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PHARMACOLOGICAL ACTIVITY OF MYRISTICA FRAGRAN'S: A REVIEW

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ABSTRACT

Myristica fragrans is a yearly spice attachment to the family Myristicaceae. It has been cultivated throughout the globe and utilize for food flavoring, essential oil implementation and in conventional medicines. Mostly nutmeg accommodate with terpenes phenylpropenes. Nutmeg is useful as an integral in devising of medicines such as for stomachache, nausea, dysentery, flatulence, vomiting, malaria, rheumatism and early stages of leprosy. Chemical compositions and antifungal belongings of nutmeg's oleoresin. Nutmegs oleoresin was chemical constituent and antifungal belongings of nutmeg's oleoresin. Nutmegs oleoresin was gained by two steps, supervened by maceration. The nutmeg's oleoresin was warmed at 100^0C, 120^0C and 180^0C. The chemical component were resolved by GC-MS, and the antifungal possession by gained colony method. The outcome of the study revealed that yield was 13.6%±0.2% and 24 composition were recognize. The nutmeg's oleoresin at 100ºC, 120ºC and 180ºC recognized 25, 21 and 20 composition. Indeed, warmed up operation on nutmeg's oleoresin did not reduced the antifungal properties. Peer-review beneath look after the arranging committee of Indonesian food by two steps, was warmed at 100^0C, 120^0C, and 180^0C the chemical components were resolved by GC-MS, and the antifungal belongings by giant colony method. The outcome of the study reveal that yield was 13.6%±0.2% and 24 composition were determined.

KEYWORDS: Myristica, Antioxidant, Diphenyl alkane; Lignan; Malbaricone C; *Myristica fragran's.* Neolignan.

➢ INTRODUCTION

In this mostly the embryo and Kernal plant part is utilise is often called as Myristica fragran's, jaiphal, javitri myristica fragrans is a conifer timber belonging to family Myristicacea, a brood of perennial herb an original to Asia, Africa, Pacific Islands, and secure America.[1] And has been familiar by most taxonomist. It is sometimes called the nutmeg family, awaited to its familiar appendage, myristica fragrans, the origin of the herb nutmeg and mace. The breed myristica comprise of about 150 breed spread in the western pacifist and Asia.[2] Nutmeg is the embryo core Inner the fruit and mace is the obese red net like skin belying on the core.[3] The acuminate dark green leaflet are organized alternatively along the offshoot and are endured on leaf stems up to 1 cm long. upper leaflet portion are shiny. The blossoms are usually sole sexed; sometimes male and female blossoms are establish on the same tree female flowers appear in groups of 1 to 3; males in accumulate of 1 to 10 blossoms are pale yellow, waxy, Obese and bell-shaped.[4] The conifer bear are 2-3 yield a span. The kernel need 3-6weeks to barren before they are prepared to utilise when fresh, the aril is flashing scarlet becoming hornier, breakable and a yellowish-brown colour when dried. The conifer do not give blossoms until around 9 years old, but once start blossoming they perceive to do so for further 75 Era. The trees bear 2 to 3 reaping an era· The seeds requires 3 to 6 weeks to dry prior to they are ready to utilize.[5] Nutmeg butter a fat obtained from the seed in utilise in perfumery, tobacco, and toothpaste medicinally, it is utilize to hold up digestion and to many more.

Figure: Myristica fragran's.

Myristicin is a congenitally takes place benzodioxole compound set up in anise, Star anise, blac *Myristica fragrans* seed is also useful in diarrhoea, mouth sore and insomnia. It has been demonstrate that Malabaricon C, acquire from Myristica fragrans, has interdict activity against various kinds of anaerobic and aerobic microorganisms.[6] Oil acquire from seeds of nutmeg remarkable reduced the manufacture of listeriolysin o which is a bacterial extracellular protein responsible for Victorious infection by Listeria monocytogenes.[7] There were no hallucinogenic or other psychoactive possessions except mild sedation.[8] Myristicin is the principal aromatic component of the volatile oil of the nutmeg. *Myristica fragrans* as a seasoning has continued of the present day. Unlike other *myristica fragrans* develop a products are till know usefull as analgesics, stomachics, digestives, hypnotics, aphrodisiacs and amenorrheal agents.[9] The objective of the review is to accentuate on the different pharmacological activities. Nutmeg (Myristica fragrans) is an evergreenery thick shady tree which producing the higher commercial value nuts and aril (mace).[10]

