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NATURAL TRANQUALITY: *MELISSA OFFICINALIS* AND *OCIMUM TENUIFLORUM* FOR STRESS AND ANXIETY RELIEF.

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ABSTRACT:
To examine the effects of lemon balm as a therapeutic herb on anxiety and depression in clinical trials, as well as any potential adverse effects, a meta-analytic approach and a systematic review were taken into consideration. The phytochemicals that underpin ***M. officinalis'*** pharmacological actions include flavonoids, terpenoids, phenolic acids, and many others. In fact, the plant may possess anti-inflammatory, antispasmodic, neuroprotective, nephroprotective, antibacterial, and antinociceptive properties. One common illness that contributes to psychological issues like anxiety and sadness is insomnia. Burns are a major cause of stress, and afterwards, many patients suffer from anxiety, depression, and insomnia. Also, the levels of serum antioxidants increase after burns, which causes problems in patients. It has been observed that ***Melissa officinalis L***. can increase serum antioxidant levels and improve mood and sleep quality. Research on its ability to particularly treat ailments like anxiety and depression dates back more than 200 years. Research has demonstrated the antistress and anxiolytic properties of ***Melissa officinalis L.*** The inotropic benefits of ***Melissa officinalis*** were first described as a fragrant herb by Avicenna, the world's first physician, who also highlighted the invigorating and strengthening effects of this herb on the heart, nerves, and brain. Holy basil, or ***Ocimum tenuiflorum***, is known as "the elixir of life" in Ayurveda and is thought to extend life and improve overall health. Clinical investigations indicate ***Ocimum tenuiflorum*** may have some anti-stress benefits, notwithstanding their limitations. While anxiety is a normal emotional activity, excessive anxiety can lead to pathological conditions such as mental and cardiovascular problems. There are numerous allopathic medications available to treat anxiety disorders; the most widely used are benzodiazepines, which have a number of systemic side effects. In India, tulsi, or ***Ocimum tenuiflorum***, has long been used to treat a variety of mental and metabolic conditions as well as asthma, common coughs, and minor upper respiratory infections. Tulsi possesses a multitude of restorative qualities, including adaptogenic, antibacterial, relaxing, cardioprotective, and immunomodulatory benefits, as demonstrated by numerous research done on humans, animals, and in vitro. The most common neurological condition, depression affects millions of people globally. Depression is the second most common chronic illness in clinical studies. In the past, anxiety disorders were treated with benzodiazepine medications such as baspiron, lorazepam (ativan), diazepam (valium), and alprazolam (xanax). But currently, antidepressants like venlafaxine, paroxetine, fluxetin, and sertaline are more commonly used.

Keywords: Anxiety disorder, stress, ***Melissa officinalis***, ***Ocimum tenuiflorum***, lemon balm, tulsi**, Lamiaceae.**

1. INTRODUCTION:

Anxiety is characterized as an uncomfortable emotional state for which the person exhibits behavioral, cognitive, and physiological reactions to dangerous circumstances or uncertainty. The cause is difficult to identify or is thought to be inescapable or uncontrollable[1]. One of these well-known plants, ***Melissa officinalis***, or lemon balm, has been used for a very long time to cure a variety of ailments, including rheumatoid arthritis, neurological disorders, gastrointestinal disorders, and headaches[2]. A perennial herb with a lemon fragrance that is grown is called lemon balm (***Melissa officinalis***). Lemon balm has been used for therapeutic purposes for over 2000 years. Paracelsus (1493–1541) recommended that lemon balm be taken for "all complaints supposed to proceed from a disordered state of the nervous system" and that it would entirely revive a man. Records of this use date back over 2000 years. Numerous herbalists have claimed that the plant has broad positive effects on the brain, including increases in memory[3]. According to recent reports, consuming ***M. officinalis*** has sedative, spasmolytic, and antibacterial effects. It has been shown to have indications for nervous disorders such as reducing excitability, anxiety, and stress as well as gastrointestinal issues and sleep disturbance (Kommission E Monograph, 1984; Bisset and Wichtl, 1994). According to a lengthy history of safe use, there have been no recorded adverse effects (Wong et al., 1998).[4]. The two most prevalent stress-related mental illnesses that disrupt the body's normal physiological balance and have a significant negative impact on public health are anxiety and depression. As per WHO data, depression affects 4.4% of the global population and is expected to become the primary cause of disability by 2030.[5]. One of the most prevalent medical conditions worldwide is burns, which can result from radiation, thermal, chemical, or electrical trauma [6]. Given the significant influence that anxiety disorders are having on our lives, it is worthwhile to consider alternate medication options for treating them. As a result, an attempt was undertaken in this study to look into the antianxiety impact of the ethanolic extract of OS leaves and to compare that effect with that of the common medication, diazepam[7]. Clinical trials for this anxiolytic drug are scarce, although at daily dosages of 1,000 and 1,200 mg, respectively, anti-stress benefits have been noted in people with generalized anxiety disorder and stress. Although studies on ***Ocimum tenuiflorum's*** ability to improve sleep have not been conducted, ***Ocimum tenuiflorum*** may have some positive impacts on the quality of sleep because hyperarousal is thought to be linked to poor sleep[8]. India's rich biodiversity is essential to Ayurveda's use of medicinal and culinary herbs, which have a range unparalleled by any other medical system. But of all the herbs used, neither **holy basil** (***Ocimum sanctum***) nor tulsi have the same level of respect as the other[9]. In everyday life, stress management has become increasingly important. While total stress avoidance is improbable, any strategy that helps raise the threshold can be helpful. Traditional therapies appear to be promising substitutes for treating stress-related diseases in order to reduce financial losses and enhance quality of life. Indian traditional medicine offers treatments based on mineral and herbal supplements as well as other therapeutic techniques to improve both physical and mental function and reduce stress[10]. A plant with great therapeutic significance, ***Ocimum tenuiflorum L***. syn. O sanctum (**Lamiaceae**) is found all throughout India and the Asian subcontinent. The leaves have an essential oil that contains a number of medicinally valuable chemicals, including limatrol, carvacrol, methyl-chavicol, eugenol, and caryophylline. Additionally, the seeds contain an oil that is sitosterol and fatty acid based. In addition, the plant possesses antibacterial, antispasmodic, antiseptic, and insect repellent qualities[11]. A debilitating mental illness, depression is thought to impact 21% of the global population. Depressive illnesses can be brought on by prolonged stress, and preclinical antidepressant evaluation frequently uses animal stress models. Major depressive disorder patients exhibit symptoms that correspond to altered levels of norepinephrine, serotonin, and dopamine in the brain[12]. Considered a "adaptogen," or anti-stress agent, are tulsi leaves. According to recent research, the leaves provide a substantial level of stress protection. Two grams of tulsi tablets will be given daily in divided dosages as part of this trial. The drug's bhavana in Rasatarangini will increase its effectiveness and facilitate easy absorption[13].

