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REVIEW ARTICLE

# Comparative summary of the ethnomedicinal use, phytochemical constituents, and pharmacological properties of *Syzygium aromaticum* and *Ocimum sanctum*

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## ABSTRACT

Medicinal plants are the primary sources of easily accessible remedies frequently used by the traditional people in developing regions. It is a common practice for sick people to combine conventional medicine with traditional medicine. Clove and Tulsi are among the most widely used herbs prescribed for their therapeutic benefits in a wide range of ailments. The purpose of this review was to accumulate and compare the benefits of both plants by focusing on their phytochemical and nutraceutical components and biological responses. Ethnomedicinal data were obtained through extracting information from journals, books, and websites belonging to the therapy. The study categorized the pharmacological properties possessed by these two plants according to their bioactive compounds, among which eugenol was found most potent and commonly present in both offering antioxidant, and anesthetic activities. Other common phytochemical components of essential oils include α-Pinene, β-Pinene, Limonene, and Camphene, 1.8-Cineole, α-Terpineol, β-Caryophyllene, Germacrene D, δ-Cadinene, α-Selinene, α-Cadinol, etc. In literature, both these plants have been reported to have a wide variety of pharmacological potentials including antimicrobial, anticancer, anti-inflammatory, chemopreventive, radioprotective, cardioprotective, hepatoprotective, anthelmintic, anticoagulant activities. The study also identified some key areas as opportunities for further scientific investigations such as assessment of safety profile of co-administration, alternative use, nutraceutical values, and disease-specific dose determination, etc. The study compiled comparative information to aid scientists for additional research and the tribal communities for specifying targeted use against particular diseases.

**Keywords**

Clove,
Tulsi,
Pharmacological Properties,
Ethnomedicinal Use,
Chemical Components,
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## INTRODUCTION

Natural plants have long been used as medicinal agents due to their biological and pharmacological activities since ancient times. Different parts of plants and their crude extracts have been employed for centuries in herbal medicine to prevent diseases, both therapeutically and prophylactically. Clove and Tulsi are known for their ethnomedicinal values and are considered abundant sources of bioactive compounds. Different compounds and plant parts of these herbs have been found to ameliorate various clinical conditions.

Clove (*Syzygium aromaticum*) is an aromatic plant, belonging to Myrtaceae family (Table 1). It is indigenous to the Maluku Islands, off the coast of east Indonesia. However, it is currently grown in Sri Lanka, India, Madagascar, Malaysia, Tanzania (Zanzibar Island) and in the northeast regions of Brazil [1]. The whole and ground cloves are used to enhance the flavor of dishes. They are utilized as a carminative to promote peristalsis and enhance gastric hydrochloric acid [2]. It has been proven to be a good anesthetic for sedating fish in a variety of invasive and noninvasive fisheries management and research techniques [3]. Furthermore, clove essential oil possesses a wide range of biological activities, including antibacterial, antioxidant, antifungal, antiseptic, and insecticidal effects [4-6]. The abundance of eugenol, a highly potent pharmacologically active compound, in clove essential oil is responsible for most of the biological activities however, other compounds are still in research.

Tulsi (*Ocimum sanctum* L.*)* is an aromatic shrub belonging to the Lamiaceae family of basil (tribe ocimeae). It originated in north-central India and is now cultivated as a native species in the eastern tropics of the world [7]. Tulsi is one of the most well-known examples of Ayurveda's holistic approach to healthcare. Tulsi has been included in spiritual and lifestyle practices in India, which is due to its wide range of health benefits. Several types of research have been conducted based on traditional Ayurvedic wisdom to investigate the medicinal benefits of tulsi and have suggested that this herb is a tonic for the body, mind, and spirit that can treat a variety of modern-day health issues. Tulsi is said to improve the appearance of the skin, the sweetness of the voice, and the development of intelligence, and stamina [8,9]. Leaves, fruits, essential oils of tulsi exert anti-tussive, antioxidant, antimicrobial, radioprotective, antihypertensive, and immunomodulatory effects [10-14].

This review mainly focused on the comparative study of *Syzygium aromaticum* (Clove) and *Ocimum sanctum* (Tulsi) depending on their nutraceutical values, compositions, essential oils, traditional applications, biological and toxic effects in order to have a clear concept of the similarities and dissimilarities between the two medicinal plants.

**Table 1**: Taxonomical classification of *S. aromaticum and O. sanctum* [15,16]

| ***Classification*** | ***S. aromaticum*** | ***O. sanctum*** |
|---|---|---|
| Kingdom | Plantae | Plantae |
| Order | Myrtales | Lamiales |
| Family | Myrtaceae | Lamiaceae |
| Genus | *Syzygium* | *Ocimum* |
| Species | *S. aromaticum* | *O. tenuiflorum* |
| Binomial Name | *Syzygium aromaticum* (L.) Merr. & L.M. Perry | *Ocimum sanctum* L. |
| General Name | Clove | Holy Basil |

### Ethnomedicinal Use

*Syzygium aromaticum* (clove) and *Ocimum sanctum* (tulsi) have been documented as the most prominent sources of traditional medicine for centuries. Approximately 80% of the world's population currently depends on traditional medicines as a primary source of health treatment [17]. Different parts of these plants are traditionally used in Ayurveda and Siddha medicine to prevent and treat a variety of illnesses and everyday ailments which have been shown in Table 2. Within Ayurveda practice, tulsi is renowned as “The Queen of Herbs,” “Mother Medicine of Nature” and is revered as an “elixir of life”. It is said that daily consumption of tulsi prevents disease, promotes general health, wellbeing, and further helps to manage the stresses of daily life. Chewing leaves helps to treat cold and sore throat [18]. In ancient times, the leaves are used to treat a variety of fevers such as boiled leaves are taken with tea as a treatment to prevent dengue and malaria fever whereas dried powder of leaf is used to cure teeth disorder [19]. On the other hand, cloves have traditionally been used as a remedy for indigestion, nausea, and vomiting. Cloves have been used to cure a variety of illnesses including malaria, cholera, and tuberculosis in tropical Asia. In America, it's used to treat different types

of worms and viruses, candida, and a number of protozoan and bacterial infections. In addition to their recreational purposes, cloves are said to be a natural anthelmintic [20].

**Table 2**: Comparison of ethnomedicinal uses between *S. aromaticum and O. sanctum* plant parts

| ***Ethnomedicinal Use*** | ***S. aromaticum*** | ***O. sanctum*** |
|---|---|---|
| Diabetes | Flower [21], Essential Oil [22,23] | Leaves [24] |
| Emetic Syndrome | Flower [25] | Leaves [26] |
| Common Colds, Headaches, Flu, Earache, Migraine, Chronic Fever | Flower [27], Essential Oil [27] | Leaves [28], Essential oil [29] |
| Cholic Pain, Arthritic Pain, Inflammation | Essential Oil [30] | Leaves [31], Seeds [32], Whole Plant [33] |
| Burn, Wound, Snakebite, Insect bite | Essential Oil [34] | Leaves [35], Whole Plant [36] |
| Ulcers, Diarrhea, Dysentery, Digestive Disorders | Flower [37] | Leaves [38,39] |
| Skin Diseases | Essential Oil [40] | Leaves [41] |
| Bronchial Asthma, Cough, Sore Throat, | Essential Oil [42] | Leaves [43] |
| Heart Disease | Flower [44] | Leaves [45], Seeds [46] |
| Night Blindness, Eye Infection, Eye Health | Essential Oil [47] | Leaves [26] |
| Scabies, Cholera, Malaria, and Tuberculosis | Flower, Whole plant [48] | Leaves [49], Root [50] |
| Bacterial, Fungal and Protozoal Infections | Flower [51], Essential Oil [52- 55] | Essential Oil [56] |
| Carcinoma | Flower [57] | Leaves [58], Seeds [59] |
| Muscular Cramp | Essential Oil [60] | Flower [61] |
| Fatigue | Not reported | Leaves [62] |
| Memory Improvement | Flower [63] | Whole Plant [64] |
| Worm Remedy | Essential Oil [65] | Flower [66], Leaves [67] |
| Immune Booster | Essential Oil [68,69] | Leaves [70] |
| Mosquito Repellent | Essential Oil [71] | Root, Stem [50] |
| Parasites | Essential Oil [72] | Not reported |
| Tooth Infections and Toothaches | Flower [73] | Not reported |
| Tonic, Stimulant | Essential Oil [36] | Leaves [27] |
| Convulsions | Not reported | Leaves [74] |
| Insomnia | Not reported | Leaves [75] |
| Mouth and Urinary Tract Infection | Not reported | Leaves [76] |
| Anxiolytic, Antidepressant | Not reported | Leaves [77], Root [78] |

Alongside, these two are popular as condiments and flavoring agents in preparing traditional dishes as well as common ingredients in formulating toothpaste commercially [79,80].

## Nutraceutical Compounds

The composition of a clove varies slightly as it is produced, processed, and stored in the agro-climatic conditions. A typical evaluation determines the following approximate chemical composition of clove: volatile oil (13.2%), non-volatile ether (15.5%), carbohydrate (57.7%), protein (6.3%), crude fibre (11.1%), mineral matter (5.0%), calcium (0.7%), phosphorus (0.11%), iron (0.01%), sodium (0.25%), potassium (1.2%), ash insoluble in HCl (0.24%), vitamins (mg/100g): Vit A: 175 I. U., Vit B1: 0.11, Vit B2: 0.04, niacin:1.55, Vit C:80.9 and calorific value (food energy): 430 calories/100g [20]. The nutritional analysis of *Ocimum sanctum* exhibits a high level of protein (30 Kcal, 4.2 g), carbohydrate (2.3 g), and fat (0.5 g) contents. It also contains vitamin A and C (25 mg per 100 g), and minerals such as calcium (25 mg), iron (15.1 mg), and phosphorus (287 mg) [9].

## Phytochemical Constitutes

The nature of compounds present in medicinal herbs can be identified through phytochemical analysis. It is also performed to evaluate the effects of available bioactive components. Phytochemical constituents such as eugenol, polyphenols, flavonoids have been considered to be a valuable source for the development of innovative pharmaceutical compounds that have been utilized to treat serious ailments [81]. Clove and tulsi possess a wide range of phytocompounds that have been compared in Table 3. Among them, the content of eugenol is found to

be the most common in both these plants apart from other mutual compounds such as gallic acid, oleanolic acid, stigmasterol, campesterol, etc. Besides, these medicinal plants also contain bicyclic sesquiterpenes, phenolic compounds, phenolic acids, triterpenes, C-glucosides, flavonoids, tannins, triterpenoid saponins, and steroids which have been demonstrated to have pharmacological actions.

