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***Review Paper***

# Syzygium aromaticum: A novel review by the phytochemical and pharmacological aspects

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## Abstract

*Chinese herbs are regarded as a valuable resource for the production of novel pharmacological substances that are previously used to treat serious association of disease. Syzygium aromaticum found as promising critical ingredients in the development of novel and successful medications. After 6 years, the trees begin to flower. After around 20 years, full bearing is achieved, and production can last up to 80 years. There is a large variation in bearing between years. Clove clusters are collected after the buds have grown to their full size, become pink, but not yet opened. They're just about 2 cm long at the moment. Ingredients extracted from dried clove buds have a wide range of therapeutic effects. Twenty additional components were discovered to be active among the total number of components obtained. Clove essential oil is mostly composed of carvacrol, thymol, eugenol, and cinnamaldehyde. 4-allyl 2-methoxyphenol, or eugenol, is the active component in clove buds, accounting about 9095 percent of the total. It describes all of Syzygium aromaticum's key activities and gives positive outcomes for all of the activities stated in the summary above. The medicinal potential of Syzygium aromatic compounds and their primary component, eugenol, in the prevention and treatment of numerous medical conditions is highlighted in this review.*

**Keywords:** Clove, Eugenol, *Syzygium aromaticum*, Anti-Inflammatory, Myrtacae.

## Introduction

In the medical system, traditional therapeutic techniques based on the use of herbal remedies continue to play a significant role. Medicinal herbs have gained widespread acceptance in recent decades as scientists have discovered that natural compounds have fewer side effects and are more effective than manufactured alternatives. Traditional medicine is still used by about 80% of the world's population as a primary source of health treatment. Anti-inflammatory, antibacterial, spasmolytic, sedative, analgesic, and local anaesthetic activities are found in a variety of herbal plants.

They have anti-inflammatory, antibacterial, spasmolytic, sedative, analgesic, and local anaesthetic characteristics and are used in embalmment and food preservation. Glycosides, saponins, flavonoids, steroids, tannins, alkaloids, terpenes, and other phytoconstituents have been shown to have pharmacological effects in a variety of plant species. Herbal medicines have been recognised as an important source for developing innovative pharmacological compounds that have been utilised to treat serious ailments up to this point. These newly discovered phytochemicals have been hailed as a promising lead compound in the hunt for a new and effective medicine[6]. Eugenol (EUG) is a phenylpropanoid with an allyl chain substituted guaiacol, also known as 4-allyl-2-methoxyphenol or 4-allyl-2-methoxyphenol. EUG is a naturally occurring compound found in a variety of plant families, including Holy basil or tulsi leaves (Lamiaceae), Eugenia caryophyllata (clove), Zingiber officinale (ginger), Cinnamomum verum (cinnamon), Curcuma longa (turmeric), and peppers (Solanaceae), as well as aromatic plants such as Cinnamomum verum (true cinnamon), Ocim (Saigon cinnamon).

Eugenia caryophyllata (syn Syzygium aromaticum) is the main normal wellspring of EUG, representing 45-90 percent. Cinnamon contains 20-50 percent EUG, however business extraction of EUG is very costly because of longer development times, while ginger, tulsi, and narrows can be fill in for cinnamon and clove as a more affordable source. EUG can be blended by guaiacol allylation with allyl chloride or created through a biotransformation cycle including microorganisms like E. coli, Corynebacterium sp., and Bacillus cereus.

EUG has a wide scope of pharmacological impacts, including antibacterial, mitigating, pain relieving, neuroprotective, antidiabetic, and anticancer abilities, making it a flexible regular component that guides in the avoidance and therapy of an assortment of ailments. EUG has been named a for the most part perceived as protected (GRAS) and nonmutagenic substance by the World Health Organization. This atom is found in nature [1].

