<sup>[33]</sup> milk of sheep<sup>[20]</sup> large dose produce *Sue halaq* (uncomfortable in throat) and *humuq* (stupidity).<sup>[26]</sup>

### Badal (Substitute)

*Jawetri/Bisbasa* (Mace, *M. fragrans* Houtt.)<sup>[13,23,31]</sup> 1½ *guna jawetri*<sup>[5,28,32]</sup> *sunbul hindi* (*balchar*, *Nardostachys jatamansi* DC.)<sup>[2,28]</sup> *sunbul* (Musk-root) 1½ *Guna* (of weight of Jaiphal)<sup>[15,29,32]</sup>

### Miqdare Khurak (Dose)

9 *masha* (9 g),<sup>2</sup> 4–9 g,<sup>[13,31]</sup> ½ to 1 *masha*,<sup>[2,12,23]</sup> *nisf* (half) *dirham* (1.75 g),<sup>[28]</sup> 2 *dirham* (7 g),<sup>[32]</sup> 2 *misqal* (9 g).<sup>[26]</sup>

### Murakkabat (Unani Formulation)

Anushdaru, arqe chob chini, arqe maullaham khas,<sup>[45]</sup> habbe a'sab,<sup>[2]</sup> habbe mumsik wa mubahhi,<sup>[45]</sup> habbe muqawwi,<sup>[27]</sup> habbe zafaran,<sup>[45]</sup> jawarishe ood shirin,<sup>[2]</sup> kushtae faulad,<sup>[46]</sup> kushtae hadtal,<sup>[45]</sup> kushtae qalai,<sup>[46]</sup> kushtae sange basari,<sup>[45]</sup>

kushtae sange jarahat,<sup>[46]</sup> kushtae shangarf,<sup>[45]</sup> kushtae tanba,<sup>[45]</sup> kushtae abrak, luboobe kabeer,<sup>[45]</sup> ma'joone chob chini,<sup>[2,27]</sup> majune aarade khurma, majune baladur, majune chob chini, majune fanjanush majune jalali majune khas majune lana majune madan mast majune muluki majune murawwihul arwah majune nankhah majune salab majune supari pak,<sup>[45]</sup> mardana sihat,<sup>[27]</sup> mufarreh mutadil,<sup>[45]</sup> roghane shangarf,<sup>[47]</sup> safoofe mughalliz jadid,<sup>[45]</sup> safoofe namake sulaimani khas,<sup>[45]</sup> salayae shangarf,<sup>[48]</sup> shangarf shagufta,<sup>[47]</sup> talae shahi,<sup>[45]</sup> tashwiae shangarf,<sup>[4]</sup> tilae khasul khas, tilae majluq.<sup>[45]</sup>

## Chemical Composition

Principal constituents of nutmeg are fixed oil, volatile oil,<sup>[14,27,48]</sup> and starch. It also contains proteins<sup>[13]</sup> cellulose, pentosans, resin, and mineral elements. Volatile oil is responsible for flavor and therapeutic action.<sup>[49]</sup> Nutmeg is a good source of potassium, phosphorus, and magnesium. Nutmeg is reported to contain moisture, 14.3%; protein, 7.5%; carbohydrates, 28.5%; fiber, 11.6%; ether extract, 36.4%; and mineral matter, 1.7%; phosphorus, 0.24%; calcium, 0.12%; and iron, 4.6 mg/100 g. It contains volatile oil (6–16%), starch (14.6–24.2%), pentosans (2.25%), furfural (1.5%), and pectin (0.5–0.6%). It is a fair source of vitamins.<sup>[50]</sup> The constituents of nutmeg can be broadly classified into terpenoids, fatty acids, phenolic acids, lignans, neolignans, and miscellaneous compounds.