**Table 3**: Comparison of phytochemical compounds of whole plants of *S. aromaticum* and *O. sanctum.*

| ***Group*** | ***S. aromaticum*** | ***O. sanctum*** |
|---|---|---|
| Essential Oil | Eugenol [27] | Eugenol [82] |
| Bicyclic sesquiterpene | β-caryophyllene [83] | Caryophyllene oxide [84] |
| Phenolic compounds | Vanillin, Eugenitin, Eugenin | Rosmarinic acid [85] |
| Triterpenes | Crategolic acid (Maslinic acid) [86] | Betulinic acid |
| Flavonoid | Kaempferol, Rhamnetin, Myricetin [87] | Apigenin, cirsimaritin, isothymusin, isothymonin, Orientin [88], Vicenin [89] |
| Phenolic acid | Gallic acid [90] | Gallic acid, p-Hydroxy-benzoic acid, Chlorogenic acid, Sinapic acid, Vanillic acid [91] |
| Fatty acid | Omega-3 [92] | Propanoic acid [9] |
| Tannin | Bicornin, gallotannic acid, methyl salicylate [93] | Not reported |
| Triterpenoid saponin | Oleanolic acid [93] | Ursolic acid, oleanolic acid [82] |
| Steroid | Stigmasterol, and campesterol [93] | β-sitosterol, stigmasterol, campesterol, ergosterol [94] |
| C-glycoside | Biflorin, Isobiflorin [95] | Not reported |

**Table 4**: Comparison of phytochemical constitutes of essential oils of *S. aromaticum* and *O. sanctum.*

| ***Terpenes*** | ***S. arometicum* [96]** | ***O. sanctum* [91]** |
|---|---|---|
| Monoterpene Hydrocarbons | α-Pinene, β-Pinene, Limonene, Δ3-Carene, Cis-β-Ocimene, Trans-β-Ocimene, Terpinene-4-o, Pulegone | α-Pinene, Camphene, Sabinene, β-Pinene, Limonene |
| Oxygenated Monoterpenes | 1.8-Cineole, Linalol, α-Terpineol, α-Terpinyl Acetate, Carvone | 1,8-cineol, cis-Sabinenehydrate, Linalool, Camphor, Borneol, α-terpinenol, D-carvone, Anethole, Eugenol |
| Sesquiterpene Hydrocarbons | α-Cubebene, α-Copaene, β-Bourbonene, ε-Cadinene, β-Caryophyllene, Zonarene, α-Caryophyllene, γ-Muurolene, Germacrene D, α-Muurolene, α-Selinene, α-Farnesene, δ-Cadinene, γ-Cadinene, Cadina-1.4-diene, α-Amorphene, Calamenene, Jasmone, Isocaryophyllene oxide | γ-Eleneme, β-Elemene, α-Gurjunene, β-Caryophyllene, β-cubebene, β-gurjunene, Alloaromadendrene, Germacrene D, β-Selinene, α-Selinene, β-Bisabolene, δ-Cadinene, 1-4, Cadinadiene, α-Calacorene |
| Oxygenated Sesquiterpenes | Epoxy-6.7-humulene, Caryophyllenol, Cubenol, Sesquiterpenol, α-Cadinol, | Nerolidol, Spathulenol, Caryophyllene oxide, α-Cadinol, Aromadendrene oxide |
| Others Compounds | 2-Heptanone, Heptyl acetate, 2-Methyl-6-methylene-1.7-octadien-3-one, Sulcatone, 2-Nonanone, 2-Undecanone, Methyl benzoate, Acetophenone, Ethyl benzoate, Dihydrocarvyl acetate, Benzyl acetate, Methyl salicylate, Methyleugenol, Acetyleugenol, Chavicol, Isoeugenol, Caryophylla-3.7-dien-6-ol, 2. 3. 4-trimethoxyacetophenone, Benzyl Benzoate | Eicosane, Tricosane |

### Phytochemical Constitutes of Essential Oil

Terpenes, or terpenoids, are the most abundant and diversified class of naturally occurring chemicals in natural plants. They are categorized as mono, di, tri, tetra, as well as sesquiterpenes depending on the number of isoprene units they contain. Table 4 categorizes monoterpene, oxygenated monoterpenes, sesquiterpene hydrocarbons, oxygenated sesquiterpenes and other compounds present in clove and tulsi. Among monoterpene hydrocarbons, both plants are enriched with α-Pinene, β-Pinene, Limonene, and Camphene. Besides, some compounds such as 1.8-Cineole, α-Terpineol, β-Caryophyllene, Germacrene D, δ-Cadinene, α-Selinene, α-Cadinol contained by sesquiterpenes are the most common in these two natural herbs [91,96].

### Toxicological Studies

Many studies have reported several therapeutic actions of *S. aromaticum* and *O. sanctum*. The World Health Organization (WHO) found that the daily amount of clove that is acceptable in humans is 2.5 mg/kg of weight whereas the daily consumption of tulsi is 30 ml/kg (Table 5). It can cause possible side effects such as liver damage, seizures, and fluid imbalances. There have not been found noteworthy evidences about clove's safety in medicinal doses [97]. However, it has been recommended to avoid its use for pregnant or breastfeeding women [97]. In respect of tulsi, studies revealed favorable therapeutic results with low or no side effects for formulations, irrespective of dose, or for any participant's age or gender [28].

**Table 5**: Toxic Dose and Safety profile of *S. aromaticum* and *O. sanctum.*

| ***Findings*** | ***S. aromaticum*** | ***O. sanctum*** |
|---|---|---|
| Toxic Dose | Equal or greater than 1500 mg/kg [98] | 55 ml/kg [99] |
| Maximum Daily Intake | 2.5 mg/kg[35] | 30 ml/kg [99] |
| LD50 | 18.2 ±5.52 mg/ml in *Danio rerio* and 21.7 ±0.8 mg/ml in *Poecilia reticulata* at 96h[100] | 42.5 ml/kg 99] |
| Adverse Reaction | Spermicidal activity in males, allergic action when used in dentistry, increased endogenous redox enzyme levels and Reduced lipid peroxidation in humans resulted in disseminated intravascular coagulopathy, generalized seizures, and hepatotoxicity, detoxification, and cardiac health effects, allergic contact dermatitis in guinea pigs[98] [101] | Clinical trial reporting transient moderate nausea [102] |

The absence of any adverse effects does not rule out the possibility of long-term side effects. However, the long traditional history of daily usage of tulsi indicating any major long-term health risks are rare and daily intake of tulsi has been reported safe [28].

### Biological Responses

Clove and Tulsi are essential therapeutic plants because of the extensive spectrum of pharmacological properties accumulated over centuries of traditional use and documented in literatures. These plants are abundant with many phytoconstitutes that leads many researchers to identify specific compounds in response to particular disease. Eugenol, the major compound of clove is reported to participate in photochemical reactions [103]and photocytotoxic properties [104]. In 1995, the radioprotective effect of *Ocimum sanctum* was first documented [105]. Besides, clove and tulsi both plants have showed antibacterial, antifungal, anticarcinogenic, analgesic, cardioprotective, anti- inflammatory, anti-fertility activities depending on their phytoconstituents. Table 6 represents biological responses of both plants according to their phytocompounds.

## RECOMMENDATIONS

The review recommends a wide range of pharmaceutical activities categorized based on their bioactive compounds. However, it also identified opportunities for further investigations in vital areas. As such, no studies were found on the co-administration (intake) of these two plants in laboratory or human model to identify their safety profile, adverse reactions or contraindications whereas, in vice versa, no report suggested their use in ailments alternatively. Moreover, very few studies documented the nutrients presents in isolated parts of these herbs. In addition, no studies were found on determining the daily intake or safe doses individually for particular diseases or disorder. Thus, current comparison

**Table 6:** Comparative summary of pharmacological properties of *S. aromaticum* and *O. sanctum* by representing the biological responses and responsible bioactive compounds.

| ***Pharmaco-logical Activity*** | ***S. aromaticum*** | | ***O. Sanctum*** | |
|---|---|---|---|---|
| | ***Biological Response*** | ***Bioactive Compounds*** | ***Biological Response*** | ***Bioactive Compounds*** |
| Antimicrobial activity | 1. Acts against non-toxigenic strains of *E. coli* O157:H7 [106]<br>2. Active against foodborne gram-positive bacteria (*S. aureus, B. cereus, E. faecalis, L. monocytogenes*) and gram-negative bacteria (*E. coli, Y. enterocolitica, S. choleraesuis, P. aerugenosa*) [51]<br>3. Suppress growth of methicillin-resistant clinical isolates at 1000 and 500mg/ml concentration[51]<br>4. Inhibits growth of 31 strains of *H. pylori* [51]<br>5. Active against yeasts and filamentous fungi [107] | Eugenol, eugenyl acetate, β-Caryophyllene, 2-heptanone, [108] acetyl-eugenol, α-humulene, methyl salicylate, iso-eugenol, methyl-eugenol, [109] phenyl propanoides, dehydrodieugenol, trans-confireryl aldehyde, biflorin, kaempferol, rhamnetin, myricetin, gallic acid, ellagic acid and oleanolic acid [110] | 1. Inhibits cell growth of *E. coli, Klebsiella, Staphylococcus aureus* and *proteus* by aqueous extract [111]<br>2. Inhibits multidrug-resistant strain of *S. aureus* and *V. cholera* by alcoholic extract [112]<br>3. Potential effect against *N. gonorrhea* resistant strains [113]<br>4. Inhibits *P. aeruginosa, S. aureus* and *B. pumilus* by *O. sanctum* fixed oil [114] | Linolenic acid [114] |
| Antioxidant activity | 1. Strong antioxidant efficiency compared to BHA and pyrogallol [115]<br>2. Suppresses linoleic acids lipid peroxidation by clove oil at 15ug/ml. Scavenging potential by lower concentration of essential oil compared to eugenol, BHA, BHI [98]<br>3. Improves kidney and liver functions as well as antioxidant status [116]<br>4. Provides potential protection against cell damages induced by $H_2O_2$ [87].<br>5. Protective effect against $CCL_4$ induced fibrosis [117] | Eugenol, β-caryophyllene, Vanillin, Kaempferol, Rhamnetin, Gallic acid, Biflorin, Myricetin [98,116] | 1. Protects membrane by flavonoids present in *O. sanctum* [118]<br>2. Reduces radiation-induced lipid peroxidation significantly in the mouse liver [119]<br>3. Processes high scavenging activity for highly reactive free radicals [34]<br>4. Decreases lipid peroxidation significantly before and after mercury ($Hgcl_2$) poisoning [120] | Orientin, vicenin [119], cirsilineol, cirsimaritin, isothymusin, apigenin, rosmarinic acid, eugenol[34] |
| Anticancer activity | 1. Exhibits anticarcinogenic and antimutagenic potential [121,122] | Oleanolic acid, Eugenol [123,91] | 1. Modulates carcinogen metabolizing enzymes such as cytochrome P450, aryl hydrocarbon hydroxylase, | Ursolic acid [130] |