## Pharmacognosy

**Synonym:** Cloves, Caryophyllum, Laung, Lavang.

**Biological Source:** Eugenia caryophyllus flower buds that have been dried. Syzygium aromaticum is another name for the plant.

**Figure-1:** Syzygium aromaticum[21]

**Geographical source:** Malacca or Clove Island, Pemba, Zanziber, Penang, Ambon, Sumatra, Indonesia, Sri Lanka, Madagascar, Seychelles, West Indies, Tanzania, and Tamil Nadu, Nilgiris, Kanyakumari, and Kottayam in India[2].

**Harvesting and processing:** In 6 years, the trees start to bloom. After around 20 years, full bearing is reached, and production can last for up to 80 years. There is a lot of difference in bearing between years. Clove clusters are plucked when the buds have grown to their full size and have turned pink but have not yet opened. They're just around 2cm long now. To guarantee uniform drying, they are spread meagerly on mats and blended frequently. Cloves that have been appropriately dried will snap conveniently across the thumbnail and weigh about 33% of their green weight. The spice value of the opening blossoms is zero. Harvesting must be done carefully to avoid injuring the branches, as this will have a severe effect on the trees' future growth. A clove tree yields between 3.5 and 7.0 kilograms per year on average, depending on its age, size, and condition[3].

**Kingdom Classification:** Mention in Table-1.

**Table-1:** Taxonomic Tree of Clove (*Syzygium aromaticum*) [4].

| | |
|---|---|
| Super kingdom | Eukaryota |
| Kingdom | Plantae |
| Phylum | Spermatophyta |
| Subphylum | Angiospermae |
| Class | Dicotyledonae |
| Super order | Rosanae |
| Order | Myrtales |
| Family | Myrtaceae |
| Genus | Syzygium |
| Species | Syzygium aromaticum[4] |

**Clove *(Syzigium aromaticum)*:** A Pharmacognostic report is as fellows.

**Table-2:** Description of macromorphology[5].

| Features | Evaluation |
|---|---|
| Organoleptic features | |
| Color | Crimson to Dark Brown |
| Odor | Aromatic and strong |
| Taste | Pungent, aromatic |
| Quantitative micromorphology | |
| Size | 10-15 mm in length, 3.5mm in width, 2 mm thick |
| Macroscopical features | |
| Shape | Hypanthium is surrounded with 4 thick acute divergent sepals surrounded by dome shaped corolla. The corolla consists of unexpanded membranous petals with several stamens & single stiff prominent style[2] |

**Microscopical characters:** In transverse section, the hypanthium below the ovary reveals heavy cuticulriized epiderms with stomata that are somewhat raised above the surface and have well-defined midomatal gaps. A one of roughly radially oriented parenchymatous cells containing timorous scholysigenous oil glands arranged in two or three more or less intermixed layers is contained within this. The nil glands have an ellipsoidal form with long radial to be and an epithelium made up of two or three layers of toned cells. Oil gland contents are soluble in alcohol and can be blackened with alcoholic ferric chloride acid.

The lackeying with ferric solution is caused by the ground mass of parenchyma. Many of the parenchymatous cells contain cluster crystals of calcium oxaline (5-25 um in diameter). A ring of bilateral vascular bundles is embedded within the oil gland layer by a zone of cells with considerably thicker walls. Calcium oxalate cluster crystals are present in the ground time of this some. The meriteles are encased in a partially lignified ring, and the xylem is made up of 3-5 lignified spinal veins. A zone of parenchyma supports the central columella within the ring of vascular bundles, consisting of air gaps separated by lamella cell thick. In the cuter region of the columella is a ring of about 17 tiny vascular bundles, the ground tissue of the column is parenchyma is especially rich in calcium oxalate clusters[6].