## Fixed Oil

Nutmeg contains 25–50% lipids as fixed oil mainly of myristic, petroselinic, and palmitic acids, the major component of fixed oil is trimyristin.<sup>[51]</sup> The expressed or extracted fixed oil is an orange-colored aromatic semisolid, also known as concrete or nutmeg butter.<sup>[16]</sup> Nutmeg butter mainly contains saturated fats (90%) with 10% unsaturated fats. The major classes of compounds constituting the oil as: Monoterpene hydrocarbons, 61–88%; oxygenated monoterpenes, sesquiterpenes, alkenes, aromatic ethers, aromatic monoterpenes, organic acids, and miscellaneous compounds. Nutmeg consists 35.7% total lipids, 74.9% of which is myristic acid.<sup>[51]</sup>

## Volatile Oil

Depending on the source, the essential oil of nutmeg contains mainly sabinene (15–50%),  $\alpha$ -pinene (10–22%) and  $\beta$ -pinene (7–18%) with myrcene (0.7–3%), 1,8-cineole (1.5–3.5%), myristicin (0.5–13.5%), limonene (2.7–4.1%), saffrole (0.1–3.2%),  $\alpha$ -thujene (2.2%), and terpinen-4-ol (0–11%), camphene (0.3%),  $\alpha$ -phellandrene (0.7%),  $\delta$ -3-carene (0.8%),  $\alpha$ -terpinene (2.2%), p-cymene (0.7%), 1,8 cineol+  $\beta$ -phellandrene (2.3%),  $\gamma$ -terpinene (3.9%), terpinolene (1.2%), (Z)-P-menth-2-en-1-ol (0.4%), trans-sabinene hydrate (0.5%), linalool (0.8%), (E)-P-menth-2-en-1-ol (0.3%),  $\alpha$ -terpineol (0.6%), eugenol (0.4%), methyl

eugenol (1.6%),  $\beta$ -caryophyllene (0.2%),  $\beta$ -cubebene (0.1%), trans-methyl isoeugenol (0.2%), trans- $\alpha$ -bergamotene (0.1%), germacrene D (0.1%), and elemicin (2.4%).<sup>[17]</sup> Oils consist 85–93% monoterpene hydrocarbons, 6.6–12% oxygenated monoterpenes and sesquiterpenes, and 3.5% aromatic ethers. Irradiation of nutmeg may leads to the breakdown of triacylglycerols, releasing free fatty acids.<sup>[52]</sup>

A study was evaluated by extraction it using absolute ethanol ratio 1:4, at 25°C using gas chromatography–mass spectrometry. The result showed that the yield ranged from 4.55 to 9.63% and 53 compounds of oleoresin have been identified to account for >90% of the total oil content. Sabinene, myristicin,  $\alpha$ -pinene, elemicin,  $\beta$ -pinene, terpinen-4-ol, limonene, and myristic acid were found as major compounds of all the nutmeg oleoresins acquired by different techniques.<sup>[53]</sup>

## Leaf Oil

The leaves of *M. fragrans* Houtt. yield 0.5–2.0% volatile oil. Myristicin and elemicin were present in the oil of the nut, mace, and leaves. The predominant leaf oil of nutmeg is monoterpenes.<sup>[54]</sup> Major identified constituents of leaf oil were sabinene+  $\beta$ -pinene (25.95–38.90%),  $\alpha$ -pinene (8.62–34.64%), and limonene (4.17–8.96%) flower oil: The chief components of the nutmeg flowers oil are sabinene, pinenes,  $\alpha$ -terpineol, terpinen-4-ol, and elemicin.<sup>[55]</sup>

The non-volatiles from nutmeg comprise lignans, phenolic acids, sterols, glycosides, and miscellaneous compounds. The fractionation of the aril of *M. fragrans* Houtt. (mace spice) guided by bioassay yielded five phenolic compounds, one new acyclic bis phenylpropanoid that displayed potent NF- $\kappa$ B inhibition (IC<sub>50</sub> = 1.5 nM and 3.4 nM, respectively).<sup>[56]</sup>

## Lignans

Several lignans and neolignans have been isolated from nutmeg.<sup>[55]</sup> It consists 8-O-4' neolignans, for example, erythro- $\Delta$ 8'-4,7-dihydroxy-3,3',5'-trimethoxy-8-O-4'neolignan and  $\Delta$ 8'-4-hydroxy-3,3',5'-trimethoxy-8-O-4'-neolignan, was determined.<sup>[57]</sup>

## Sterols

The sitosterol sterols were predominant in nutmeg. Other sterols reported were campesterol, desmosterol, and lanosterol.<sup>[58]</sup>