➢ CHEMICAL COMPOSITION

The important constituents of Myristica fragrans have been confirmed to be alkyl benzene derivatives e.g. Myristicin, elemicin, safrole, etc essential.[11] The kernel contains about 10% essential oil. Which is widelyelemicin, in the kernel of M. fragrans is one of the cause for its intoxicating effects (Sonavane et al. terpinene, limonene, myrcene (60% to 90%), terpene derivation (linalool, geraniol, terpineol-5% to composed of terpene hydrocarbons (a-pinenes, camphene, p-cymene, sabinene, b-phellandrene, and phenylpropanes (myristicin, elemicin, safrole -2% to 20%.[12]

➢ Table of chemical constituent with according to their therapeutic effect.[13]

Active constituent	Therapeutic activity
Myristicin	Antioxidant
Malbaricone	Antibacterial
Dihydroguaiaretic acid	Cytotoxity
Macelignan	Hepatoprotective
Myristicin+pyretrum	Insecticidal
Myristicin, Trimyristin	Molluscidal
Myristicin	Memory enhancing
Myristicin	Hyperlipidemiac
Myristicin	Aphrodisiac

- **Pharmacological Actions**

1. **Anti-bacterial Action**
2. **Hypoglycemic Action**
3. **Hypo-lipedemiac and platelets Action**
4. **Hepatoprotective Action**
5. **Anti-inflammation Action**
6. **Anti-cancer Action**
7. **Memory intensity Action**
8. **Anti-diarrhoeal Action**
9. **Anti depressants Action**
10. **Anti-oxidant Action**

The explanation of pharmacological effects are given below

1) Antibacterial Action

The antibacterial activity of the volatile oil acquired from the kernels of *Myristica fragrans* was examined in a study which consist of various bacterial strains and it was determined that it was equally efficacious against the bulkiness of gram positive and gram negative microorganism. Essential oil acquired from *Myristica fragrans* kernel having the extension restraint ability of bacterial spores and useful as a food preservatives.[14] It has been determined experimentally that take out from the dried kernel seal of nutmeg has two composition which shows the antioxidant powerful antifungal activity and antibacterial

activities.[15] It has been determined experimentally and demonstrated that *Myristica fragrans* has the strong antimicrobial activity.[16] It also useful as preservatives antiseptic and disinfectant.[17] In further study, it was set up that ethyl acetate take-out of the flesh of *Myristica fragrans* had the powerful bactericidal activity oppose to some cariogenic Gram positive and Gram negative bacteria.[18] In a study, a number of frequently utilize pieces were assess for antifungal activity and turmeric and nutmeg were established to be almost energetic Antifungal combination were separated from *Myristica fragrans,* which were derived of neoligans and euginol.[19]

2) Hypoglycemic and antidaibetic Actions

It was determined that when rats were treated with the pre-treatment with the agent petroleum ether (60-80º C) remove of *Myristica fragrans*, at dose of 200 mg/kg, a notable reduce in blood glucose level, ($P<0.05$), Was acquired, i.e. blood glucose level lower from 145.75±9.65 to 81.5±4.03 mg% in oral glucose tolerance test (OGTT) after 30 min contrast to Sway group of glucose-fed rats. In alloxan convince diabetic rats, when petroleum ether take out of *Myristica fragrans*was specified daily for couples of week, the blood sugar level reduce notable from 326.25±7.05 to 268.0±9.6 mg %.[20] The nutmeg take out has signal peroxisome proliferator-activated receptor(PPAR) α/γ dual agonist performance, but its vigour is less than PPAR αand PPAR γ full agonist. Therefore, nutmeg (*Myristica fragrans*) take out being a natural dual agonist PPAR α/γ can be evolve as a potential anti-diabetic agent for the therapy of type 2 diabetes.[21]

