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Review Article

THERAPEUTIC PROPERTIES OF JATIPAL - *MYRISTICA FRAGRANCE*. HOUTT

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A B S T R A C T

Myristica fragrans Houtt, traditionally known as Jatiphal and Javitri in India, belongs to the family Myristicaceae is known for its flavour and therapeutic action since 18th centaury in alternative medicinal systems. It is a good body detoxifier, stimulates the brain. Ethanol extract shows antifungal, spasmolytic, carminative, hepatoprotective, antiviral, anticarcinogenic, antioxidant, antimicrobial properties. Nutritionally, nutmeg is rich in energy, carbohydrates, proteins and dietary fibre. Seed is a rich source of vitamins. It also contains electrolytes minerals and phytonutrients including carotene-B and crypo-xanthin . *Myristica fragrans* has a lot of industrial applications in liqueurs, soap production and cosmetics. This review article elucidates the information regarding the phytochemistry and pharmacological activity of the plant which provides the basis for further research.

Keywords: Myristica, Myristicin, Detoxifier, Jatiphala, Nutmeg.

INTRODUCTION

Nutmeg (*Myristica fragrans*) Houtt (Family: Myristicaceae), an aromatic plant whose seed is widely used as a spice, is a tropical, dioeciously evergreen tree native to the Moluccas or Spice Island of Indonesia, in India it is found mostly in Tamil Nadu and to some extent in Kerala, Andhra Pradesh and Assam. Nutmeg has a characteristic pleasant fragrance and is slightly warm taste, mostly related to various activities of their essential oils, such as antimicrobial, antioxidant, antifungal spasmolytic, carminative, hepatoprotective, antiviral, anticarcinogenic (O.A. Olajide, F.F.1999) (Tajuddin, *et.al* 2003), memory enhancer, antidiarrheal (J.K. Grover, S. Khandkar *et.al*.,2002), anti inflammatory etc. It is found effective as a stimulant, carminative as well as for intestinal catarrh and colic. It stimulates appetite, control flatulence, and has a reputation as an emmenagogue (to promote and regulate menstrual flow) and abortifacient (Green, 1959; Panayotopoulos and Chisholm, 1970).

It is used in alternative medicine as it has been reported to have a variety of active phytochemicals including vitamins, carotenoids, terpenoids, alkaloids, flavonoids, lignans and phenolics, etc. These compounds render their effects via different mechanisms such as radical scavenging, metal chelating, and inhibition of lipid peroxidation and quenching of singlet oxygen to act as antioxidants.

Nutmeg is used to flavour many kinds of baked goods, confections, puddings, meats, sausages, saucers, vegetables, and beverages (Panayotopoulos and Chisholm, 1970). It is also used as components of curry powder, teas and soft drinks, or mixed in milk and alcohol.

The herbal drug yields two kinds of oils i.e., the compressed fatty oil and the steam distilled essential oil.

Because of the inhibition of prostaglandin synthesis in the mucosa and sub mucosa of the colon it is used as anti-diarrheal agent for the patients with medullar carcinoma of thyroid.

The Genus

There are 150 species of *Myristica*

Common Names(s)

Sanskrit: Jatiphala,Jaiphol , **Telugu**: Jjajikaya **Bengali**: Jatiphala, Jayaphala,**Gujarati**:

Jayaphala,**Hindi:** Jati-phal, Jayaphal **Kannada:** Jakayi, **Malayalam:** Jathikka, **Marathi**: Jatiphala, **Nepali**: Jaiphal, **Oriya**: Jasiphala,**Punjabi**: Jafal,**Tamil**: cati-k-kay.

Distribution

Myristica species are cosmopolitan in distribution but abundant in Moluccas and Banda Islands in the South Pacific. Tropical regions, like Indonesia, Grenada in the West Indies and Sri Lanka cultivate nutmeg. (Purseglove, 1968; Bown, 1995). Five species are found in South India (Gamble, 1921). *M. dactyloides* Gaert. is reported in the W. Ghats of Tamil Nadu (Mathew, 1999;Henry *et.al;*1987)