| *Pharmaco-logical Activity* | *S. aromaticum* | | *O. Sanctum* | |
|---|---|---|---|---|
| | *Biological Response* | *Bioactive Compounds* | *Biological Response* | *Bioactive Compounds* |
| Anticancer activity (cont.) | 2. Plays chemopreventive role for lung, skin and digestive cancers [87]<br>3. Prevents tumor growth and encourages cell cycle arrest and apoptosis [123]<br>4. Interferes with NF-κB and other cells signaling pathways [87]<br>5. Inhibits malignant melanoma, of both anchorage-dependent and anchorage-independent growth, reduce tumors size and blocks melanoma invasion and metastasis [124]<br>6. Prevents cervical carcinoma and gemcitabine at low concentrations [ 91]<br>7. Decreases the possibility of apoptosis of Bcl-2, COX-2 and IL-1β, lessens inflammation, and facilitates the efficacy of gemcitabine [87]<br>8. Displays better remedial effects in skin malignancy and melanoma [87] | (cont.) | cytochrome b5, and glutathione S-transferase by the alcoholic extract of tulsi leaves [125]<br>2. Inhibits human fibrosarcoma cells in vitro to reduce cytoplasm, condensed nuclei, and fragmented DNA [126]<br>3. Reduces benzo(a)pyrine induced forestomach neoplasia in mice as well as 3'-methyl-4-dimethylaminoazobenzene induced hepatomas in rats [127]<br>4. Inhibits chemically induced skin papillomas in mice [128]<br>5. Induces papillomagenesis significantly to reduce the tumour incidence, average number of papillomas or/and cumulative number of papillomas in mice [129]<br>6. Elevates reduced GSH content and GST activities [129]<br>7. Prevents early events of DMBA induced buccal pouch carcinogenesis by oral treatment[130]<br>8. Blocks or suppresses the events associated with chemical carcinogenesis by inhibiting metabolic activation of the carcinogen [131]<br>9. Protects Swiss Albino mice against Ehrlich ascites carcinoma (EAC) and S 180 tumors [132] | (cont.) |
| Anti-inflammatory activity | 1. Inhibits respiratory inflammation by essential oil [133]<br>2. Lessens musculoskeletal pain and nasal congestion by COX-2 inhibition [134]<br>3. Alleviates cold, cough, asthma, bronchitis and sinusitis through inhalation of aromatic oil [135]<br>4. Mimics endolac at 0.025 and 0.1 ml/kg and Indomethacin at 0.05 and 0.2ml/kg doses.<br>5. Decreases the volume of pleural exudates keeping the total blood leukocyte count unchanged at 200 and 400 mg/kg [136] | Flavonoids including kaempferol, rhamnetin and β-Caryophyllene [135] and eugenol [136] | 1. Shows analgesic, antipyretic, anti-inflammatory effects in acute and chronic inflammations in rats [137]<br>2. Restores the stress alteration caused by noise stress (leucopenia, elevated corticosterone level, and neutrophil functions) values to normal levels, showing a stress-relieving action [138] | Flavonoids [139] |

| ***Pharmaco-logical Activity*** | ***S. aromaticum*** | | ***O. Sanctum*** | |
|---|---|---|---|---|
| | ***Biological Response*** | ***Bioactive Compounds*** | ***Biological Response*** | ***Bioactive Compounds*** |
| Chemo-preventive activity | 1. Inhibits cell multiplication during carcinogenesis.<br>2. Lowers COX-2 levels 13.49 % and 55.93%, by clove infusion on 17th and 26th weeks of carcinogenesis [59] | Eugenol [140] | 1. Promotes antiproliferative and chemopreventive activities in mice [141]<br>2. Elevates levels of reduced GSH in liver, lung and stomach tissues [141] | Apigen [142] |
| Radio-protective activity | 1. Promotes radioprotective activity by inhibiting lipid peroxidation, showing strong reducing power, and superoxide radical scavenging activity [143] | Polyphenol, trace element [144] | 1. Protects human lymphocytes against clastogenic effects of radiation at low and non-toxic doses [112]<br>2. Potentiates radioprotective action in humans by increasing protection of bone marrow cells and lower toxicity of WR-2721 [145] | Flavonoids- orientin and vicenin [118]<br>Rosemarinic acid [142] |
| Anti-hypertensive and cardio-protective activities | 1. Minimizes the risk of cardiovascular disease, arterial sclerosis, and many other conditions linked to oxidative stress. [35]<br>2. Responsible for reversible and negative inotropic effects in the heart muscle.[35]<br>3. Acts as smooth muscle relaxant and hypotensive agent [35] | Eugenol [35] | 1. Prevents temporary and long-term cerebral ischemia and hypoperfusion [34]<br>2. Shows hypotensive effect in anesthesia due to peripheral vasodilatory activity.<br>3. Protects Wister rats from isoproterenol-induced myocardial necrosis by increasing endogenous antioxidants [146]<br>4. Inhibits the transcriptional expression of genes modulating atherogenesis controlling lipid metabolism, cytotoxin production and cellular activity within the arterial wall [147]<br>5. Lowers serum cholesterol, LDL + VLDL cholesterol and triacylglycerol indicating a hypocholesterolemic effect [9]<br>6. Decreases blood total cholesterol, triglyceride, phospholipids, and LDL-cholesterol levels, as well as a significant increase in HDL-cholesterol and total fecal sterol levels [148] | Linoleic and linolenic acids [149] |
| Hepato-protective activity | 1. Lowers alkaline phosphatase activity indicating hepatoprotective effect of clove oil [150] | Flavonoids and polyphenolic [150] | 1. Protects liver injury induced by paracetamol by oral administration [151]<br>2. Prevents carbon tetrachloride (0.2 ml/100 g, subcutaneously)-induced liver damage in Albino rats [89] | Eugenol, flavonoid and ursolic acid, linoleic acid [152] |

| ***Pharmaco-logical Activity*** | ***S. aromaticum*** | | ***O. Sanctum*** | |
|---|---|---|---|---|
| | ***Biological Response*** | ***Bioactive Compounds*** | ***Biological Response*** | ***Bioactive Compounds*** |
| Anthelmintic activity | 1. Reveals anthelmintic property against *H. contortus* worms.<br>2. Effectively kills worms at high concentrations where 100% mortality was attained within minutes of exposure [153] | Phenolics, Tannins and Alkaloids[154] | 1. Shows putative anthelmintic activity on Caenorhabditis elegance model [155]<br>2. Impacts in non-hatching of eggs, non-development of larvae, and paralysis and death of larvae of gastrointestinal nematodes [156] | Eugenol [155], Tannins [156] |
| Analgesic activity | 1. Helps to inhibit inflammatory mediators such as prostaglandins, leukotrienes [87]<br>2. Inhibits pain perception by suppressing sensory receptor [157]<br>3. Lowers the action potential conduction [158]<br>4. Inhibits NMDA - GABA receptor stimulation which are involved in pain sensitivity [159] | Eugenol [157] | 1. Effective against acetic acid induced writhing method in mice in a dose dependent manner [89]<br>2. Processes combined inhibitory effects of prostaglandins, histamine and acetylcholine [160] | Not reported |
| Central Nervous System (CNS) depressant activity | 1. Prevents convulsions through inhibitory activity via strychnine and picrotoxin effects at glycine and GABAA receptor sites, respectively by clove essential oil [87]<br>2. Promotes hypnotic and anxiolytic effects by increasing the concentration of GABA in the brain[99] | Eugenol, B-Caryophyllene, Humulene [99] | 1. Extends the period of lost reflex, lowers the time of recovery and severity of electroshock and pentylenetetrazole-induced convulsions in mice [89]<br>2. Reduces apomorphine-induced fighting time and ambulation [161]<br>3. Increases swimming time indicating a CNS stimulant or antidepressant mimicking desipramine [162]<br>4. Increases sleeping time in rats induced by pentobarbitone [46]<br>5. Enhances the levels of dopamine (DA), serotonin (5-HT), and 5-HT turnover in numerous distinct brain areas during sub-chronic noise exposure [163]<br>6. Prevents the noise-induced increase in levels of neurotransmitters without affecting normal levels indicating probable herbal treatment for noise-induced biogenic amine alterations [164] | Not reported |
| Antipyretic activity | 1. Mimics acetaminophen intragastrically and intravenously to treat fever [165] | Eugenol [165] | 1. Reduces the febrile response indicating its antipyretic activity against typhoid-paratyphoid A/B vaccine-induced pyrexia in rats [166], mimics aspirin in antipyretic effect at a dose of 3 ml/kg [166] | Not reported |

| ***Pharmaco-logical Activity*** | ***S. aromaticum*** | | ***O. Sanctum*** | |
|---|---|---|---|---|
| | ***Biological Response*** | ***Bioactive Compounds*** | ***Biological Response*** | ***Bioactive Compounds*** |
| Antidiabetic activity | 1. Contributes hypoglycemic effect via molecular dynamics, molecular mechanic and molecular Docking [167] | Acetyleugenol, Eugenol, alpha-Humulen [167] | 1. Potentiates the action of exogenous insulin, improves fasting blood glucose and glucose tolerance[168]<br>2. Reduces fasting and postprandial blood glucose levels in a randomized trial [169]<br>3. Processes aldose reductase activity to decrease the complications of diabetes such as cataract, retinopathy, etc [170] | Not reported |
| Antiulcer activity | 1. Prevents ethanol- and indomethacin-induced stomach ulcers in rat model [172]<br>2. Improves gastrointestinal health, particularly in chronic alcohol users [171]<br>3. Provides gastroprotective effect via synthesis of mucus [172] | Eugenol, Clovinol [171,172] | 1. Elicits notable antiulcer activity against aspirin, indomethacin, , reserpine, histamine, alcohol (ethanol 50%) , serotonin or stress-induced ulcers in rats [166]<br>2. Possesses antiulcer activity due to lipoxygenase inhibitory effects, histamine antagonistic, and antisecretory activities [173] | Not reported |
| Antiarthritic activity | 1. Promotes bone-preserving efficacy by the hydroalcoholic extract of dried clove buds in ovariectomised rat model of osteoporosis [174] | Eugenol [30] | 1. Improves in formaldehyde induced arthritis in rats as comparable to aspirin[166]<br>2. Inhibits inflammatory mediators (e.g., serotonin, histamine, bradykinin and PGE2) in experimentally induced arthritis and joint edema [175] | Not reported |
| Adaptogenic activity/anti-stress activity | 1. Shows significant antidepressant like activity against monoamineoxidase in CD-1(ICR) mice [176] | Eugenol [176] | 1. Shows adaptogenic activity via immunostimulant capacity [177]<br>2. Increases resistance to a variety of stress-induced biological changes [89] | Not reported |
| Anesthetic Activity | 1. Exhibits slight anesthetic activity in humans and fish by S. aromaticum oil[178, 179]<br>2. Blocks prostaglandin H (PHS) production [180]<br>3. Able to anesthetize rabbit fish (*Saiganus lineatus*), rainbow trout (*Oncorhynchus mykiss*), and coral reef fish (*Pomacentrus amboinensis*), crabs [181]<br>4. Generates fast anesthesia in Zebra fish with a short recovery time [87] | Eugenol [180] | 1. Exhibits the shortest induction time indicating the highest anesthetic activity to fish. | Methyl eugenol |