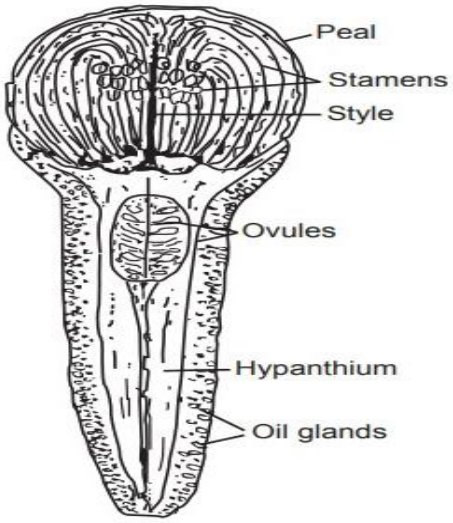


**Figure-2:** Microscopy of Clove[22].

Several researches have been conducted to identify the ingredients of Syzygium aromaticum[1,7]. Clove buds contain 15-20% medicinal oil, which is generally made out of eugenol (70-85%), eugenyl acetic acid derivation (15%), and β-caryophyllene (5-12%). Vanillin, crategolic corrosive, tannins, gallotannic corrosive, methyl salicylate, flavonoids, eugenin, kaempferol, rhamnetin, eugenitin, and triterpenoids such oleanolic corrosive are a portion of the other medicinal oil parts in clove oil. Methyl amyl ketone, methyl salicylate, humulene, benzaldehyde, and carvicol are among the oil's fixings.

The typical pleasant odour of cloves is caused by minor ingredients such as methyl amyl ketone, methyl salicylate, and others. In the hydrocarbon part of recently refined Indian clove bud oil, Gopalakrishnan et al. recognized six sesquiterpenes: - cubebene (1.3 percent), - copaene (0.4 percent), humulene (9.1 percent), - caryophyllene (64.5 percent), - cadinene (2.6 percent), and - cardinene (2.6 percent)[8].

**Phytochemicals:** Phytochemicals are mention in Table-3.

**Table-3:** Chemical constituent's names and molecular formulas.

| Name of the Compound | Formula |
|---|---|
| Toluene | $C_7H_8$ |
| 2-Pentanone-3-methylene | $C_6H_{10}O$ |
| 2-Pentanone, 4-hydroxy-4-methyl | $C_6H_{12}O_2$ |
| m-Doxane-4-ol, 2,6-diethyl-5-methylacetate | $C_{11}H_{20}O_4$ |
| 2,4,4,6-Tetramethyl-4,5-dihydro-1,3-oxazine | $C_8H_{15}NO$ |
| 3-Allyl-6-methoxyphenol | $C_{10}H_{12}O_2$ |
| Copaene | $C_{15}H_{24}$ |
| Caryophyllene | $C_{15}H_{24}$ |
| 1,4,7-Cycloundecatriene, 1,5,9,9-tetramethyl-Z,Z,Z-α-Farnesene | $C_{15}H_{24}$ |
| Eugenol acetate | $C_{12}H_{14}O_3$ |
| Caryophyllene oxide | $C_{15}H_{24}O$ |