Systemic Position

Plantae
Angiosperms
Magnoliids
Magnoliales
Myristicaceae
Myristica

Morphology of the Plant

The South Indian species of *Myristica* are identified on the basis of inflorescence, leaf venation, fruit shape and colour of the aril. *Myrstica fragrans* is moderate sized evergreen tree grows up to 25 meters in height. Root is tap root, Stem is aerial, erect , branched , woody , Leaves are elliptic or oblong – lanceolate, shiny above and dull beneath with reticulate venation. Inflorescence is Flowers creamy yellow, fragrant, and unisexual. Perianth is fused into an urn-shaped enclosure. The female flowers are small, with one pistil containing a single ovule while male flowers contain fused stamens. Fruits yellow, broadly pyriform or globose, fleshy pericarp, split into two equal halves when mature. Seed ellipsoid, 20-30 mm long and about 20 mm broad, brown with a dark points and lines slightly furrowed reticulately indicating the position of the radical a groove running along the line of raphe to the darker chalaza of embryo.

Pollinator: *Formicomus braminus* (Beetle)

Useful part: Seeds (nutmeg) and aril (mace)**.**

Nutritional Value

Nutmeg is a rich source of vitamins (Vit. A, C. and E), electrolytes (Sodium and Potassium) minerals (calcium, copper, iron, magnesium, manganese, zinc and Phosphorus), phytonutrients(carotene-B and crypo-xanthin B) , moisture (14.3%) either extract (36.4%), fibre (11.6%) volatite oil(6-16%), starch (4.6-24.24.2%), pentosans (2.25%), furtural (1.5%) and pectin (0.6%) (Gordon, 2005).

Anatomy of Fruit

Pericarp (Fruit Wall)

It is reported to be around 7mm thick and three layers(N.Parimala1 & S.Amerjothy 2013).

Epidermis- It is considered to be the epicarp and is made up of unistratose and consists of narrowly oblong thick walled cells with prominent cuticle**. Hypodermis-** Tangentially stretched parenchymatous cells are present in this zone. **Sclereid Zone –** A discontinuous zone made up of brachysclereids.

Mesocarp- Composed of multilayered parenchymatous, polyhedral cells.

Twig bearing Fruits

Inflorescence

L.S. of Male Flower

L.S of Fruit with Seed & Aril

Dried Aril

Seeds

Buds **Pollen on Anther**

L.S of Male & Female Flower

Vascular Bundles- Small vascular strands are found scattered in the mesocarp found in clusters of three, they are collateral and conjoint, xylem with angular thickening and prominent phloem.

Anatomy of Seed

It has 140 µm in thick seed coat

Epicarp (Seed Coat)

Outer layer of cells are small, squarish and inner layer of the cells made up of radially elongated palisade like cells, this layers also shows the presence of tannin cells.

Vascular Bundles-Vascular Bundles are scattered in inner layers.

Perisperm-Differentiated in three layers

Outer zone- It is 450-500µm thick and consist of angular parenchymatous cells and Calcium Oxalate crystals.

Middle zone- Made up of radial elongated row of cells.

Inner zone- Cells with dark amorphous cells with variable shapes and sizes. Many elongated thread like cells that are 2mm long and 450µm made up of spongy parenchyma cells these threads in the interior show well developed collateral vascular bundles.

Endosperm

Young Endosperm- Occupies maximum portion of the seed.

Matured Endosperm- Due to the intrusion of perisperm many radial lobes are formed called ruminated endosperm this is made up of soft parenchymatous cells.

Is flat, ribbon like repeatedly lobed creamy when young and dark red when matured and easily separable from the seed. It is 400µm thick in the middle and 150µm thick at the ends.

Epidermis- The epidermal cells are 10µm thick.

Cortex - 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 outline and fairly thick walled. The idioblasts are 40µm wide,

in between the idioblasts are smaller, angular or spindle shaped parenchyma cells.

Vascular Bundles-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

Anatomy of Mace (aril)

The aril is 400µm thick in the middle and 150µm thick at the ends, differentiated in to parenchymatous epidermis, parenchymatous cortex with idioblasts (40µ wide) and in the centre lie prominent discrete vascular bundles.(N.Parimala1 & S. Amerjothy 2013)