## Aroma Glycosides

The principal glycosidical bound volatiles of nutmeg were p-cymene-7-ol rutinoside and methyl eugenol glucosides of eugenol, and  $\alpha$ -terpineol.<sup>[59]</sup> The main aglycones as isoeugenol (46.1%) and methoxy eugenol (27.7%). The aglycones, namely, pulegone (5.6%), *cis*-isoeugenol (3.7%),  $\beta$ -thujone

(3.4%), cuminol (3.3%), isoelemicin (3%), eugenol (2.8%), and isoeugenol (2.3%) in minor quantities terpinen-4-ol (1%) were present.<sup>[60]</sup>

### Elemental Contents of Nutmeg

The quantity of element in nutmeg is Mg (0.45%), Al (210 mg/kg), Si (167 mg/kg), P (0.17%), S (0.14%), Cl (402 mg/kg), K (0.63%), Ca (0.30%), Ti (13 mg/kg), Mn (124 mg/kg), Fe (151 mg/kg), Cu (73 mg/kg), Zn (44 mg/kg), Br (95 mg/kg), Rb (32 mg/kg), and Sr (11 mg/kg).<sup>[49]</sup> Current information shows furanocoumarins in nutmeg could be useful in the development of new drugs for the treatment of different diseases that suggest an opportunity that furanocoumarins can be further developed as a potential disease-curing remedy.<sup>[61]</sup>

### Reported Pharmacological Activity

#### Antimicrobial activity

Nutmeg oil showed a strong antibacterial activity against 25 genera of bacteria.<sup>[62]</sup> It exhibited strong activities against *Bacillus subtilis*, *Saccharomyces cerevisiae*, and *Escherichia coli*.<sup>[63]</sup> Camphene presents in the oil that has strong antibacterial, antifungal, and insecticidal properties.<sup>[64]</sup> The extract of nutmeg possessed strong antibacterial activity against non-pathogenic and pathogenic *E. coli*, but the strain O157 showed more sensitive to  $\beta$ -pinene than non-pathogenic *E. coli* strains.<sup>[65]</sup> The seeds extract in chloroform showed potent antibacterial activity against Gram-positive and Gram-negative bacteria. Trimyristin and myristic acid also showed good antibacterial activity that was isolated from the extract.<sup>[66]</sup>

Methanol extract of nutmeg possessed strong inhibition against *Streptococcus mutans*, a pathogen associated with the happening of dental caries. The minimum inhibitory concentration (MIC) of macelignan against *S. mutans* was 3.9  $\mu\text{g/mL}$ , which was much lower than of other natural agents having anticariogenic activity such as 15.6  $\mu\text{g/mL}$  of sanguinarine, 250  $\mu\text{g/mL}$  of eucalyptol, 500  $\mu\text{g/mL}$  of menthol and thymol, and 1000  $\mu\text{g/mL}$  of methyl salicylate. In the bactericidal test, macelignan at a concentration of 20  $\mu\text{g/mL}$  inactivated *S. mutans* completely in 1 min. The specific activity and quick effect of macelignan against oral bacteria powerfully suggest that it could be employed as a natural antibacterial agent in useful foods or oral care products.<sup>[67]</sup>

#### Insecticidal and Repellent Activity

Essential oil extracted from nutmeg was tested against *Lasioderma serricorne* for insecticidal and repellent activity. The study shows that its active constituents would be suitable for its development as a natural insecticides and repellents to control *L. serricorne*.<sup>[68]</sup> Insecticidal activity of nutmeg

oil has a powerful antifeedant activity, contact toxicity, and fumigant toxicity against the stored product insects.<sup>[64]</sup>

#### Antiamebic Activity

The nutmeg essential oil at a concentration of 0.5  $\mu\text{L/mL}$  is active against *Entamoeba histolytica*.<sup>[69]</sup> The nematicidal activity of essential oil of nutmeg exhibits potent nematicidal activity against the root-knot nematode, *Meloidogyne incognita*.<sup>[70]</sup>