| ***Pharmaco-logical Activity*** | ***S. aromaticum*** | | ***O. Sanctum*** | |
|---|---|---|---|---|
| | ***Biological Response*** | ***Bioactive Compounds*** | ***Biological Response*** | ***Bioactive Compounds*** |
| Anticoagulant activity | 1. Inhibits human platelet aggregation on stimulated platelet activating factor, arachidonic acid (AA) or collagen [87]<br>2. Protects PAF against AA at induced thrombosis [87]<br>3. Reduces the production of thromboxane A2 and 12-HETE by human platelets treated with [C [14]] AA. [182]<br>4. Suppresses in vitro prostaglandin biosynthesis, formation of thromboxane B2, and arachidonic acid-induced platelet aggregation in vitro [83][183]<br>5. Supersedes aspirin in preventing platelet aggregation induced by arachidonate, adrenaline and collagen.<br>6. Exerts equivalent efficacy to indomethacin in arachidonate induced aggregation [184] | Eugenol and acetyl eugenol [184] | 1. Prolongs blood clotting time indicating the antiaggregatory action of oil on platelets as compared to aspirin [149]<br>2. Increases blood clotting time and percentage which is and could be due to inhibition of platelet aggregation | Linoleic acid [166] |
| Immuno-modulatory activity | 1. Increases humoral and cell-mediated immune responses via immunomodulatory action[185] | Not reported | 1. Modifies humoral immune response via antibody formation [82]<br>2. Influences both humoral and cell-mediated immune responses, and GABAergic pathways [186] | Ursolic acid, oleanolic acid and salrigenin [186] |
| Antifertility activity | 1. Decreases and distorts pattern of spermatozoa, thickening of the membrane, vacuolization within seminiferous<br>2. Decreases length and weight of testis considerably [187]<br>3. Inhibits testicular activity administering high and mid dose points a biphasic effect of clove flower bud [188] | Not reported | 1. Decreases total sperm count, sperm motility and weight of testis [189]<br>2. Reduces sperm count, sperm motility, and male reproductive organ weight for long-term feeding [89]<br>3. Reduces the sexual behavioral score in mature male Wistar rats [190] | Ursolic acid [191] |
| Memory enhancer activity | 1. Improves learning and memory subsequently through reduction in lipid peroxides [63]<br>2. Improves scopolamine-induced memory deficit at a relatively higher dose (0.1 ml/kg). | Not reported | 1. Ameliorates the amnesic impact of scopolamine (0.4 mg/kg) as well as aging-induced memory impairments [192]<br>2. Improves step-down latency (SDL) and acetylcholinesterase inhibition in treating cognitive diseases including dementia and Alzheimer's disease [192] | Not reported |

recommends further phytochemical and pharmacological analysis to establish clove and tulsi as prescribed natural agents.

## CONCLUSION

The role of natural plants in medicine have always been well-documented in literatures. This review was focused on the comparison of traditional uses, biological responses, chemical compositions, toxicity and safety profiles of clove and tulsi herbs. Alongside the comparative analysis, the study also revealed common constituents and common pharmacological activities among these two plants; which have indicated the role of different bioactive compounds for same biological responses. The review concludes that both clove and tulsi are highly potent pharmacological agents and can be used for different ailments prior assessing their safe dose profile against the particular disease or disorder.

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### Authors' Contributions

Authors MNI structured and organized the project. Author JS collected the findings and prepared the manuscript.

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Authors agreed on the article before submission and had no conflict of interests.

## REFERENCES

1. Cortés-Rojas DF, de Souza CRF, Oliveira WP. Clove (*Syzygium aromaticum*): A precious spice. *Asian Pac J Trop Biomed*. 2014;4(2):90-96. doi:10.1016/S2221-1691(14)60215-X
2. Nassan M, Mohamed E, Abdelhafez S, Ismail T. Effect of clove and cinnamon extracts on experimental model of acute hematogenous pyelonephritis in albino rats: Immunopathological and antimicrobial study. *Int J Immunopathol Pharmacol*. 2015;28(1):60-68. doi:10.1177/0394632015572075
3. Prince A, Powell C. Clove oil as an anesthetic for invasive field procedures on adult rainbow trout. *North American Journal of Fisheries Management*. 2000;20(4):1029-1032. doi:10.1577/1548-8675(2000)020<1029:COAAAF>2.0.CO;2
4. Lee KG, Shibamoto T. Antioxidant property of aroma extract isolated from clove buds [*Syzygium aromaticum* (L.)Merr. et Perry]. *Food Chemistry*. 2001;74(4):443-448. doi:10.1016/S0308-8146(01)00161-3
5. Núñez L, D'Aquino M, Chirife J. Antifungal properties of clove oil (*Eugenia caryophylata*) in sugar solution. *Braz J Microbiol*. 2001; 32:123-126. doi:10.1590/S1517-83822001000200010
6. Zainol SN, Said SM, Abidin ZZ, Azizan N, Majid F a. A, Jantan I. Synergistic benefit of *Eugenia Caryophyllata* L. and *Cinnamomum Zeylanicum* Blume essential oils against oral pathogenic bacteria. *Chemical Engineering Transactions*. 2017;56:1429-1434. doi:10.3303/CET1756239
7. Bast F, Rani P, Meena D. Chloroplast DNA phylogeography of Holy Basil (*Ocimum tenuiflorum*) in Indian subcontinent. *The Scientific World Journal*. 2014;2014: e847482. doi:10.1155/2014/847482
8. Mohan L, Amberkar MV, Kumari M. *Ocimum sanctum* Linn (Tulsi) - an overview. *International Journal of Pharmaceutical Sciences Review and Research*. 2011;7(1):51-53.
9. Pattanayak P, Behera P, Das D, Panda SK. *Ocimum sanctum* Linn. A reservoir plant for therapeutic applications: an overview. *Pharmacogn Rev*. 2010;4(7):95-105. doi:10.4103/0973-7847.65323
10. Mondal S, Mirdha BR, Mahapatra SC. The science behind sacredness of Tulsi (*Ocimum sanctum* Linn.*).Indian J Physiol Pharmacol*. 2009;53(4):291-306.
11. Tiwari M, Murugan R, Tulsawani R, et al. Factors affecting radioprotective efficacy of *Ocimum sanctum* (Tulsi) extract in mice. *JAMPS*. 2016;9(9):1-12. doi:10.9734/JAMPS/2016/28152
12. Mondal S, Varma S, Bamola VD, et al. Double-blinded randomized controlled trial for immunomodulatory effects of Tulsi (*Ocimum sanctum* Linn.) Leaf extracton healthy volunteers. *J Ethnopharmacol*. 2011;136(3):452-456. doi:10.1016/j.jep.2011.05.012
13. Meghwani H, Prabhakar P, Mohammed SA, et al. Beneficial effect of *Ocimum sanctum* (Linn*)* against monocrotaline-induced pulmonary hypertension in rats. *Medicines (Basel)*. 2018;5(2):34. doi:10.3390/medicines5020034
14. Deore SL, Jaju PS, Baviskar BA. Simultaneous estimation of four antitussive components from herbal cough syrup by HPTLC. *Int Sch Res Notices*. 2014; 2014:1-7. doi:10.1155/2014/976264
15. Integrated Taxonomic Information System - Report (ITIS): *Syzygium aromaticum.* Accessed February 11, 2022. https://www.itis.gov/servlet/SingleRpt/SingleRpt?search_topic=TSN&search_value=506167#null

16. Dash BK, Azam M, Or-Rashid A, Hafiz F, Sen M. Ethnomedicobotanical study on *Ocimum sanctum* L. (Tulsi) -A review. *Mintage Journal of Pharmaceutical & Medical Sciences*. 2013; 2.
17. Ekor M. The growing use of herbal medicines: Issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol*. 2014;4(177):1-7. doi:10.3389/fphar.2013.00177
18. 7 health benefits of Tulsiplant. Care Health Insurance. Updated February 01, 2022. Accessed February 11, 2022. https://www.careinsurance.com/blog/health-insurance-articles/remarkable-health-benefits-of-tulsi-leaves-you-must-know
19. M. S, Shanmugam KR, Bhasha DS, G. V. *Ocimum sanctum*: A review on the pharmacological properties. *International Journal of Basic & Clinical Pharmacology*. 2016;5(3):558-565. doi:10.18203/2319-2003.ijbcp20161491
20. Bhowmik D, Kumar K, Yadav A, Paswan S. Recent trends in Indian traditional herbs *Syzygium aromaticum* and its health benefits. *Journal of Pharmacognosy and Phytochemistry*. 2012; 1 (1):13-23.
21. Kuroda, M., Mimaki, Y., Ohtomo, T., Yamada, J., Nishiyama, T., Mae, T., Kishida, H., & Kawada, T. Hypoglycemic effects of clove (*Syzygium aromaticum* flower buds) on genetically diabetic KK-Ay miceand identificationof the active ingredients. *Journal of Natural Medicines*.2012;66(2):394–399. https://doi.org/10.1007/s11418-011-0593-z
22. Tahir HU, Sarfraz RA, Ashraf A, Adil S. Chemical composition and antidiabetic activity of essential oils obtained from two spices (*Syzygium aromaticum* and *Cuminum cyminum*). *International Journal of Food Properties*. 2016;19(10):2156-2164. doi:10.1080/10942912.2015.1110166
23. Prasad RC, Herzog B, Boone B, Sims L, Waltner-Law M. An extract of *Syzygium aromaticum* represses genes encoding hepatic gluconeogenic enzymes. *Journal of Ethnopharmacology*. 2005;96(1-2):295-301. doi:10.1016/j.jep.2004.09.024
24. Vats V, Grover JK, Rathi SS. Evaluation of anti-hyperglycemic and hypoglycemic effect of *Trigonella foenum-graecum* Linn, *Ocimum sanctum* Linn and *Pterocarpus marsupium* Linn in normal and alloxanized diabetic rats. *Journal of Ethnopharmacology*. 2002;79(1):95-100. doi:10.1016/S0378-8741(01)00374-9
25. Singh J, Baghotia A, SP G. *Eugenia caryophyllata* Thunberg (Family Myrtaceae): A Review. Int. J. Res. Pharm. Biomed. Sci. 2012;3(4):1469–1475.
26. Sethi L, Bhadra P. A review paper on Tulsi plant (*Ocimum sanctum* L.). *Indian Journal of Natural Sciences*. 2020; 10(60):20854-20860.
27. Vicidomini C, Roviello V, & Roviello GN. Molecular basis of the therapeutical potential of clove (*Syzygium aromaticum* L.*)* and clues to its anti-COVID-19 utility. *Molecules*. 2021;26(7):1880. doi: 10.3390/molecules26071880
28. Jamshidi N, Cohen MM. The clinical efficacy and safety of Tulsi in humans: A systematic review of the literature. *Evidence-Based Complementary and Alternative Medicine*. 2017; 2017:1-13. doi:10.1155/2017/9217567
29. Ahmadifard M, Yarahmadi S, Ardalan A, Ebrahimzadeh F, Bahrami P, Sheikhi E. The efficacy of topical basil essential oil on relieving migraine headaches: A randomized triple-blind study.*Complement Med Res*. 2020;27(5):310-318. doi: 10.1159/000506349
30. Grespan R, Paludo M, Lemos H de P, et al. Anti-arthritic effect of eugenol on collagen-induced arthritis experimental model. *Biological & Pharmaceutical Bulletin*. 2012;35(10):1818-1820. doi:10.1248/bpb.b12-00128
31. Komeh-Nkrumah SA, Nanjundaiah SM, Rajaiah R, Yu H, Moudgil KD. Topical dermal application of essential oils attenuates the severity of adjuvant arthritis in Lewis rats: Antiarthritic activity of essential oils. *Phytother Res*. 2012;26(1):54-59. doi:10.1002/ptr.3509
32. Mirje MM, Zaman SU, Ramabhimaiah S. Evaluation of the anti-inflammatory activity of *Ocimum sanctum* Linn (Tulsi) in Albino rats. 2014;3(1):198-205.
33. Calderón Bravo H, Vera Céspedes N, Zura-Bravo L, Muñoz LA. Basil seeds as a novel food, source of nutrients and functional ingredients with beneficial properties: A review. *Foods*. 2021;10(7):1467. doi:10.3390/foods10071467
34. Kelm MA, Nair MG, Strasburg GM, DeWitt DL. Antioxidant and cyclooxygenase inhibitory phenolic compounds from *Ocimum sanctum* Linn. *Phytomedicine*. 2000;7(1):7-13. doi:10.1016/S0944-7113(00)80015-X
35. El-Saber Batiha G, Alkazmi LM, Wasef LG, Beshbishy AM, Nadwa EH, Rashwan EK. *Syzygium aromaticum* L. (Myrtaceae): Traditional uses, bioactive chemical constituents, pharmacological and toxicological activities. *Biomolecules*. 2020;10(2):202. doi:10.3390/biom10020202
36. Kumar KS, Bhowmik D,Biswajit, et al. Traditional Indian herbal plants Tulsi and its medicinal importance.*Research Journal of Pharmacognosy and Phytochemistry.* 2010;2(2): 93-101.
37. Leung AY, Khan IA, Abourashed EA . Leung's Encyclopedia of Common Natural Ingredients Used in Food, Drugs, and Cosmetics. A John Wiley & Sons, Cop; 2010.
38. Dharmani P, Kuchibhotla VK, Maurya R, Srivastava S, Sharma S, Palit G. Evaluation of anti-ulcerogenic and ulcer-healingproperties of *Ocimum sanctum* Linn. *Journal of Ethnopharmacology*. 2004;93(2-3):197-206. doi:10.1016/j.jep.2004.02.029
39. Vaseem A, Ali M, Afshan K. Activity of Tulsileaves(*Ocimum sanctum* linn) in protecting gastric ulcer in ratsbycold restrains method. *International Journal of Basic & Clinical Pharmacology*. 2017;6(10):2343-2347. doi:10.18203/2319-2003.ijbcp20174356
40. Fu Y, Chen L, Zu Y, et al.The antibacterial activity of clove essential oil against propionibacterium acnes and its mechanism of action. *Arch Dermatol*. 2009;145(1):86-88.doi:10.1001/archdermatol.2008.549
41. Mohammadi Nejad S, Özgüneş H, Başaran N. Pharmacological and toxicological properties of eugenol.