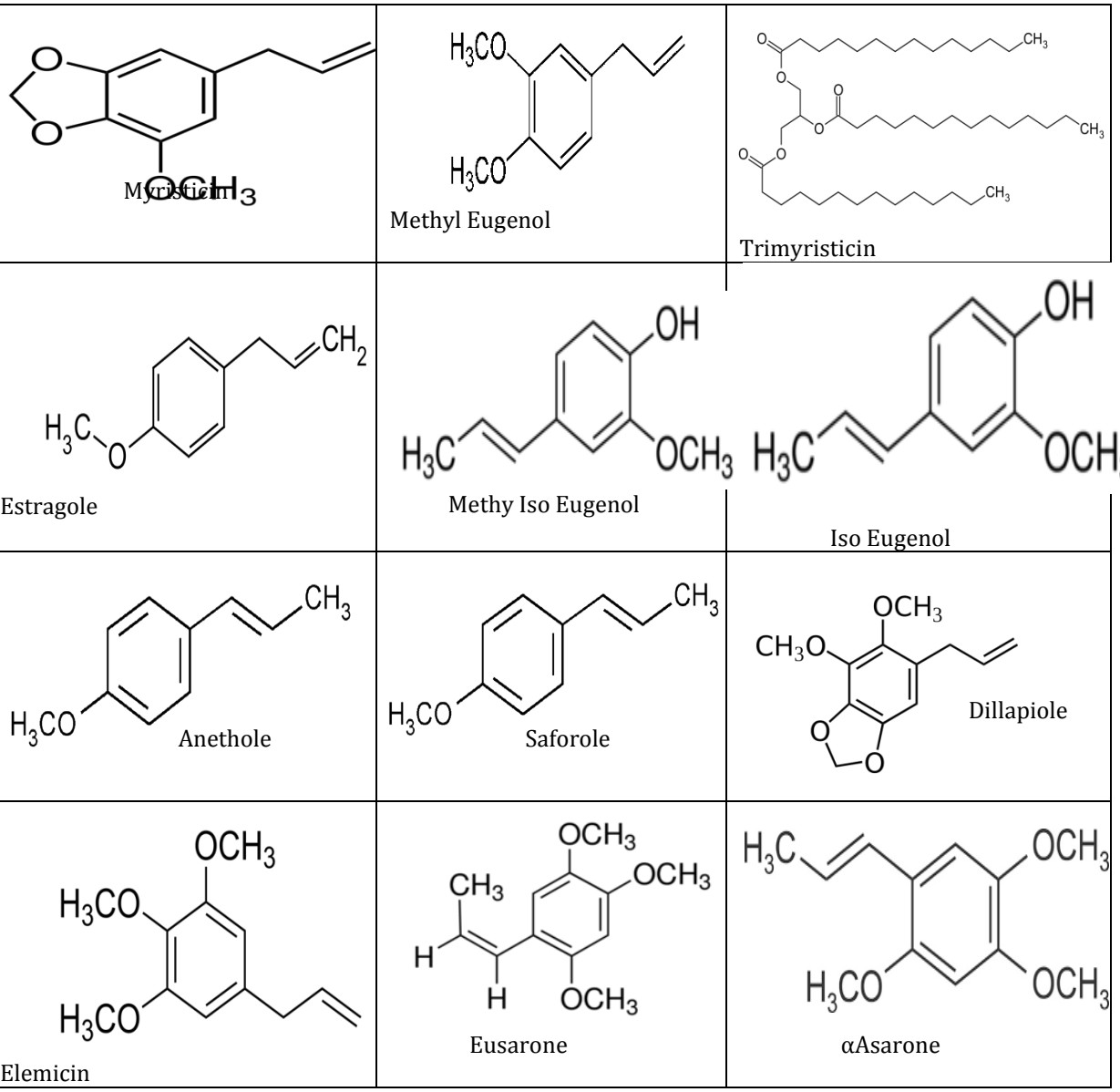
Phytochemistry of Seed

The chemical composition of the acetone extract of nutmeg seed said to contain 32 different compounds representing 99.49% of the total extract (Ashish Deep Gupta 2013). Sabinene (28.61%), b-pinene (10.26%), apinene (9.72%)

(G.R. Mallavarapu 1998). Other important compounds are terpinen-4-ol (5.80%), myristicin (4.30%), limonene (3.76%), c-terpinene (3.71%), (Z)-p-menth-2-en-1-ol (3.21%), isoeugenol (2.72%), elemicin (2.67%), (E)-p-menth-2-en-1-ol (2.15%), myrcene (2.14%), a-phellandrene (1.84%),p-cymene (1.81%), terpinolene (1.63%) and linalool (1.12%).Difference in the chemical composition of the nutmeg has been reported which could be an attribute of difference in climate, cultivar, soil factor and solvent used for the extraction (G.R. Mallavarapu 1998).