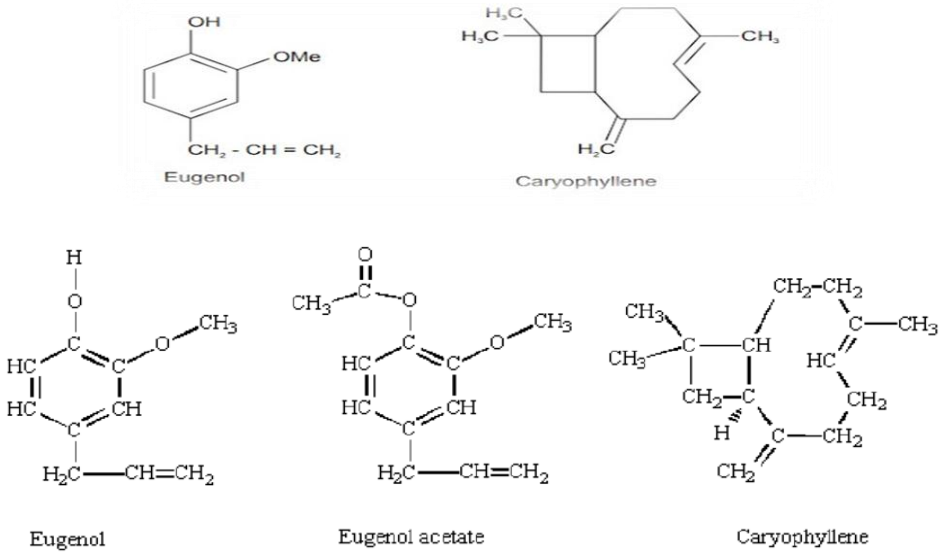


**Figure-3:** Chemical moieties prsesent in clove[23,24].

**Pharmacological account of *Syzygium aromaticum*:**

**Table-4:** Various Phytochemicals from *Syzygium aromaticum* have different pharmacological effects.

| Name of Phytoconstituent | Pharmacological Activity |
|---|---|
| Eugenol | Antimicrobial, Analgesic, Antioxidant, Anticancer, Anthelmintic, Antiulcer,Anti-inflammatory, Antidepressant, Bonepreserving, Antipyretic, Antithrombic |
| B-caryophyllene | Antitumor, Antiapotopic, Anaesthetic, Antilishmanial, Anti-inflammatory, Antioxidant, Antibiotic |
| Vanillin | Antimicrobial, Antioxidant, Antidepressant |
| Crategolic acid(Maslinic acid) | Antitumor |
| Kaempferol | Antioxidant, Antimicrobial, Anticancer, Anti-inflammatory |
| Rhamnetin | Anti-inflammatory, Antioxidant, Cardioprotective, Antifungal |
| Eugenitin | Antifungal |
| Eugenin | No action detailed |
| Gallic acid | Antimicrobial, Antioxidant |
| Biflorin | Anti-inflammatory, Antibacterial, Antioxidant, Anticancer |
| Myricetin | Antimicrobial, Antioxidant, Anticancer, Anti-inflammatory |
| Campesterol | Antibacterial, Antinociceptive, Anticarcinogenic |
| Stigmasterol | Antimicrobial, Antitumor, Acarcidal, Block cartilage degradation |
| Oleanolic acid | Antidiabetic, Antimicrobial, Anticancer |
| Bicornin | No action detailed |