#### Antifungal Activity

Nutmeg seeds extract in methanol showed strong antifungal activity *in vitro* and *in vivo* against numerous plant pathogens. From the methanol extract, the three lignans isolated, namely, erythro-austrobailignan-6 (EA6), meso-dihydroguaiaretic acid, and nectandrin-B (NB), showed varied antimicrobial activity on the target species.<sup>[71]</sup> The potentials of essential oil and acetone extract of nutmeg as antifungal, antibacterial, and antioxidant were carried out by different techniques. Radical scavenging capacity was carried out on 2, 2'-diphenyl-1-picrylhydrazyl radical, and they showed potent scavenging activity in comparison with synthetic antioxidants with reducing power. Major component was sabinene (20.22%), followed by terpinen-4-ol (12.08%), safrole (10.32%),  $\alpha$ -pinene (9.7%),  $\beta$ -phellandrene (6.56%), and  $\gamma$ -terpinene (5.93%).<sup>[72]</sup> Rahman *et al.* reported antifungal activity of essential oil from nutmeg.<sup>[64]</sup>

#### Hypolipidemic Activity

Ram *et al.* evaluated ethanolic extract of nutmeg kernels as a hypolipidemic activity in albino rabbits. 500 mg/kg of the extract administered per day for 60 days in the hyperlipidemic rabbits resulted in significantly lower levels of lipoprotein lipids.<sup>[73]</sup>

#### Antioxidant Activity

The aglycone fraction from glycosidically bound volatiles of nutmeg had a stronger antioxidant activity compared with free volatiles from its essential oil.<sup>[60]</sup> Higher antioxidant activity of nutmeg oil was reported at 180°C. This might be due to the volatilization of the hydrocarbons at higher temperature, resulting in the accumulation of phenolic constituents in the remaining oil. Administration of eugenol (10.7 mg/kg of body weight/day) removes the oxidative stress from rats imposed by CCl<sub>4</sub>. Eugenol, an allylbenzene and ingredient of nutmeg, that inhibits the accumulation of lipid peroxidation products in red blood cells and maintains the antioxidant enzymatic activities such as superoxide dismutase, glutathione peroxidase, catalase, glutathione-S-transferase(s), glutathione reductase, and glucose-6-phosphate dehydrogenase at normal levels.<sup>[74]</sup>



Anticholinesterase activity tested of the ethyl acetate fraction of the methanol extract of *M. fragrans* Houtt. seeds isolated by various chromatographic techniques demonstrate it could be used beneficially in the treatment of Alzheimer's disease.<sup>[75]</sup>

### Anticancer Activity

The lignan constituents in the nutmeg are anticarcinogenic. The essential oil of nutmeg possesses admirable anticarcinogenic activity, which have been well documented involving animals. The essential oil interferes with the activities of the host enzymes associated with activity and detoxicity of xenobiotic compounds including chemical carcinogens and mutagens.<sup>[76]</sup> *In vitro* and *in vivo* mutagenic and antimutagenic effects of aqueous fraction of *M. fragrans* Houtt. (AFMF) leaves on TA100 strain of *Salmonella typhimurium* and *Mus musculus* (male Swiss albino mice), respectively, reveal that phytochemical is responsible for the observed antimutagenic activity. AFMF seems to contain a promising chemotherapeutic agent for the prevention of genetic damage that is crucial for cancer development.<sup>[77]</sup>

The water extracts from the seeds of *M. fragrans* Houtt. inhibit the *in vitro* enzymatic activity of lactate dehydrogenase. The results showed as a potential candidate for the development into a novel drug against cancer through inhibition of lactate dehydrogenase activity.<sup>[78]</sup> A study of myrislignan on A549 cells *in vitro* and *in vivo* reveal a potential mechanism for the anticancer effect of myrislignan on human lung cancer, while suggesting that myrislignan may be a capable compound for the management of lung cancer.<sup>[79]</sup>

### Aphrodisiac Activity

The nutmeg and clove extracts were found to stimulate the mounting behavior of male mice, and also to considerably increase their mating performance. Hence, ethanolic extracts (50%) of nutmeg and clove improved the sexual behavior of male mice.<sup>[80]</sup> Oral administration of the extract of nutmeg at the dose of 500 mg/kg produced significant and constant increase in the sexual power of normal male rats without any noticeable adverse effects indicates that the 50% ethanolic extract possesses aphrodisiac activity, increasing both potency and libido, which could be attributed to its nerve stimulating property. The study provides a scientific rationale and justification for the traditional use of nutmeg in the management of male sexual disorders.<sup>[81]</sup>