3) Hypolipidemiac and platelets anti-aggregatory Action

The hypolipidemiac and platelets anti-aggregatory undertaking of the take out of kernel of *Myristica fragrans* were deliberate in albino rabbits. It was perceive that ethanolic withdraw of Nutmeg, at an oral administration of500 mg/kg for 60 d, in albino rats, remarkably lower the complete cholesterol in heart and liver. Low-density lipoproteins (LDL) andvery low-density lipoproteins (VLDL) levels were also noticeable lower. The high-density lipoprotein (HDL) cholesterol was enlarge, but it was not remarkable. The total cholesterol: HDL ratio and LDL: HDL ratios were remarkable lower in the act towards brute contrast to power l group. The virulent study that there is absolutely not unpropitious effect on various hematological and biochemical parameters. It also been revealed platelets anti-aggregatory undertaking.[22] The pip take out of *Myristica fragrans* when operate hypercholesterolemia rabbits, noteworthy lower serum cholesterol & LDL cholesterol and upraised the lower LDL:

HDLratio. It also the aggregation of phospholipids, triglyceride and cholesterol in heart, aorta and liver and assist in the Cessation of athermanous plaque in the aorta. Eradication of cholesterol and phospholipids through faecal matter was developed notable; in rabbits fed with kernel extract out.[23]

4) Hepatoprotective Endeavour Action

Myristicin, the premier combination, in *Myristica fragrans* has potential to Impede the lipopolysaccharide plus d-galactosamine persuade improvement of antibody TNF-alpha centralize in mice consequently, it was counsel that of Myristicin venture Perchance be due to the hampering of cancer decease factor (TNF)-alpha free from macrophages.[24] Mace is accept to enclose hepatic detoxification system convince a Pursuit a study control Lenitive effects of a areca nut was convey out by Regulate the levels of enzymes of the hepatic detoxification system, such as cytochrome P-450, cytochrome b5, glutathione S-transferase (GST) and it was windup that areca nut reduces the mace-induced enlarge in hepatic sulfhydryl (-SH) and GST level sand raised levels of cytochrome P-450 and cytochrome b5.[25] An additional contemporary education revealed that mace lignan isolated from Myristica fragrans had a hepatoprotective upshot on cisplatin-convince hepatotoxicity in mice.[26] In a further work, it was establish that nutmeg aqueous takeout had noteworthy hepatoprotective and antioxidant pursuit against isoproterenol persuade hepatotoxicity and oxidative strain.[27]

5) Anti-inflammatory Action

The anti-inflammatory activity of *Myristica fragrans* was assessing carrageenan-induced edema in rats and acetic acid convince vascular penetrable in mice. It was determined to that the anti-inflammatory effect was about the same as that of Indomethacin. The results put forward that myristicin in attendance in mace is in charge of for anti-inflammatory action.[28] The anti-inflammatory possession of myristicin strength be due to reticence of chemokines, cytokines, nitrous oxide and growth factors in double-stranded RNA (dsRNA) Restorative macrophages via the calcium pathway.[29] The methanol takeout from pip of Myristica fragrans worn for the therapy of inflammatory illness also had interdict result on nitric oxide (NO) production.[30] In a further education, ethanolic take out of nutmeg kernel be seen in high anti-inflammatory activity by impede the inflammatory cytokines and Nitric oxide manufacturing. Quercetin was establish to be the active composite In charge of for the anti-inflammatory activity.[31] Many authors conclude anti-inflammatory activity of nutmeg as

well as its oil.[32] Equal to non-steroidal anti-inflammatory drugs, pharmacological activities also showed by nutmeg oil.[33] But anti-inflammatory activity is shown only by petroleum ether extracts. The total extract of nutmeg activated an enzyme that is AMP-activated protein kinase enzyme (potential therapeutic target) for curing the metabolic syndrome including type-2 diabetes and obesity's. Seven combination like tetrahydrofuroguaiacin B2,5-bis-aryl-3,4-dimethyl tetrahydrofuranlignans, fragransinC_1, saucernetindiol, nectandrinB, verrucosin, galbacin and nectandrin a were separated from this extract as an active composition. Some of the separate combinations bring about effective AMPK increase in different C_2C1_2 cells, at 5μM concentration. Nutmeg and its active composition not only useful in the treatment of type-2 diabetes and obesity but also for the enlargement of agents other metabolic disorders.[34]