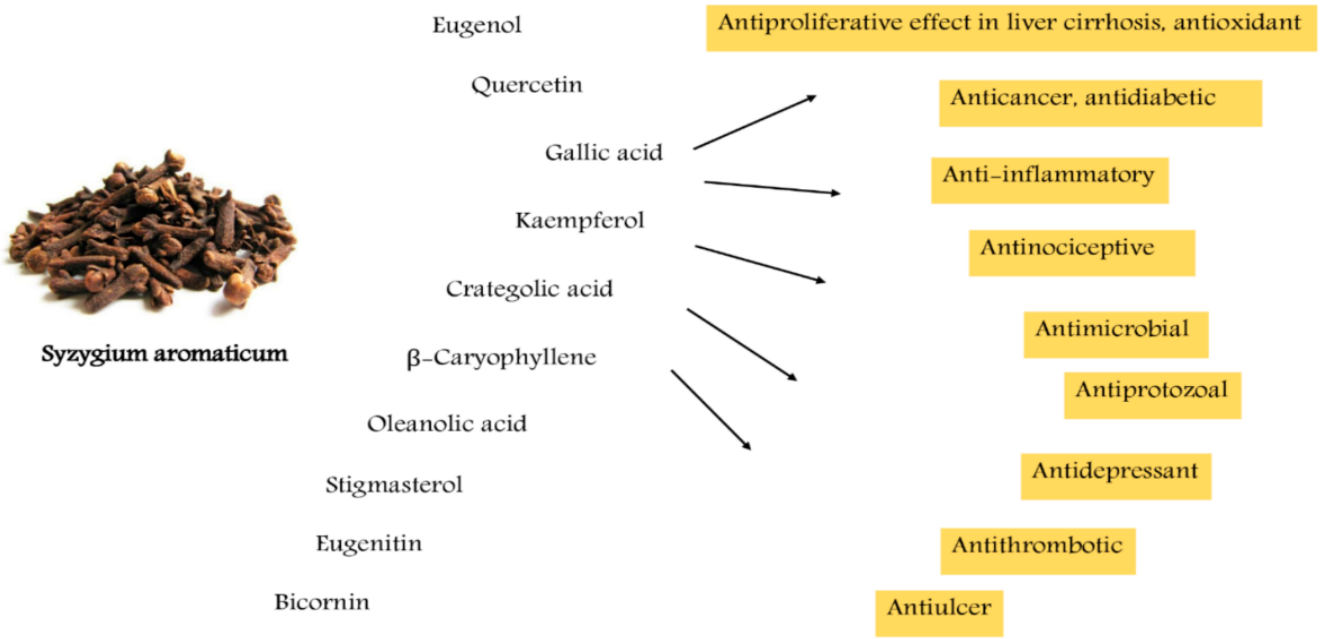


**Figure-4:** Pharmacological activities of Syzygium aromaticum[25].

**Anaesthetic activity:** Despite the fact that clove has been regularly utilized in dentistry for a really long time, its effective sedative properties stay obscure. Clove is perhaps the main wellsprings of phenolic synthetic substances in plant. Clove oil is gotten from the Syzygium aromaticum plant. Clove and clove oils can be found in an assortment of food varieties, refreshments, and even toothpastes. The feeling of calcium and chloride directs in ganglion cells is believed to be the component behind clove oil's pain relieving activity. Its pain relieving activity was also supported by voltage-subordinate impacts in sodium and calcium channels, as well as trigeminal ganglion receptors. At measurements of 50, 75, and 100mg/kg, eugenol was found to have pain relieving impact in the fringe sensory system[9].

**Anti-Inflammatory:** The mitigating viability of clove oil was analyzed in mice utilizing the recently settled carrageenan-initiated paw oedema test8. In particular, 0.02ml of a newly delivered suspension of the phlogistic specialist carrageen an in saline (10mg/ml) was infused sub-plantar into the right rear paw of each mouse in three gatherings of six creatures. Mice were treated with clove oil thirty minutes prior to getting carrageenan infusions, while negative and positive control mice got typical saline and indomethacin, individually. A micrometer was utilized to evaluate paw thickness previously and 3 hours after carrageenan infusion (Mitutoyo, Japan).

The degree of acute inflammation and oedema was determined by the increase in paw thickness. The rate concealment of the incendiary reaction was determined utilizing the equation beneath for each mouse in contrast with saline-treated mice.

Percent inhibition ¼ 100 ½ðEPT=CPTÞ _____ 100

EPT represents exploratory paw thickness, while CPT represents for control paw thickness[10]. The anti-inflammatory actions of eugenol have led to the conclusion that this molecule can reduce the expression of the cyclo-oxygenase II enzyme. Eugenol dimers can stop macrophages from producing cytokines that are activated by polysaccharides. Eugenol also inhibits cell proliferation by suppressing the transcription factor NF-Kappa B (NF-B) [11].

**Anti- Microbial:** Eugenol, carvacrol, and thymol, antimicrobial components of cloves, are phenolic chemicals found in cinnamon, cloves, sage, and oregano. When these chemicals are present in cinnamon and cloves, they act as mould inhibitors as well as giving flavour and scent to baked goods. Antibiotics now in use (such as ampicillin, chloramphenicol, and co-trimoxazole) are becoming ineffective against certain infections, making treatment of infectious disorders challenging.