Phytochemistry of Mace

The oil of mace contains the same aromatic component as that of seed but in slightly different amounts and flavour. Apart from monoterpene hydrocarbons, p-dimethylstyrene has been identified along with seven esters, eight sesquiterpene hydrocarbons and two unsaturated aliphatic compounds namely 3-methyl -4-decan-l-ol and its acetate (Schenk & Lamparsky 1981).Red colour of the mace is identified to lycopene (Gopalakrishnan 1979) neolignans,fragnasol C and D and myristicanol A and D have been reported (Rastogi & Mehrotra 1995; Miyasawa et al 1996).



Essential oils of Seed

The percentage phytochemical compounds present in seed essential oil are Thujene 0.78, Pinene 10.23, Camphene 0.16, Sabinene 21.38,Myrcena 2.38,Terpinene 2.72, Limonene 5.57,Ocimene 0.03,Terpinene 3.98, *Trans*-Sabinene Hydrate 0.03, Terpinolene 1.62, Linalool 0.75, Fenchyl Alcohol 0.05, *Cis*-Sabinene Hydrate 0.06, 4-Terpineol 13.92,Terpineol 3.11, Citronellol 0.77, Linalyl Acetate 0.06, Bornyl Acetate 0.24, Safrole 4.28, Methyl Eugeunol 0.77, Isoeugeunol 1.74, Myristicin 13.57, Elimicin 1.42, Metoxyeugeunol 0.10,Asaron 0.03, Myristic Acid 0.11, Ethyl Miristate 0.04, Palmitic Acid 0.03, Ethyl Palmitate 0.07, Stearic Acid 0.01, Ethyl Oleate 0.01(Muchtaridi *et.al*. 2010) and triglyceride Trimyristin that has anxiogenic activity and is used in polyherbal formulations.

Pharmacological Properties

Antiangiogenic Activity

Compounds like myristicin, limonene, eugenol and terpinen-4-ol of nutmeg essential oil attribute antiangiogenic activity. Myristicin have been reported to induce cytotoxicity in human neuroblastoma SK-N-SH cells by mean of apoptotic mechanism (Lee BK *et.al*., 2005). D-limonene is a chemo preventive agent in hepatocellular carcinoma models(Parija T *et.al*., 2000., DK Patel *et.al* 2010 and terpinen-4-ol and Eugenol showed that they can induce apoptosis in human melanoma cells(Calcabrini A *et al*., 2004) (Hussain A *et.al* 2009).

Antimicrobial

Extracts of nutmeg showed antimicrobial activity against gram positive (*Bacillus subtilis and S. aureus*) Orabi *et al*., 1991; De *et al*., 1999; Dorman & Deans, 2000, gram negative (*Pseudomonas putida and P. aeruginosa*) bacteria and pathogenic fungi (*Aspergillus fumigatus, A. niger and A. flavus*) .Ethanol extract of fresh, seed and mace of *Myristica fragrans* is a classic remedy for the periodontal diseases that occurs by accumulation of *Actinomyces viscosus, Porphyromonas gingivalis, Streptococcus mutans and streptococcus sanguis* in the form of an adherent plaque (Zaleha Shafiei *et.al* 2012) these properties are attributed by myristin and triglyceride Trimyristin

Antioxidant

Anti-oxidant properties has been determined by the ferric reducing antioxidant power and trolox equivalent antioxidant capacity (Tan KP et al 2013). Anti-oxidant property of nutmeg is contributed by various phytochemicals, mainly vitamins, carotenoids, terpenoids, alkaloids, flavonoids, lignans, simple phenols and phenolic acids (Tan KP et al 2013),caffic acid and catechin (Shan B2005)(Gowri Pendyalan *et al.*,2008)

Aphrodisiac

Since 18th century, the spice is being used to treat male sexual dysfunctions it is clinically proved by Orabi *et al*., 2000 (Tajuddin *et al*. 2005).

Anti-inflammatory

Triglyceride Trimyristin of nutmeg oil shows anti-inflammatory properties and is used as local message to reduce muscular pain and rheumatic pain of joints (Pamphona-Roger, 1999).It reduces joint swelling and treats rheumatic fever (Duke and Edward, 1985; Ernest, 2002).

Antidiabetic activity

Macelignan present in the seeds enhanced the insulin sensitivity and improved lipid metabolic disorders by activating peroxisome proliferator receptor and attenuating endoplasmic reticulum stress, suggesting that it is an ant diabetic agent for the treatment of type 2 diabetes (Han *et al*., 2008).