*Turk J Pharm Sci*. 2017;14(2):201-206. doi:10.4274/tjps.62207

42. Aisha AFA, Abu-Salah KM, Alrokayan SA, Siddiqui MJ, Ismail Z, Majid AMSA. *Syzygium aromaticum* extracts as good source of betulinic acid and potential anti-breast cancer.*Rev bras farmacogn*. 2012;22(2):335-343. doi:10.1590/S0102-695X2011005000185
43. Rai V, Iyer U, Mani UV. Effect of Tulasi (*Ocimum sanctum*) leaf powder supplementation on blood sugar levels, serum lipids and tissues lipids in diabetic rats. *Plant Food Hum Nutr*. 1997;50(1):9-16. doi:10.1007/BF02436038
44. Chegu K, Mounika K, Rajeswari M, et al. In vitro study of the anticoagulant activity of some plant extracts. *World Journal of Pharmacy and Pharmaceutical Sciences*. 2019;7: 904-913. doi:10.20959/wjpps20185-11492
45. Suanarunsawat T, Boonnak T, Ayutthaya WDN, Thirawarapan S. Anti-hyperlipidemic and cardioprotective effects of *Ocimum sanctum* L.fixed oil in rats fed a high fat diet. *Journal of Basic and Clinical Physiology and Pharmacology*. 2010;21(4):387-400. doi:10.1515/JBCPP.2010.21.4.387
46. Singh S, Rehan HMS, Majumdar DK. Effect of *Ocimum sanctum* fixed oil on blood pressure, blood clotting time and pentobarbitone-induced sleeping time. *Journal of Ethnopharmacology*. 2001;78(2-3):139-143. doi:10.1016/S0378-8741(01)00336-1
47. Mohamed M, Abdallah A, Mahran M, Shalaby A. Potential alternative treatment ofocular bacterial infections by oil derived from *Syzygium aromaticum* flower (Clove). *Current Eye Research*. 2018;43(7):873-881.doi:10.1080/02713683.2018.1461907
48. DeFilipps RA,Krupnick GA. The medicinal plants of Myanmar. *PhytoKeys*. 2018;(102):1-341. doi:10.3897/phytokeys.102.24380
49. Inbaneson SJ, Sundaram R, Suganthi P. In vitro antiplasmodial effect of ethanolic extracts of traditional medicinal plant *Ocimum* species against *Plasmodium falciparum*. *Asian Pacific Journal of Tropical Medicine*. 2012;5(2):103-106. doi:10.1016/S1995-7645(12)60004-2
50. Patel RR. Tulsi: The queen of medicinal herbs.*Journal of Bioequivalence & Bioavailability.*2020;12(6):407.
51. A.Mounika AM, M.Sushma MS, Sidde L, Malathi S, Rajani K. Invitro evaluation of antimicrobial activity of Clove buds (*Euginea aromatica*).*International Journal of Indigenous Herbs and Drugs*. 2020;5(4):25-33. doi:10.46956/ijihd.vi.95
52. Chee HY, Lee MH. Antifungal activity of Cloveessential oil and its volatile vapouragainstdermatophytic fungi. *Mycobiology*. 2007;35(4):241-243. doi:10.4489/MYCO.2007.35.4.241
53. Schmidt E, Jirovetz L, Wlcek K, et al. Antifungal activity of eugenol and various eugenol-containing essential oils against 38 clinical isolates of *Candida albicans*. *Journal of Essential Oil Bearing Plants*. 2007;10(5):421-429. doi:10.1080/0972060X.2007.10643575
54. Xu JG, Liu T, Hu QP, Cao XM. Chemical composition, antibacterial properties and mechanism of action of essential oil from Clovebuds against *Staphylococcus aureus*. *Molecules*. 2016;21(9):1194. doi:10.3390/molecules21091194
55. Kalemba D, Kunicka A. Antibacterial and antifungal properties of essential oils. *Current Medicinal Chemistry*. 2003;10(10):813-829. doi:10.2174/0929867033457719
56. Amber K, Aijaz A, Immaculata X, Luqman KA, Nikhat M. Anticandidal effect of *Ocimum sanctum*essential oil and its synergy with fluconazole and ketoconazole. *Phytomedicine*. 2010;17(12):921-925. doi:10.1016/j.phymed.2010.02.012
57. Banerjee S, Panda CKr, Das S. Clove (*Syzygium aromaticum* L.), a potential chemopreventive agent for lung cancer. *Carcinogenesis*. 2006;27(8):1645-1654. doi:10.1093/carcin/bgi372
58. Bhattacharyya P, Bishayee A. *Ocimum sanctum* Linn. (Tulsi): An ethnomedicinal plant for the prevention and treatment of cancer. *Anti-Cancer Drugs*. 2013;24(7):659-666. doi:10.1097/CAD.0b013e328361aca1
59. Prakash J, Gupta SK. Chemopreventiveactivity of *Ocimum sanctum* seed oil. *Journal of Ethnopharmacology*. 2000; 72(1-2):29-34. doi:10.1016/S0378-8741(00)00194-X
60. Parle M, Khanna D. Clove: A champion spice. *International Journal of Research in Ayurveda and Pharmacy*. 2010;2(1):47-54.
61. Kaur G, Jaggi AS, Singh N. Exploring the potential effect of *Ocimum sanctum* in vincristine-induced neuropathic pain in rats. *J Brachial Plex Peripher Nerve Inj*. 2010; 5:3. doi:10.1186/1749-7221-5-3
62. Kassab R, Bauomy A. The neuroprotective efficency of the aqueous extract of Clove (*Syzygium aromaticum*) in aluninium-induced neurotoxicity. *International Journal of Pharmacy and Pharmaceutical Sciences*. 2014; 6:503-508.
63. Halder S, Mehta AK, Kar R, Mustafa M, Mediratta PK, Sharma KK. Cloveoil reverses learning and memory deficits in scopolamine-treated mice. *Planta Med*. 2011;77(8):830-834. doi:10.1055/s-0030-1250605
64. Giridharan VV, Thandavarayan RA, Konishi T. *Ocimum sanctum* Linn. (Holy Basil) to improve cognition. *Diet and Nutrition in Dementia and Cognitive Decline*.2015:1049-1058. doi:10.1016/B978-0-12-407824-6.00098-7
65. Pant A, Prakash P, Pandey R, Kumar R. *Syzygium aromaticum* (L.) Elicits lifespan extension and attenuates age-related Aβ-induced proteotoxicity in *Caenorhabditis elegans*. *Cogent Biology*. 2016;2(1):1218412. doi:10.1080/23312025.2016.1218412
66. Anees AM. Larvicidal activity of *Ocimum sanctum* Linn. (Labiatae) against *Aedes aegypti (L.)* and *Culex quinquefasciatus* (Say). *Parasitol Res*. 2008;103(6):1451-1453. doi:10.1007/s00436-008-0991-7
67. Buchineni M, Pathapati RM, Kandati J, Buchineni M. Anthelmintic activity of tulsi leaves (*Ocimum Sanctum* Linn)-An in-vitro comparative study.*Saudi Journal of Medical and Pharmaceutical Sciences.*2015;1(2):47-49.
68. Dibazar SP, Fateh S, Daneshmandi S. Clove (*Syzygium aromaticum*) ingredients affect lymphocyte subtypes expansion and cytokine profile responses: An in vitro

evaluation. *Journal of Food and Drug Analysis*. 2014;22(4):448-454. doi:10.1016/j.jfda.2014.04.005