The antibacterial efficacy of methanolicclove and ethanolicclove extracts against three food-associated gramme positive and gram negative bacteria (Staphylococcus aureus, E. coli, and Pseudomonas aeruginosa) is empowering, according to an antibacterial susceptibility experiment. The antimicrobial activity of the methanolicclove extract was superior to that of the ethanolicclove extract against all test species, with the methanolicclove extract showing superior results[12].

**Anti-Cancer:** The battle against the exceptionally vindictive public foe known as "disease" has seethed for centuries, and people have often been on the losing end. It is notable as one of the fundamental driver of mortality around the world, with 7.6 million fatalities (around 21,000 disease passings each day) kept in 2008. Malignant growth is an expansive term that incorporates in excess of 200 unique human illnesses brought about by typical cells denounced any kind of authority, bringing about atypical cell multiplication that spreads all through or attacks the body, in the end prompting demise on the off chance that not made due. Cloves' cytotoxic impact against MCF-7 human bosom malignant growth cell lines is being examined in this review.

MTT measure, the anticancer capability of various portions of water extract, ethanol concentrate, and medicinal balm of cloves was analyzed in vitro. The rejuvenating oil, trailed by ethanol and water separate, had the most grounded cytotoxic impact in both BSLT and MTT measures. The medicinal oil had a LD50 worth of 37g/mL in the 24-hour BSLT. Moreover, the rejuvenating ointment's IC 50 qualities in 24-and 48-hour MTT measures were 36.43 g/mL and 17.6 g/mL, separately[13].

**Anti-fungal:** Clove medicinal oil (EO) and its primary constituent, eugenol were tested for antifungal activity. S. aromaticum clove oil was purchased for commercial use. Clove medicinal oil and its unstable fume have antifungal properties against Candida albicans and Epidermophyton floccosum, which are dermatophytic fungus. Trichophyton rubrum, Microsporangium, and Microsporum mentagrophytes were studied. Clove medicinal oil and its volatile vapour both effectively suppress dermatophytic fungus spore germination and mycelial proliferation. Clove essential oil's volatile vapor has fungicidal activity, while clove essential oil applied directly had fungistatic activity. On solid media, clove medicinal oil's volatile vapor had fungistatic action; however in broth medium, the oil had fungicidal activity. As a result, we believe that clove essential oil and its volatile vapor have antifungal action against the test fungus in distinct ways. Clove essential oil's volatile vapor was found to be an efficient antifungal agent against various human pathogenic fungi[14].

**Anti-Bacterial:** The agar well dissemination technique was utilized to decide the impacts of eugenol on the development of Gram-positive (Bacillus cereus; Bacillus subtilis; Staphylococcus aureus) and Gram-negative (Escherichia coli; Salmonella typhi; Pseudomonas aeruginosa) microorganisms. At a convergence of 1000g/mL, eugenol has been found to restrict P. aeruginosa growth[11].

**Antioxidant effect:** Nagababu and associate's research has shown that eugenol can be used as a medicinal antioxidant. The production of thiobarbituric acid reactive substances (TBARS) was reduced by eugenol at doses of 4-15M in their investigation. It has also been shown that eugenol-grafted chitosan hydrogel has an antioxidant effect. Eugenol inhibits lipid peroxidation and low-density lipoprotein oxidation. Eugenol-like substances inhibit copper-dependent oxidation of low-density lipoprotein as well as lipid peroxidation and $Fe^2$ autooxidation[15].