### Anxiogenic, Analgesic, and Sedative Activities

Sonavane *et al.* tested n-hexane extract of *M. fragrans* Houtt. seeds, acetone-insoluble part of the n-hexane extract (AIMF), and trimyristin (TM) for their anxiogenic activity when given intraperitoneally exhibited anxiogenic activity.<sup>[82]</sup>

*M. fragrans* Houtt. increased the duration of pentobarbitone-induced sleep and amplified the severity of haloperidol-induced catalepsy. The extract of nutmeg reduced the acetic acid-induced writhing and increased reaction time when placed on the hot plate. The extract of nutmeg exhibited a wide margin of safety and did not produce mortality in dose up to 3.0 g/kg, i. p.<sup>[83]</sup>

### Antidepressant Activity

N-hexane extract of *M. fragrans* Houtt. seeds studied on depression in mice using the forced swim test (FST) and the tail suspension test (TST), extract elicited significant antidepressant-like effect in both the TST and the FST.<sup>[84]</sup>

### Anti-inflammatory Activity

Five new 8-O-4' type neolignans, named myrifralignan A-E (1-5), together with five known analogs (6-10), were isolated from the seeds of *M. fragrans* Houtt. Their chemical structures were established using several spectroscopic methods. These results illustrated that the 8-O-4' type neolignans are capable candidates as anti-inflammatory agents.<sup>[85]</sup> A study was evaluated in which used the CFA-injected rats as a sustainable pain model to test the anti-inflammatory and analgesic effect of nutmeg oil. The result showed to be a potential chronic pain reliever through inhibition of COX-2 expression and blood substance P level.<sup>[86]</sup>

### Hepatoprotective Activity

Study done on in rats with liver damage caused by lipopolysaccharide (LPS) plus d-galactosamine (D-GalN) revealed that myristicin one of the major essential oils of nutmeg markedly suppressed LPS/D-GalN-induced enhancement of serum tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ) concentrations and hepatic DNA fragmentation in mice, suggests hepatoprotective activity of myristicin may be due to the inhibition of TNF- $\alpha$  release from macrophages.<sup>[87]</sup> Sohn *et al.* investigated protective effect of macelignan, isolated from *M. fragrans* Houtt. against cisplatin-induced hepatotoxicity in mice showed protective effects of macelignan on cisplatin-induced hepatotoxicity.<sup>[88]</sup>

### Anticonvulsant Activity

Volatile oil of nutmeg tested for its effects in maximal electroshock, subcutaneous pentylenetetrazole, strychnine, and bicuculline seizure tests. The results indicate its effect against grand mal and partial seizures, it prevents seizure. Slight potentiation of clonic seizure activity limits its use for the treatment of myoclonic and absence seizures.<sup>[89]</sup>

### Anticariogenic Activity

Extract of *M. fragrans* Houtt. possessed strong inhibitory activity against *S. mutans*. The anticariogenic compound macelignan isolated from the methanol extract of *M. fragrans*, MIC of macelignan against *S. mutans* was 3.9 µg/mL, which was much lower than those of other natural anticariogenic agents such as 15.6 µg/mL of sanguinarine, 250 µg/mL of eucalyptol, 500 µg/mL of menthol and thymol, and 1000 µg/mL of methyl salicylate. Macelignan also possessed preferential activity against other oral microorganisms such as *Streptococcus sobrinus*, *Streptococcus salivarius*, *Streptococcus sanguis*, *Lactobacillus acidophilus*, and *Lactobacillus casei* in the MIC range of 2–31.3 µg/mµ.<sup>[67]</sup>

### Antidiarrheal Activity

Nutmeg crude suspension and petroleum ether (PE) decreased the mean number of loose stools or increased the latency period. Overall, extracts of nutmeg showed a good antidiarrheal effect, with a significant sedative property. The extracts possessed only a weak analgesic effect.<sup>[90]</sup>