Dental Care

Eugenol of nutmeg relieves from toothache (Duke *et al*., 2002; Kokwaro 2009), prevents bad breath (Barceloux, 2009)

Memory enhancing activity

Parle *et al*. (2004) have investigated the effect of *M. fragrans* seeds on learning capabilities and memory level in mice. Administration of the *n*-hexane extract of *M. fragrans* at the lowest dose of 5 mg/kg body weight for 3 successive days significantly improved the learning and memory level of young and aged mice. The extract said to have reversed scopolamine and diazepam-induced impairment in learning and memory of young mice. The observed memory enhancing effect of *M. fragrans* may be attributed to a variety of properties (individually or in combination) such as antioxidant, anti-inflammatory, or procholinergic activity.

Digestive

The decoction of the nutmeg is used for the treatment of flatulence, nausea and vomiting (Kurian, 2010).External application of the oil relieves the stomach pain. Freshly prepared decoction with honey has been used to relief of nausea, gastritis and indigestion ailment (Doman *et al.*, 2000).

Piles relieving
Piles are cured by applying nutmeg past mixed with Vaseline.

Heart Functioning
Nutmeg proves to be an excellent tonic for the cardiovascular system. It increases the blood circulation and stimulates the heart functions (Balick and Paul, 2000).

Antifungal
Essential oils of nut meg posses antifungal properties against *Colletotrichum gloeosporoides, Colletotrichum musae, Fusarium oxysporum , Fusarium semitectum , Aspergillus niger and Aspergillus glaucus* (V. Pooja et.al .,2012)

Spasmolytic
Nutmeg is helpful in clearing up the congestion resulting from cold and thus, is widely used in cough syrups. It's even helpful in aroma therapy (Gill, 1992; Iwu, 1993).

Carminative
Nutmeg is said have good carminative properties(Seenivasan et.al.,2006)

Hepatoprotective
Morita *et al*. (2003) have reported that myristicin from *M. fragrans* (nutmeg) possessed most potent hepatoprotective activity to rats with liver damage induced by lipopolysaccharide (LPS) plus D-galactosamine (D-GalN). It was reported that myristicin markedly suppressed LPS/D-GalN-induced enhancement of serum TNF-alpha concentrations and hepatic DNA fragmentation in mice. These findings suggest that the hepatoprotective activity of myristicin may be, at least in part, due to the inhibition of TNF-alpha release from macrophages. Sohn *et al*. (2008) observed that the hepatoprotective effects of macelignan, isolated from *M. fragrans* is related to activation of the mitogen activated protein kinase (MAPK) signaling pathway, especially JNK and c-Jun.

Insomnia
Nutmeg seeds increase the levels of serotonin that brings the relaxation of the body.(Pandey, 2005).

Anticarcinogenic
Extracts of nutmeg suppressed the growth of human lymphoid leukaemic cells, Molt 4 B (Moteki et al. 2002). Myristicin, present in the volatile oil of M. fragrans is a potential cancer chemo preventive agent (Zheng et al.1992). The essential oil is reported to modulate the formation of DNA adducts by aflatoxinin vitro (Hashim et al. 1994). The dihydroguaiaretic acid from M. fragrans mace suppressed leukaemic cells, colon cancer and lung cancer cells in vitro (Park et al. 1998). The mace of M. fragrans protected from bone marrow genotoxicity in male Swiss albino mice (Kumari 1992). It also significantly protected from methylcholanthrene-induced carcinogenesis in uterine cervix of mice (Hussain & Rao 1991) and had chemo preventive effects on dimethylbenz anthracene (DMBA)-induced papillo-magenesis in the skin of mouse (Jannu et al. 1991).

Jaiphal for pimple
A paste of nutmeg made with water or milk is applied externally to treat pimple and acne scar. Ground nutmeg powder made into a paste with Sandalwood, Kumkumadi taila, olive oil etc can be used for face

Weedicidal
The essential oil, obtained from the leaves is toxic to weeds hence used as weedicides, could also be use in the preparation of chewing gums and other flavouring essences (Pandey, 2005).

Pesticidal properties
The aqueous decoction of seed is toxic to cockroaches (Krishnamurthy et al. 2001). Nematicidal activity of M. Fragrans seed against Meloidogyne incognita has been reported (Gotke & Maheswari 1990).