Lemon balm (*Melissa officinalis*):

The family **Lamiaceae** includes lemon balm (*Melissa officinalis L.*), which is extensively distributed throughout central and southern Europe as well as Asia minor. It can also be found in tropical nations like Brazil, where it's referred to as Melissa and Erva-cidreira. It is a perennial plant with a lemony scent that can grow up to one meter tall. Dried leaves, frequently with flowering tops, are the parts most commonly utilized[14]. ***Melissa officinalis L***. is a perennial herbaceous plant in the mint family Lamiaceae, sometimes referred to as **lemon balm, honey balm, balm mint, garden balm, or common balm.** Primarily prevalent in the Mediterranean region of the world, it may also be found in other parts of the world such Central Asia, Iran, Europe, Serbia, America, and Africa. The leaves have an oval shape and are dark greenish in colour (Figure 1); they smell slightly of lemon, almost like mint. Its tiny white blooms, which are loaded of nectar and draw bees, arrive throughout the summer [18,23].

Figure 1. The aerial parts of ***M. officinalis***.

1. Biochemical compounds *of Melissa officinalis:*

Numerous phytochemicals, such as phenolic compounds, flavonoids, tannins, and terpenes (monoterpenes, sesquiterpenes, and triterpenes) have been found in ***M. officinalis*** by phytochemical studies (Allahverdiyev et al., 2004, Moradkhani et al., 2010). The primary active ingredients in ***M. officinalis*** are triterpenes (such as ursolic acid and oleanolic acid), phenolics (such as cis-and trans-RA), and volatile compounds (such as geranial, neral, citronellal, and geraniol).[15]. The primary active ingredients in ***Melissa officinalis*** are flavonoids (quercetin, rhamnocitrin, luteolin), phenolic compounds (rosmarinic acid, caffeic acid, and protocatechuic acid), volatile chemicals (geranial, neral, citronellal, and geraniol), and triterpenes (ursolic acid and oleanolic acid). [16,19].