69. Han X, Parker TL. Anti-inflammatory activity of clove (*Eugenia caryophyllata*) essential oil in human dermal fibroblasts. *Pharmaceutical Biology*. 2017;55(1):1619-1622. doi:10.1080/13880209.2017.1314513
70. Das R, Raman RP, Saha H, Singh R. Effect of *Ocimum sanctum* Linn. (Tulsi) extract on the immunity and survival of *Labeorohita* (Hamilton) infected with *Aeromonas hydrophila*. *Aquac Res*. 2015;46(5):1111-1121. doi:10.1111/are.12264
71. Barnard DR. Repellency of essential oils to mosquitoes (Diptera: Culicidae). *J Med Entomol*. 1999;36(5):625-629. doi:10.1093/jmedent/36.5.625
72. Yang YC, Lee HS, Clark JM, Ahn YJ. Insecticidal activity of plant essential oils against*Pediculus humanus capitis* (Anoplura: Pediculidae). *J Med Entomol*. 2004;41(4):699-704. doi:10.1603/0022-2585-41.4.699
73. Kothiwale SV, Patwardhan V, Gandhi M, Sohoni R, Kumar A. A comparative study of antiplaque and antigingivitis effects of herbal mouth rinse containing tea tree oil, clove, and basil with commercially available essential oil mouth rinse. *J Indian Soc Periodontol*. 2014;18(3):316-320. doi:10.4103/0972-124X.134568
74. Jaggi R, Madaan R, Singh B. Anticonvulsant potentialof Holy Basil, *Ocimum sanctumLinn*and its cultures. *Indian journal of experimental biology*. 2003;41:1329-1333.
75. N BA, Ghosh, AR, M, CH, S, NH, R, PB, Dr. Krishna KL. Review on nutritional, medicinal and cns activities of tulsi (*Ocimum. sanctum*). *Journal of Pharmaceutical Sciences and Research*. 2020;12(3):420-426.
76. Ali H, Dixit S. in vitro antimicrobial activity of flavanoids of *Ocimum sanctum* with synergistic effect of their combined form. *Asian Pacific Journal of Tropical Disease*. 2012; 2(1):S396-S398. doi:10.1016/S2222-1808(12)60189-3
77. Chatterjee M, Verma P, Maurya R, Palit G. Evaluation of ethanol leaf extract of *Ocimum sanctum* in experimental models of anxiety and depression. *Pharmaceutical Biology*. 2011;49(5):477-483. doi:10.3109/13880209.2010.523832
78. Dhingra D, Sharma A. A review on antidepressant plants. *Indian Journal of Natural Products and Resources.* 2006; 5(2):144-152.
79. Wilson L. Spices and Flavoring Crops: Leaf and Floral Structures. *Encyclopedia of Food and Health*. 2016; 9 : 84-92. doi:10.1016/B978-0-12-384947-2.00780-7
80. Pal RS, Pal Y, Saraswat N, Wal P. A review on the recent flavoring herbal medicines of today. *Open Medicine Journal*. 2020;7(1):1-6. doi:10.2174/1874220302007010001
81. Lahlou M. The Success of natural products in drug discovery. *Pharmacology & Pharmacy*.2013; 4:17-31. doi:10.4236/pp.2013.43A003
82. Anandjiwala S, Kalola J, Rajani M. Quantification of eugenol, luteolin, ursolic acid, and oleanolic acid in black (*Krishna Tulasi*) and green (*Sri Tulasi*)varieties of *Ocimumsanctum Linn*. using high-performance thin-layer chromatography. *Journal of Aoac International*. 2006;89(6):1467-1474. doi:10.1093/jaoac/89.6.1467
83. Jirovetz L, Buchbauer G, Stoilova I, Stoyanova A, Krastanov A, Schmidt E. Chemical composition and antioxidant properties of clove leaf essential oil. *J Agric Food Chem*. 2006;54(17):6303-6307. doi:10.1021/jf060608c
84. Upadhyay R. Tulsi: A holy plant with high medicinal and therapeutic value. *International Journal of Green Pharmacy*. 2017; 11:S1-S12.
85. Sundaram RS, Ramanathan M, Rajesh R, Satheesh B, Saravanan D. Lc-Ms quantification of rosmarinic acid and ursolic acid in the *Ocimum Sanctum Linn*. leaf extract (holy basil, tulsi). *Journal of Liquid Chromatography & Related Technologies*. 2012;35(5):634-650. doi:10.1080/10826076.2011.606583
86. Ladurner A, Zehl M, Grienke U, et al. Allspice and clove as source of triterpene acids activating the g protein-coupled bile acid receptor TGR5. *Front Pharmacol*. 2017; 8: 1-13. doi:10.3389/fphar.2017.00468
87. Mittal M, Gupta N, Parashar P, Mehra V, Khatri M. Phytochemical evaluation and pharmacological activity of *Syzygium aromaticum*: a comprehensive review. *International Journal of Pharmacy and Pharmaceutical Sciences*.2014:6(8):67-72.
88. Lam KY, Ling APK, Koh RY, Wong YP, Say YH. A review on medicinal properties of orientin. *Adv Pharmacol Sci*. 2016; 2016:1-9. doi:10.1155/2016/4104595
89. Pandey G, Sharma M. Pharmacological activities of *Ocimum sanctum* (Tulsi): A review. *International Journal of Pharmaceutical Sciences Review and Research*. 2010; 5: 61-66.
90. Shan B, Cai YZ, Sun M, Corke H. Antioxidant capacity of 26 spice extracts and characterization of their phenolic constituents.*J Agric Food Chem*. 2005;53(20):7749-7759. doi:10.1021/jf051513y
91. Hussain AI, Chatha SAS, Kamal GM, Ali MA, Hanif MA, Lazhari MI. Chemical composition and biological activities of essential oil and extracts from *Ocimum sanctum*. *International Journal of Food Properties*. 2017;20(7):1569-1581. doi:10.1080/10942912.2016.1214145
92. Chaula D, Laswai H, Chove B, et al. Effect of clove (*Syzygium aromaticum)* and Seaweed (*Kappaphycus alvarezii*) water extracts pretreatment on lipid oxidation in sun-dried sardines (*Rastrineobola argentea*) from Lake Victoria, Tanzania. *Food Sci Nutr*. 2019;7(4):1406-1416. doi:10.1002/fsn3.975
93. Bao L, Eerdunbayaer E, Nozaki A, et al. Hydrolysable tannins isolated from *Syzygium aromaticum*: Structure of a new C-glucosidic ellagitannin and spectral features of tannins with a tergalloyl group. *ChemInform*. 2012; 85(2): 365-381. doi:10.1002/chin.201225223
94. Kadian R, Parle M. Therapeutic potential and phytopharmacology of tulsi. *International Journal of Pharmacy & Life Sciences*. 2012; 3(7):1858-1867.
95. Lee HH, Shin JS, Lee WS, Ryu B, Jang DS, Lee KT. Biflorin, isolated from the flower buds of *Syzygium aromaticum* L.,suppresses LPS-induced inflammatory mediators via

STAT1 inactivation in macrophages and protects mice from endotoxin shock. *J Nat Prod*. 2016;79(4):711-720. doi:10.1021/acs.jnatprod.5b00609

96. Amelia B, Saepudin E, Cahyana AH, Rahayu DU, Sulistyoningrum AS, Haib J. GC-MS analysis of clove *(Syzygium aromaticum*) bud essential oil from Java and Manado. Paper presented at:2nd International Symposium on Current Progress in Mathematics and Sciences;November 1-2, 2016:Depok, Jawa Barat, Indonesia. doi:10.1063/1.4991186
97. Bhowmik D, Kumar KPS, Yadav A, Srivastava S, Paswan S, Sankar A. Recent trends in Indian traditional herbs *Syzygium aromaticum* and its health benefits. *Journal of Pharmacognosy and Phytochemistry*.2012; 1(1):13-22.
98. Doleželová P, Mácová S, Plhalová L, Pištěková V, Svobodová Z. The acute toxicity of clove oil to fish *Danio Rerio* and *PoeciliaReticulata*. *Acta Vet Brno*. 2011;80(3):305-308. doi:10.2754/avb201180030305
99. Satapathy S, Das N, Bandyopadhyay D, Mahapatra SC, Sahu DS, Meda M. Effect of tulsi(*Ocimum sanctum* Linn.) supplementation on metabolic parameters and liver enzymes in young overweight and obese subjects. *Ind J Clin Biochem*. 2017;32(3):357-363. doi:10.1007/s12291-016-0615-4
100. Mishra RK, Singh SK. Safety assessment of *Syzygium aromaticum* flower bud (clove) extract with respect to testicular function in mice. *Food and Chemical Toxicology*. 2008;46(10):3333-3338. doi:10.1016/j.fct.2008.08.006
101. Mihara S, Shibamoto T. Photochemical reactions of eugenol and related compounds: Synthesis of new flavor chemicals. *J Agric Food Chem*. 1982;30(6):1215-1218. doi:10.1021/jf00114a053
102. Ogata M, Hoshi M, Urano S, Endo T. Antioxidant activity of eugenol and related monomeric and dimeric compounds. *Chem Pharm Bull (Tokyo)*. 2000;48(10):1467-1469. doi:10.1248/cpb.48.1467
103. Devi PU, Ganasoundari A. Radio-protectiveeffect of leaf extract of Indian medicinal plant*Ocimum sanctum*. *Indian J Exp Biol*. 1995;33(3):205-208.
104. Burt SA, Reinders RD. Antibacterial activity of selected plant essential oils against *Escherichia Coli* O157:H7. *Lett Appl Microbiol*. 2003;36(3):162-167. doi:10.1046/j.1472-765X.2003.01285.x
105. Pinto E, Vale-Silva L, Cavaleiro C, Salgueiro L. Antifungal activity of the clove essential oil from *Syzygium aromaticum* on *Candida, Aspergillus* and *Dermatophyte* species. *Journal of Medical Microbiology*. 2009;58(11):1454-1462. doi: 10.1099/jmm.0.010538-0
106. Chaieb K, Zmantar T, Ksouri R, et al. Antioxidant properties of the essential oil of *Eugenia Caryophyllata* and its antifungal activity against a large number of clinical *Candida*species. *Mycoses*. 2007;50(5):403-406. doi:10.1111/j.1439-0507.2007.01391.x
107. Yang YC, Lee SH, Lee WJ, Choi DH, Ahn YJ. Ovicidal and adulticidal effects of *Eugenia caryophyllata* bud and leaf oil compounds on *Pediculus capitis*. *J Agric Food Chem*. 2003;51(17):4884-4888. doi:10.1021/jf034225f
108. Cai L, Wu CD. Compounds from *Syzygium aromaticum* possessing growth inhibitory activity against oral pathogens.*J Nat Prod*. 1996;59(10):987-990. doi:10.1021/np960451q
109. Samak G, Vasudevan D, Kedlaya R, Deepa S, Ballal M. Activity of *Ocimum sanctum* (The traditional Indian medicinal plant) against the enteric pathogens. *Indian Journal of Medical Sciences*. 2001; 55(8):434-438, 472.
110. Aqil F, Khan MSA, Owais M, Ahmad I. Effect of certain bioactive plant extracts on clinical isolates of β-lactamase producing methicillin resistant*Staphylococcus aureus*. *J Basic Microbiol*. 2005;45(2):106-114. doi:10.1002/jobm.200410355
111. Shokeen P, Ray K,Bala M, Tandon V. Preliminary studies on activity of *Ocimum sanctum, Drynaria quercifolia*, and *Annona squamosa* against *Neisseria gonorrhoeae*. *Sexually Transmitted Diseases*. 2005;32(2):106-111. doi:10.1097/01.olq.0000152821.23777.90
112. Singh S, Malhotra M, Majumdar DK. Antibacterial activity of *Ocimum sanctum* L. Fixed oil. *Indian J Exp Biol*; 2005:43(9):835-837.
113. Dorman HJD, Surai P, Deans SG. In vitro antioxidant activity of a number of plant essential oils and phytoconstituents. *Journal of Essential Oil Research*. 2000;12(2):241-248. doi:10.1080/10412905.2000.9699508
114. Gülçin İ, Elmastaş M, Aboul-Enein HY. Antioxidant activity of clove oil – A powerful antioxidant source. *Arabian Journal of Chemistry*. 2012; 5(4):489-499. doi:10.1016/j.arabjc.2010.09.016
115. Bakour M, Soulo N, Hammas N, et al. The antioxidant content and protective effect of argan oil and *Syzygium aromaticum* essential oil in hydrogen peroxide-induced biochemical and histological changes. *International Journal of Molecular Sciences*. 2018; 19(2):1-14.610. doi:10.3390/ijms19020610
116. Calleja MA, Vieites JM, Montero-Meterdez T, et al. The antioxidant effect of β-caryophyllene protects rat liver from carbon tetrachloride-induced fibrosis by Inhibiting hepatic stellate cell activation. *Br J Nutr*. 2013;109(3):394-401. doi:10.1017/S0007114512001298
117. Saija A, Scalese M, Lanza M, Marzullo D, Bonina F, Castelli F. Flavonoids as antioxidant agents: Importance of their interaction with biomembranes. *Free Radical Biology and Medicine*. 1995;19(4):481-486. doi:10.1016/0891-5849(94)00240-K
118. Uma Devi P, Ganasoundari A, Vrinda B, Srinivasan KK, Unnikrishnan MK. Radiation protection by the *ocimum* flavonoids orientin and vicenin: Mechanisms of action. *Radiation Research*. 2000;154(4):455-460. doi:10.1667/0033-7587(2000)154[0455:RPBTOF]2.0.CO;2
119. Sharma MK, Kumar M, Kumar A. Protection against mercury-induced renal damage in swiss albino mice by *Ocimum sanctum*. *Environmental Toxicology and Pharmacology*. 2005;19(1):161-167. doi:10.1016/j.etap.2004.06.002
120. Zheng GQ, Kenney PM, Lam LK. Sesquiterpenes from clove(*Eugenia caryophyllata*) as potential anticarcinogenic