Insecticidal
Jung *et al*. (2007) have reported the insecticidal properties of *M. fragrans* seed compounds against adult females of *Blattella germanica* (Dictyoptera: Blattellidae). Myristicin present in the kernel may be employed as an additive to pyrethrum to enhance the toxicity of the latter to houseflies, although myristicin itself is inactive (Anonymous, 1995). The aqueous decoctions of *M. fragrans* have been found to be toxic to cockroaches (Anonymous, 1995). Essential oil of *M. fragrans* has insecticidal activity against larvae of *Lycoriella ingenua* (Park *et al*., 2008) and *Callosobruchus chinensis* (Chaubey, 2008).

Adverse effects and Toxicity
No evident of adverse physiological or neurological is said to reported when used in minimum but large doses of raw nutmeg has psychoactive effects due the presence of myristicin, a monoamine oxidase inhibitor and psychoactive substance (Helena Hallstrom *et.al* 1997). Myristicin poisoning can induce convulsions, palpitations, nausea, eventual

dehydration, and generalized body pain (Demetriades, AK *et.al* 2005). In human beings 6-7 mg/kg body weight of nutmeg is enough to cause psycho pharmacological effects. 1-2 mg myristicin/ kg body weight obtained from 5gm of seeds causes intoxication (Helena Hallstrom 1997). Prostaglandin production is inhibited by Myristica extract that leads to hallucinogens that may affect the foetus if consumed in large quantities (Herb and drug safety chart Herb and drug safety chart from Baby Centre UK).

Toxicological effects including weak pulse, hypothermia, delirium, vertigo and nausea associated with ingestion of M. fragrans has been reported (Hallstrom & Thuvander 1997). Zaki & El (1987) reported teratogenic effects of nutmeg in foetus of rats. Randerath et al. (1993) reported the development of covalent

DNA adducts in the liver of adult and foetal mice, treated with extracts of nutmeg or mace or myristicin, the major spice constituent of nutmeg. Safrole, a minor constituent of nutmeg also produced DNA adducts in the liver of mice.

Myristica fragrans in Ayurveda

Sanskrit name-Jaitiphala, Malatiphala

Rasa : Katu, Tikta

Guna : Laghu, Tiksna

Virya : Usna

Vipaka : Katu

Karma : Dipana, Grahi,Vrsy,Mukhakledanasaka,Mukhadaurgandhyanasaka,Kaphavatapana

Important formulations – Jatiphaladi Curna, Dadimavaleha,Nasika Churna, Mrita Sanjivani Gulika

Therapeutic uses – Atisara , Svasa , Chardi , Kasa , Pinasa , Grahami ,Mukharoga , Sukrameha.

Dose - 0.5 - 1.0 g of the drug in powder form.

Unani Medicine

Javetri or Bisbasa (Mace) in Unani therapeutic is used for cardiac diseases (Amraz-e-Qalb), indigestion (Sue Hazim) and sexual debility (Zofe Bah).

Some formulations with Bisbasa

Jawarish Bisbasa - Buroodat Meda (coldness of gastric), Sue Hazm (Dyspepsia), Riyahi Dard (Gaseous Pain)

Chinese Medicine

SuHeXiang Wan (SHXW), a polyherbal (15 herbs) Chinese traditional drug administered to treat central nervous depression, seizures, infantile convulsion, stroke. (Jeon S *et al*., 2011)

Folk Lore Medicine

Sugalis tribes of Chittoor and Cuddapah use warm nutmeg oil to gently press on the umbilical cord for early drying. (M. Hamambara Reddy.et.al., 2000)

The Nag clan of the Rai Ghatual tribe residents of Tanki Tila village in Moulvibazar district of Bangladesh use leaves of Andrographis paniculata , Ocimum tenuiiflorum and Justicia adhatoda along with seeds of Myristica fragrans and Nigella sativa to treat of fever and loss of appetite. The plant parts are crushed and juice obtained made in to pills administered orally.(Protiva Rani Das.et.al.,2013)

Nandurbar tribes of Maharastra district use decoction of nutmeg seeds for vomiting and hiccups. (S. K. Tayade. et. D. A. Patil 2010).

Conservation Status

International Union for Conservation of Nature and Natural Resources Red List-2015 of Threatened Species 1998: e.T33986A9820569 of Myristica fragrance has placed it under the category & criteria of Data Deficient ver. 2.3

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