**Microbicidal activity:** Essential oils may contain unique antibacterial constituents that are effective against bacterial infections. Essential oils from plants have antibacterial properties that have been utilised practically for millennia, but they have only lately been examined scientifically. The microorganisms utilized were E. coli ATCC 25922, S. aureus ATCC 6538 P, and Pseudomonas aeruginosa ATCC 27853. Bacterial subcultures were done on tryptone soy agar (Oxoid) and suspended in 1% peptonized water to accomplish a centralization of around 109cfu/mL. Fritzsche S. A. I. C. A. given the essential oils (ECO). The ECO was broken down in 50% v/v propylene glycol (PPG). The survivor's log discoveries have been adjusted for time, and the death rate steady qualities for every temperature and fixation have been determined. Bacterial aversion to clove natural balm at 21°C was 1.514 (Escherichia coli) > 1.334 (Pseudomonas aeruginosa) > Staphylococcus aureus, as indicated by their inactivation rate (k) (0.995)[10].

**Nematicidal activity:** Meloidogyne incognita was used to test the nematicidal activity of plant extracts. Clove (Syzygium aromaticum L) extracts killed the nematode with an EC50 5-10 times lower than synthetic pesticides chlorpyrifos, carbosulfan, and deltamethrin in laboratory evaluation. Meloidogyne incognita Kofoid and White (Chitwood) (Tylenchida: Heteroderidae), a major plant-parasitic nematode species that affects the quantity and quality of crop production in many annual and periodical crops. Root galling, stunting, and nutrient shortage, especially nitrogen deficiency, are all frequent features of infected plants.

In the Netherlands, the laboratory experiment was carried out in triplicate at Wageningen University's Sub Department of Nematology. Zincognita was the nematode species studied, and it was obtained using Barker's method. Abbott's formula was used to adjust the nematode death rates in the exposure groups (PO) for mortality in the solvent controls (PC):

$$PT\ (\%) = [100 \times (PO-PC)/PC]$$ [16]

**Pediculicidal Activity:** The 3 major lice that infest humans are Pediculus humanus capitis (head louse), Pthirus pubis (crab louse) and Pediculus humanus (body louse). The humans head lice are a nuisance for millions of people worldwide with high generality in children. Head lice have been treated by methods that include the physical removal of lice, various domestic treatments and conventional insecticides. Insecticidal activity of essential oil specially clove oil and eucalyptus oil and compare the relative toxicity of essential oil[1].

**Shelf life of Strawberry:** Shelf existence of strawberry fruit changed into recorded via way of means of each 2 days in ordinary room temperature for distinctive clove oil software situations and fruit ripening stages. The boom of shelf existence supported via way of means of clove oil software at excessive dosage utilization. We discover that the shelf existence of strawberry culmination on the mature culmination changed into better depended to clove oil software evaluate to immature culmination significantly. Post-garage shelf existence (days) of strawberries at everyday room situations changed in to found via way of means of 15 as a report for shelf-existence period evaluate to 10 days as control[17].

**Aphrodisiac activity:** Syzygium aromaticum flower buds have long been used in Yunani medicine for the treatment of male sexual disorders. Effects of 50% ethanolicclove extract on general mating behavior and negative effects on sexually normal males. The results showed that 50% ethanolicclove extract significantly and persistently increased sexual activity in normal male rats without noticeable gastric ulcers or side effects. Therefore, the aphrodisiac properties that result from the extract support its traditional use claims in sexual disorders[18].

## Conclusion

From the information gathered above, this review concludes various phytochemical and pharmacological aspects of Syzygium aromaticum, clove and its main component, eugenol. Ingredients extracted from dried clove buds provide many therapeutic effects. Of all the components obtained, it was observed that mainly 20 more components were in the active form. The main components of clove essential oil are carvacrol, thymol, eugenol and cinnamaldehyde.

4-allyl 2-methoxyphenol, or eugenol, is the active ingredient that makes up about 90-95 percent of the total clove buds. Here we explain all the main activities of Syzygium aromaticum and report satisfactory results for the various activities mentioned in the overview above. This overview catches up to highlight the therapeutic potential of Syzygium aromaticum and its main component, eugenol, in the prevention and treatment or treatment of various medical emergencies. I hope the information I collect here in this review will guide scientists and researchers to create new plant-derived herbal natural medicines from clove essential oils and eugenol.

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