6) Anticancer Action

In one study, it was perceive that, on build on indispensable oil of *Myristica fragrans* in various concentrations to the Michigan CancerFoundation-7 (MCF-7) breast cancer unit line and A-357 epidermal skin cancer unit line, there was cytotoxic result.[35] The indispensable of nutmeg showed notable reticence on the enlargement of a colon cancer cell line (undifferentiated Caco-2 cells) in an in vitro study.[36] The methanol takeout of *Myristica fragrans* Houtt source cell death of Jurkat leukemia T cell line by implement require SIRTI mRNA down regulation.[37] It has been demonstrate that Myristica fragrans impede the dare growth microorganism using 20%v/v of the takeout.[38] The casing of the kernels of nutmeg has chemo inhibitory possession It remarkable lower the Prevalence of a skin papilloma in Swiss albino mice.[39] The inhibitory action of Nutmeg was studied on methylcholanthrene-induced carcinogenesis in the uterine cervix in Swiss albino mice. After a dose of 10 mg/mouse/day for 90 d there was a notable reduced in the enlarge of carcinoma.[40] Ethanolic extract of *Myristica fragrans* was useful totes anti-cancer activity opposed to human cancer cell lines and it be in view more than 70% growth reticence at a concentration of100μg/ml.[41]

1. Memory intensify Action

The effect of *Myristica fragrans* takeout, on recovery ability of learning and remembrance, were studied on aged and young mice in oppose to their disability persuade by scopolamine (0.4 mg/intraperitoneal) and diazepam (1 mg/kg intraperitoneal). N-hexane Takeout of *Myristica fragrans* was given orally for 3 consecutive days in three doses (5, 10, & 20 mg/kg) and begin with the dose of 5 mg/kgp. o. Significantly ameliorate. The reminiscence and

learning of youthful bandaged mice. The implement of action was not evoke in these studies, but the authors be convinced that it is a mechanism based on the dopamerginic -cholinergic activities, anti-inflammatory and anti-oxidant of this plant.[42] Alzheimer's disease is treated on the basis of anticholinesterase reticence by let fall the empirical decrease arising by lower cholinergic deficiency. In one study, it was Start that a hydro alcoholic take out of Nutmeg did show notable (50%) reticence of acetylcholinesterase for the treatment.[43]

2. Anti-diarrhoeal Action

Crude suspension and petroleum ether take out of nutmeg were evaluated for anti-diarrhoeal activity and it showed a decrease in the mean number of loose stools and increased in the latency period. The crude suspension of nutmeg showed a good anti-diarrhoealeffect.[44] In another study, hexane soluble portion of ethanol extract of the dehydrated fruits and flowers of *Myristica fragrance* observedanti-secretory possession in the ileum of rabbit and guinea pig oppose Escherichia coli enterotoxins.[45]

9. Antidepressant Action

The n-hexane extract of M. fragrans kernel was studied in mice for its antidepressant effect by utilize the forced swim test (FST) and the tail suspension test (TST) at 3 distinct oral doses of 5, 10, and 20mg/kg body weight. The highly potent dose was established to be 10 mg/kudos, as it shown a maximum reduced in the immobility of mice when comparison to control. Addition to this dose also shown similar strength to Imipramine (15 mg/kg) and Fluoxetine (20 mg/kg). Thus, the extract of nutmeg was competent to give remarkable antidepressant effect in mice, when assessed by TST and FST. The antidepressant effect of the nutmeg kernel extract could be due to interchange with the dopaminergic, adrenergic and serotonergic systems.[46]

10) Anti-oxidant Action

Antioxidant activity of some spices was comparison with a part food antioxidants like butylated hydroxyanisole (BHA), butylated hydroxytoluene (BHT), Propyl gallate, Anise, Nutmeg, Liquorice and shown good activity in the deoxyribose assay. Propyl gallate, Liquorice, Ginger and nutmeg rises the firmness of a part fixed fats such as olive, sunflower and corn oil and oils such as margarine and butter as well prevents oxidation at 110 °C. The antioxidant activity of nutmeg was set up to be higher than BHT in the trolox equal to antioxidant capacity (TEAC) assay.[47] In another study, it was reported that metabolic extract of nutmeg Kernel showed good antioxidant activity by methods of 1,1-diphenyl-2-