agents.*J Nat Prod*. 1992;55(7):999-1003. doi:10.1021/np50085a029
121. Miyazawa M, Hisama M. Suppression of chemical mutagen-induced sos response by alkyl phenols from clove (*Syzygium aromaticum*) in the *Salmonella typhimurium* TA1535/pSK1002 umu test. *J Agric Food Chem*. 2001;49(8):4019-4025. doi:10.1021/jf0103469
122. Liu H, Schmitz JC, Wei J, et al. Cloveextract inhibits tumor growth and promotes cell cycle arrest and apoptosis.*oncol res*. 2014;21(5):247-259. doi:10.3727/096504014X13946388748910
123. Ghosh R, Nadiminty N, Fitzpatrick JE, Alworth WL, Slaga TJ, Kumar AP. Eugenol causes melanoma growth suppression through inhibition of e2f1 transcriptional activity. *J Biol Chem*. 2005;280(7):5812-5819. doi:10.1074/jbc.M411429200
124. Banerjee S, Prashar R, Kumar A, Rao AR. Modulatory influence of alcoholic extract of *ocimum* leaves on carcinogen-metabolizing enzyme activities and reduced glutathione levels in mouse.*Nutrition and Cancer*. 1996;25(2):205-217. doi:10.1080/01635589609514443
125. Karthikeyan K, Gunasekaran P, Ramamurthy N, Govindasamy S. Anticancer activity of*Ocimum sanctum*. *Pharmaceutical Biology*. 1999;37(4):285-290. doi:10.1076/phbi.37.4.285.5801
126. Aruna K, Sivaramakrishnan VM. Anticarcinogenic effects of some indian plant products.*Food and Chemical Toxicology*. 1992;30(11):953-956. doi:10.1016/0278-6915(92)90180-S
127. Devi Pu. Radioprotective, anticarcinogenic and antioxidant properties of the Indian holy basil, *Ocimum sanctum* (Tulasi). *Indian J Exp Biol*. 2001;39(3):185-90.
128. Prashar R, Kumar A, Banerjee S, Rao A. Chemopreventive action by an extract from *Ocimum sanctum* on mouse skin papillomagenesis and its enhancement of skin glutathione s-transferase activity and acid soluble sulfydryl level: *Anti-Cancer Drugs*. 1994;5(5):567-572. doi:10.1097/00001813-199410000-00008
129. Harsha M, Mohan Kumar KP, Kagathur S, Amberkar VS. Effect of *Ocimum sanctum* extract on leukemic cell lines: A preliminary in-vitro study. *J Oral MaxillofacPathol*. 2020;24(1):93-98. doi:10.4103/jomfp.JOMFP_181_19
130. Bhagat N, Chaturvedi A. Spices as an alternative therapy for cancer treatment. *SRP*. 2016;7(1):46-56. doi:10.5530/srp.2016.7.7
131. Sharma M, Pandey G, Sahni Y, Khanna A. Anticancer effect of a herbal drug proimmu on the experimental uterine cancer in rat. *Phytomedica*. 2010;11:51-58.
132. Öztürk A, Özbek H. The anti-inflammatory activity of *Eugenia caryophyllata* essential oil: An animal model of anti-inflammatory activity. *Electron J Gen Med*. 2005;2(4):159-163. doi:10.29333/ejgm/82334
133. Kim EH, Kim HK, Ahn YJ. Acaricidal activity of clove bud oil compounds against *Dermatophagoides farinae* and *Dermatophagoides pteronyssinus* (Acari: Pyroglyphidae). *J Agric Food Chem*. 2003;51(4):885-889. doi:10.1021/jf0208278
134. Ghelardini C, Galeotti N, Di Cesare Mannelli L, Mazzanti G, Bartolini A. Local anaesthetic activity of beta-caryophyllene. *Farmaco*. 2001;56(5-7):387-389. doi:10.1016/s0014-827x(01)01092-8
135. Daniel AN, Sartoretto SM, Schmidt G, Caparroz-Assef SM, Bersani-Amado CA, Cuman RKN. Anti-inflammatory and antinociceptive activities of eugenol essential oil in experimental animal models.*Rev bras farmacogn*. 2009; 19: 212-217. doi:10.1590/S0102-695X2009000200006
136. Godhwani S, Godhwani JL, Vyas DS. *Ocimum sanctum*: An experimental study evaluating its anti-inflammatory, analgesic and antipyretic activity in animals. *J Ethnopharmacol*. 1987;21(2):153-163. doi:10.1016/0378-8741(87)90125-5
137. Archana R, Namasivayam A. Effect of *Ocimum sanctum* on noise induced changes in neutrophil functions. *Journal of Ethnopharmacology*. 2000;73(1-2):81-85. doi:10.1016/S0378-8741(00)00281-6
138. Bawankule D, Kumar A, Agarwal K, et al. Pharmacological and phytochemical evaluation of *Ocimum sanctum* root extracts for its anti-inflammatory, analgesic and antipyretic activities. *Phcog Mag*. 2015;11(42):217. doi:10.4103/0973-1296.157743
139. Prashar A, Locke IC, Evans CS. Cytotoxicity of clove (*Syzygium aromaticum*) oil and its major components to human skin cells. *Cell Prolif*. 2006;39(4):241-248. doi:10.1111/j.1365-2184.2006.00384.x
140. Prakash J, Gupta SK. Chemopreventive activity of *Ocimum sanctum* seed oil. *Journal of Ethnopharmacology*. 2000;72(1-2):29-34. doi:10.1016/S0378-8741(00)00194-X
141. Baliga MS, Jimmy R, Thilakchand KR, et al. *Ocimum sanctum* L (Holy Basil or Tulsi) and its phytochemicals in the prevention and treatment of cancer. *Nutrition and Cancer*. 2013;65Suppl 1:26-35. doi:10.1080/01635581.2013.785010
142. Nada AS. Efficacy of clove oil in modulating radiation-induced some biochemical disorders in male rats. *Journal of Radiation Research and Applied Sciences*. 2011; 4(2B):629-647.
143. Samarth RM, Samarth M, Matsumoto Y. Medicinally important aromatic plants with radioprotective activity. *Future Science OA*. 2017;3(4):FSO247. doi:10.4155/fsoa-2017-0061
144. Ganasoundari A, Uma Devi P, Rao BSS. Enhancement of bone marrow radioprotection and reduction of WR-2721toxicityby *Ocimum sanctum*. *Mutation Research/Fundamental and Molecular Mechanisms of Mutagenesis*. 1998;397(2):303-312. doi:10.1016/S0027-5107(97)00230-3
145. Sood S, Narang D, Dinda AK, Maulik SK. Chronic oral administration of *Ocimum sanctum* Linn. augments cardiac endogenous antioxidants and prevents isoproterenol-induced myocardial necrosis in rats. *Journal of Pharmacy and Pharmacology*. 2010;57(1):127-133. doi:10.1211/0022357055146