### Antiplatelet Activity

Han *et al.* investigated the antiplatelet activity of a series of neolignans isolated from *M. fragrans* Houtt. using human

platelets. Compound 1 showed the strong IC<sub>50</sub> value of 3.2 ± 0.4, it displayed antiplatelet activity.<sup>[91]</sup>

## DISCUSSION AND CONCLUSION

The present review illustrates therapeutic importance of nutmeg in Unani medicine text as well as recent research activities performed on it. Several Unani formulations containing nutmeg and nutmeg itself are indicated as digestive, carminative, appetizer, exhilarant and mood elevator, antitussive, antiemetic, sexual stimulants, demulcent, nervine tonic, aphrodisiac, stomachic, antidiarrheal, liver tonic, cardiogenic, and uterine tonic. Recent researchers also validated the indications of *M. fragrans* Houtt. in Unani Medicine. Besides, traditional therapeutic utilization in Unani medicine its new indications such as antimicrobial, antiamebic, antifungal, hypolipidemic, antioxidant, anticancer, anxiogenic, sedative, analgesic, and anti-inflammatory activity make it more valuable and important easily available household drug [Table 1]. Further, scope of research can also be explored with the help of traditional knowledge exist in Unani and other traditional medicine.

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**Table 1:** Some useful pharmacological activities of *M. fragrans* and its constituents

Pharmacological activities	Chemical constituents
Antibacterial activity <sup>[62-67]</sup>	Trimyristin and myristic acid, <sup>[66]</sup> macelignan <sup>[67]</sup>
Insecticidal and repellent activity <sup>[64,68]</sup>	Essential oil <sup>[64]</sup>
Antiamebic activity <sup>[69,70]</sup>	Essential oil <sup>[70]</sup>
Antifungal activity <sup>[64,72]</sup>	Lignans-EA6, MDA and NB, <sup>[71]</sup> sabinene, terpinen-4-ol, safrole, α-pinene, β-phellandrene, and γ-terpinene <sup>[64]</sup>
Hypolipidemic activity <sup>[73]</sup>	Ethanol extract <sup>[73]</sup>
Antioxidant activity <sup>[60,74,75]</sup>	Eugenol <sup>[74]</sup>
Anticancer activity <sup>[76-79]</sup>	Myrislignan <sup>[79]</sup>
Aphrodisiac activity <sup>[80,81]</sup>	Ethanol extract <sup>[80,81]</sup>
Anxiogenic, analgesic and sedative activities <sup>[82,83]</sup>	N-hexane extract and trimyristin <sup>[82]</sup>
Antidepressant activity <sup>[84]</sup>	N-hexane extract <sup>[84]</sup>
Anti-inflammatory activity <sup>[85,86]</sup>	8-O-4' type neolignans, named myrifralignan A-E (1-5) <sup>[85]</sup>
Hepatoprotective activity <sup>[87,88]</sup>	Myristicin, <sup>[87]</sup> macelignan <sup>[88]</sup>
Anticonvulsant activity <sup>[89]</sup>	Volatile oil <sup>[89]</sup>
Anticariogenic activity <sup>[67]</sup>	Macelignan <sup>[67]</sup>
Antidiarrheal activity <sup>[90]</sup>	Crude suspension and PE extract <sup>[90]</sup>
Antiplatelet activity <sup>[91]</sup>	Series of neolignans <sup>[91]</sup>

Some chemical constituents of *M. fragrans*. Fixed oil - myristic, petroselinic, palmitic acids, and trimyristin.<sup>[51]</sup> Volatile oil - sabinene, α-pinene, and β-pinene.<sup>[52]</sup> Lignans - 8-O-4' neolignans,<sup>[57]</sup> sterols - sitosterol, campesterol, desmosterol, and lanosterol.<sup>[58]</sup> Aroma glycosides - p-cymene-7-ol rutinoside and methyl eugenol glucosides of eugenol, and α-terpineol,<sup>[59]</sup> EA6: Erythro-austrobailignan-6, MDA: Meso-dihydroguaiaretic acid, NB: Nectandrin-B, PE: Petroleum ether



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