picrylhydrazyl (DPPH) and ferric reduces antioxidant power(FRAP) due to high content of tannin, flavonoid and terpenoids.[48] Acetone extract appear good antioxidant activity by the DPPH radical scavenging assay due to the appearance of several terpenoidslike sabinene, myristicin and eugenol.[49] Nutmeg Has the antioxidant activity due to the apperance different amalgamation consisting of β-caryophyllene and eugenol, have the hydrogen molecule in the allylic or benzylic place. Since it is relatively simple abstraction of atomic hydrogen from these functional groups, these amalgations have high antioxidant activity. The abstraction of atomic hydrogen is done by peroxy radicals that build under oxidative stress. In another view, bit part of Eugenol in nutmeg favors the antioxidant possession by encouraging the endeavor of superoxide dismutase, catalase, glucose-6-phosphate dehydrogenase, glutathione peroxidase and glutamine transferase enzymes.[50] The amalgam having catechol like structure as in caffic acid are advised to be good antioxidants as they easily donate electrons or phenolic hydrogen to the acceptors, such as lipid peroxyl groups or responsive oxygen species. Calliste et al (2010) set up that lignan derivatives are advised as a class of amalgam that shows the antioxidant potential of nutmeg kernel. After absorption of lignans and their glycosides into the body, they are assimilate to generate biologically active amalgamation having catechol construction that are in charge of high antioxidant possess of nutmeg kernel.[51]

11. Antimicrobial Action

The essential oil and various extracts of aromatic plants have shown powerful antimicrobial activity oppose diversity of fungi as well as bacteria.[52] Narasimhan et al (2006) determine the antibacterial activity by arranging chloroform extract of nutmeg oppose the both gram negative and gram positive bacteria. They set up myristic acid and Trimyristin are the main antibacterial combination extracted from nutmeg kernel. Researchers isolated three lignan. (mesihydroguaiaretic acid, nectandrin-B and erythro-austrobailignan-6) showing antifungal activity, from the methanolic extract of nutmeg seeds.[53] The evolvement of wheat leaf rust and rice blast was repressed by these three lignans. Some combination like caracole, γ-cymene, α-. α-Pinene and β-pinenes which are monoterpene hydrocarbons are also antimicrobial agents. They are advised to be implicated in membrane disruption. Carvacol is another important combination for antimicrobial activity. Carvacol works in the similar way as the other phenolic combination., which work through membrane eradication and the, outcome will be the rise in imbibition of membrane to potassium ions and protons, proton-motive Pinene, β-Pinene, and β-caryophyllene are reported to be antimicrobial appear in

essential oil of nutmeg pip.[54] Some plant phenolics are also describe for Antimicrobial activity. Antifungal and anti-inflammatory activities of plant essential oil are due to the appearance of β-caryophyllene which conclude moderate of the membrane while alone shows weak antibacterial activity.[55]

➢ **Uses *of myristica fragran's***

- *Myristica fragrans* has many usage ranging from culinary to medicinal. *Myristica fragrans* has been utilize in cooking for millennia. It is utilise in soups as well as in meats and vegetables. It is easily blended with other spices like white pepper, clove sand ginger; further, all spice and cinnamon are optional ingredients.
- *Myristica fragrans* Essential oils are also used in the manufacture of camphor, plasticizers, bases, solvents, and perfume and pine oils. *myristica fragrans* contains many chemical composition that are identified as anti-oxidant, health promoting properties and disease preventing. Spicy nuts with a non-greasy Trimyristin-like texture and essential (flexible) essential oils provide flavor aromatic flavor to *myristica fragrans*.
- These active compounds in *myristica fragrans* have numerous curative uses in traditional medicines as anti-depressant, anti-fungal, digestive, aphrodisiac, and carminative From ancient times the traditional Chinese and Indian medicines nutmeg and its oil have been used for diseases related to the digestive and nervous systems.
- Ingredients such as elemicin and myristicin in this spice contain stimulants and cooling agents. In dentistry, for tooth ache eugenol has been used to relief the pain.
- To reduces rich taste and freshness to recipes. Recently, research showed that mace lignin could be utilizes a white skin agent because it effectively inhibits melanin biosynthesis.[56]

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