146. Kaul D, Shukla AR, Sikand K, Dhawan V. Effect of herbal polyphenols on atherogenic transcriptome. *Mol Cell Biochem*. 2005;278(1-2):177-184. doi:10.1007/s11010-005-7497-8
147. Sarkar A, Lavania SC, Pandey DN, Pant MC. Changes in the blood lipid profile after administration of*Ocimum sanctum* (Tulsi) leaves in the normal albino rabbits. *Indian J PhysiolPharmacol*. 1994;38(4):311-312.
148. Singh S, Rehan HMS, Majumdar DK. Effect of *Ocimum sanctum* fixed oil on blood pressure, blood clotting time and pentobarbitone-induced sleeping time. *Journal of Ethnopharmacology*. 2001;78(2-3):139-143. doi:10.1016/S0378-8741(01)00336-1
149. Othman GA, Ahmed DAEM, Alghamdi HA, Radwan AM. Antifungal activity of *Syzygium aromaticum* (Dianthus) against toxigenic *Rhizopus stolonifera* and its immunomodulatory effects in aflatoxin-fed mice. *Trop J Pharm Res*. 2019; 17(10):1991-1997. doi:10.4314/tjpr.v17i10.14
150. Chattopadhyay RR, Sarkar SK, Ganguly S, Medda C, Basu TK. Hepatoprotective activity of *O. sanctum* leaf extract against paracetamol induced hepatic damage in rats. *Indian J Pharmacol*. 1992; 24(3):,163-165.
151. Lahon K, Das S. Hepatoprotective Activity of *Ocimum sanctum* alcoholic leaf extract against paracetamol-induced liver damage in albino rats.*Pharmacognosy Res*. 2011; 3(1):13-18. doi:10.4103/0974-8490.79110
152. Charitha V, J DA, Malakondaiah P. In Vitro Anthelmintic activity of *Syzygium aromaticum* and *Melia Dubia* against *Haemonchus contortus* of sheep. *Indian Journal of Animal Sciences*. 2017; 87:968-970.
153. Athanasiadou S, Kyriazakis I, Jackson F, Coop RL. Direct Anthelmintic effects of condensed tannins towards different gastrointestinal nematodes of sheep: In vitro and in vivo studies. *Veterinary Parasitology*. 2001;99(3):205-219. doi:10.1016/S0304-4017(01)00467-8
154. Asha MK, Prashanth D, Murali B, Padmaja R, Amit A. Anthelmintic activity of essential oil of *Ocimum sanctum* and eugenol. *Fitoterapia*. 2001;72(6):669-670. doi:10.1016/S0367-326X(01)00270-2
155. Kanojiya D, Shanker D, Sudan V, Jaiswal AK, Parashar R. Anthelmintic activity of*Ocimum sanctum*leaf extract against ovine gastrointestinal nematodes in India. *Research in Veterinary Science*. 2015; 99:165-170. doi:10.1016/j.rvsc.2015.01.017
156. Raghavenra H, Diwakr BT, Lokesh BR, Naidu KA. Eugenol-The active principle from cloves inhibits 5-lipoxygenase activity and leukotriene-C4 in human PMNL cells. *Prostaglandins Leukot Essent Fatty Acids*. 2006;74(1):23-27. doi:10.1016/j.plefa.2005.08.006
157. Kozam G. The effect of eugenol on nerve transmission. *Oral Surg Oral Med Oral Pathol*. 1977;44(5):799-805. doi:10.1016/0030-4220(77)90390-5
158. Hosseini MM, Asl M, Rakhshandeh H. Analgesic effect of clove essential oil in mice. *Avicenna J Phytomed*. 2011:1(1):1-6. doi: 10.22038/AJP.2011.114
159. Singh S, Majumdar DK. Analgesic activity of *Ocimum sanctum* and its possible mechanism of action. *International Journal of Pharmacognosy*. 1995;33(3):188-192. doi:10.3109/13880209509065361
160. Galal A, Abdellatief S. Neuropharmacological studies on *Syzygiumaromaticum* (clove) essential oil. *International Journal of Pharma Science*. 2015; 5:1013-1018.
161. Singh E, Sharma S, Dwivedi J, Sharma S. Diversified potentials of *Ocimum sanctum* Linn (Tulsi): An exhaustive survey. J Nat Prod Plant Resour. 2012,2(1):39-48.
162. Sakina MR, Dandiya PC, Hamdard ME, Hameed A. Preliminary psychopharmacological evaluation of *Ocimum sanctum* eaf extract. *Journal of Ethnopharmacology*. 1990;28(2):143-150. doi:10.1016/0378-8741(90)90023-M
163. Samson J, Sheela Devi R, Ravindran R, Senthilvelan M. Biogenic amine changes in brain regions and attenuating action of *Ocimum sanctum* in noise exposure. *Pharmacology Biochemistry and Behavior*. 2006;83(1):67-75. doi:10.1016/j.pbb.2005.12.008
164. Ravindran R, Devi RS, Samson J, Senthilvelan M. Noise-stress-induced brain neurotransmitter changes and the effect of *Ocimum sanctum (Lin*n*)* treatment in albino rats. *J Pharmacol Sci*. 2005;98(4):354-360. doi:10.1254/jphs.FP0050127
165. Feng J, Lipton JM. Eugenol: Antipyretic activity in rabbits. *Neuropharmacology*. 1987;26(12):1775-1778. doi:10.1016/0028-3908(87)90131-6
166. Singh S, Taneja M, Majumdar DK. Biological activities of *Ocimum sanctum* L. Fixed Oil— an overview. *Indian J Exp Biol*. 2007; 45(5):403-412.
167. Bouchentouf S, Said G, Noureddine M, Allali H, Bouchentouf A. A note study on antidiabetic effect of main molecules contained in clove using molecular modeling interactions with DPP-4 enzyme. *International Journal of Computational and Theoretical Chemistry*. 2017;5:9-13. doi:10.11648/j.ijctc.20170501.12
168. Hussain EHMA, Jamil K, Rao M. Hypoglycaemic, hypolipidemic and antioxidant properties of tulsi(*Ocimum sanctum* Linn) on streptozotocin induced diabetes in rats. *Indian J Clin Biochem*. 2001;16(2):190-194. doi:10.1007/BF02864859
169. Antora RA, Salleh RM. Antihyperglycemic effect of *Ocimum* plants: A short review. *Asian Pacific Journal of Tropical Biomedicine*. 2017;7(8):755-759. doi:10.1016/j.apjtb.2017.07.010
170. Halder N, Joshi S, Gupta SK. Lens aldose reductase inhibiting potential of some indigenous plants.*Journal of Ethnopharmacology*. 2003;86(1):113-116. doi:10.1016/S0378-8741(03)00052-7
171. Issac A, Gopakumar G, Kuttan R, Maliakel B, Krishnakumar IM. Safety and anti-ulcerogenic activity of a novel polyphenol-rich extract of clove buds *(Syzygiumaromaticum L*). *Food Funct*. 2015;6(3):842-852. doi:10.1039/C4FO00711E
172. Santin JR, Lemos M, Klein-Júnior LC, et al. Gastroprotective activity of essential oil of the*Syzygiumaromaticum* and its

major component eugenol in different animal models. *Naunyn-Schmied Arch Pharmacol*. 2011;383(2):149-158. doi:10.1007/s00210-010-0582-x

173. Singh S, Majumdar DK. Evaluation of the gastric antiulcer activity of fixed oil of *Ocimum sanctum* (Holy Basil). *Journal of Ethnopharmacology*. 1999;65(1):13-19. doi:10.1016/S0378-8741(98)00142-1
174. Karmakar S, Choudhury M, Das AS, Maiti A, Majumdar S, Mitra C. Clove *(SyzygiumaromaticumLinn)*extract rich in eugenol and eugenol derivatives shows bone-preserving efficacy. *Natural Product Research*. 2012;26(6):500-509. doi:10.1080/14786419.2010.511216
175. Singh S, Majumdar DK. Effect of fixed oil of *Ocimum sanctum* against experimentally induced arthritis and joint edema in laboratory animals.*International Journal of Pharmacognosy*. 1996;34(3):218-222. doi:10.1076/phbi.34.3.218.13205
176. Tao G, Irie Y, Li DJ, Keung WM. Eugenol and its structural analogs inhibit monoamine oxidase a and exhibit antidepressant-like activity. *Bioorganic & Medicinal Chemistry*. 2005;13(15):4777-4788. doi:10.1016/j.bmc.2005.04.081
177. Godhwani S, Godhwani JL, Was DS. *Ocimum sanctum*— A preliminary study evaluating its immunoregulatory profile in albino rats. *Journal of Ethnopharmacology*. 1988;24(2-3):193-198. doi:10.1016/0378-8741(88)90151-1
178. Taylor PW, Roberts SD. Cloveoil: An alternative anaesthetic for aquaculture. *North American Journal of Aquaculture*. 1999;61(2):150-155. doi:10.1577/1548-8454(1999)061<0150:COAAAF>2.0.CO;2
179. Diyaware MY, Suleiman SB, Akinwande AA, Aliyu M. Anesthetic Effectsof clove(*Eugenia aromaticum*) seed extract on *Clariasgariepinus* (Burchell, 1822)fingerlings under semi-arid conditions. *Journal of Agricultural Sciences, Belgrade*. 2017;62(4):411-421. doi:10.2298/jas1704411d
180. Pongprayoon U, Baeckström P, Jacobsson U, Lindström M, Bohlin L. Compounds inhibiting prostaglandin synthesis isolated from *Ipomoea pes-caprae*. *Planta Med*. 1991;57(06):515-518. doi:10.1055/s-2006-960196
181. Hamackova J, Kouril J, Kozak P, Stupka Z. Cloveoil as an anaesthetic for different freshwater fish species.*Bulgarian Journal of Agricultural Science*. 2006; 12:185-194.
182. Saeed SA, Gilani AH. Antithrombotic activity of clove oil. J *Pak Med Assoc.* 1994;44(5):112-5.
183. Rasheed A, Laekeman G, Totté J, Vlietinck AJ, Herman AG. Eugenol and prostaglandin biosynthesis. *N Engl J Med*. 1984;310(1):50-51. doi:10.1056/NEJM198401053100115
184. Srivastava KC. Antiplatelet principles from a food spice clove(*Syzgium aromaticum* L). *Prostaglandins, Leukotrienes and Essential Fatty Acids*. 1993;48(5):363-372. doi:10.1016/0952-3278(93)90116-E
185. Islamuddin M, Chouhan G, Want MY, Ozbak HA, Hemeg HA, Afrin F. Immunotherapeutic potential of eugenol emulsion in experimental visceral leishmaniasis.*PLoSNegl Trop Dis*. 2016;10(10):1-23.e0005011. doi:10.1371/journal.pntd.0005011
186. Mukherjee R, Dash PK, Ram GC. Immunotherapeutic potential of *Ocimum sanctum* (L) in bovine subclinical mastitis. *Research in Veterinary Science*. 2005;79(1):37-43. doi:10.1016/j.rvsc.2004.11.001
187. Bhakta S, Awal M, Das S. Herbal contraceptive effect of *Abrus precatorius, Ricinus communis*, and *Syzygium aromaticum*on anatomy of the testis of male Swiss albino mice. *J Adv Biotechnol Exp Ther*.2019;2(2):36-43. doi:10.5455/jabet.2019.d23
188. Choi D, Roh HS, Kang DW, Lee JS. The potential regressive role of *Syzygium aromaticum*on the reproduction of male golden hamsters. *Development &Reproduciton*. 2014;18(1):57-64. doi:10.12717/DR.2014.18.1.057
189. Ahmed M, Ahamed RN, Aladakatti RH, Ghosesawar MG. Reversible anti-fertility effect of benzene extract of *Ocimum sanctum* leaves on sperm parameters and fructose content in rats. *Journal of Basic and Clinical Physiology and Pharmacology*. 2002; 13(1):51-59. doi:10.1515/JBCPP.2002.13.1.51
190. Kantak NM, Gogate MG. Effect of short term administration of tulsi (*Ocimum sanctum* Linn.) on reproductive behavior of adult male rats. *Indian J PhysiolPharmacol.*1992; 36(2):109-111.
191. Singh V, Amdekar S, Verma O. *Ocimum sanctum* (tulsi): Bio-pharmacological activities. *WebmedCentralPharmacology*. 2010;1(10):1-7. doi:10.9754/journal.wmc.2010.001046
192. Joshi H, Parle M. Cholinergic basis of memory improving effect of *Ocimum tenuiflorum* Linn. *Indian Journal of Pharmaceutical Sciences*. 2006; 68(3):364-365. doi:10.4103/0250-474X.26680