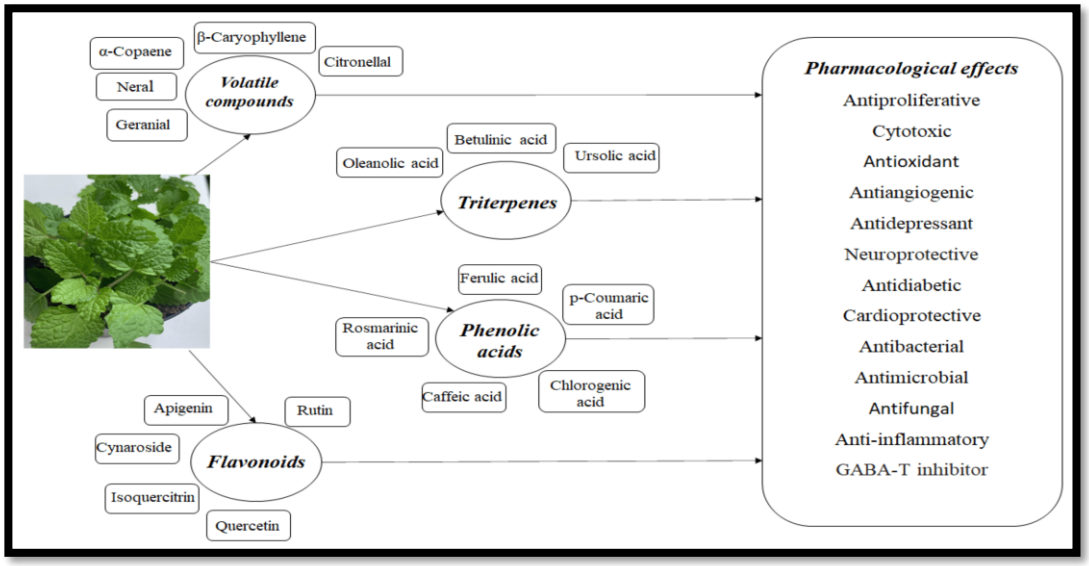

Figure 2. The composition of ***Melissa officinalis*** and its pharmacological effects [17].

1.1 Volatile compounds:

Unlike other plants in the **Lamiaceae** family, ***Melissa officinalis*** leaves yield a volatile oil that is extracted and has pharmacological effects. This oil is acquired in modest quantities. The volatile chemicals present in varying amounts are the primary and secondary constituents of the essential oil extracted from the dried leaves of ***Melissa officinalis*** [17].

Nurzynska-Wierdak et al. [21] looked into how the dried oil of Polish Melissa officinalis leaves changed chemically during their first and second growing seasons. By hydrodistilling air-dried leaves, they were able to extract 0.3% essential oil; GC-MS and GC-FID analysis revealed 106 compounds, with geranial accounting for 45.2% and 45.1% and neral accounting for 32.8% and 33.8%. In a comparative analysis of ***Melissa officinalis*** from two separate cities in Tunisia, Germany, and France, Souihi et al. [22] noted that there was a significant concentration of germacrene D but not citral. Due to variations in weather during the research years, the study by Seidler-Łożykowska et al. [24] revealed that the essential oil level ranged from 0.08 to 0.20%. Regarding the fluctuations in the composition and concentration of essential oils, Kittler et al. Nouri et al. [20] studied the essential oil and rosmarinic acid content of ***Melissa officinalis*** grown in southern Iran. They found a high amount of rosmarinic acid compared to prior research and a total yield of 0.37% (v/w), rich in neral and geranial. The chemical makeup and in vitro antibacterial activity of an essential oil extracted from ***Melissa officinalis*** leaves grown in Algeria were examined in a different study [23]. Said-Al Ahl et al.'s findings [25] indicate that the essential oil content and quality of ***Melissa officinalis*** are influenced by the time of harvesting.

1.2 Triterpenes:

M. officinalis yielded the discovery of several novel triterpenes. Six novel ursane-type triterpenes have been identified by Mencherini and associates from ***M. officinalis*** leaves [26]. From the aerial portions of ***M. officinalis***, three novel ursene triterpene glycosides
(melissiosides A–C) with promising antibacterial properties have recently been discovered [27]. Ji and associates extracted serratagenic acid, ursolic acid, oleanolic acid, 2α,3β,23,29tetrahydroxyolean-12-en-28-oic acid, and ursolic acid from ***M. officinalis*** leaves in 2015 [28]. The methanol extract from the dried aerial portions of lemon balm also contained ursolic and oleanolic acids [29].

1.3 Phenolic Compounds:

M. officinalis leaves contain 8.962% phenyl-propane derivatives expressed in caffeic acid and 0.64% flavonoids expressed in rutoside, according to research by Hanganu and co-authors (2008) [31]. Six polyphenolic substances were found in the ethyl-ether, ethyl acetate, and 1buthanol extracts of ***M. officinalis*** leaves, namely caftaric acid, caffeic acid, p-cumaric acid, ferulic acid, luteolin, and apigenin [30]. According to Toth and co-authors, RA was a significant phenolic active ingredient of ***M. officinalis*** [32]. A novel glycoside molecule, 7-O-beta-Dglucopyranoside-3'-O-beta-D-glucuronopyranoside, was initially isolated by Patora and Klimek from ***M. officinalis*** leaves in 2002 [33]. In 2015, Ji and co-authors isolated thirteen compounds, including protocatechuyl aldehyde, vanillin, luteolin, rosmarinic acid, luteolin-7O- β-D-glucoside from the ***M. officinalis*** leaves [28]. From the leaves of ***M. officinalis***, luteolin, luteolin 7-O-beta-glucopyranoside, apigenin 7-O-beta-D-glucopyranoside, luteolin 7O-beta-D-glucuronopyranoside, luteolin 3'-O-beta-D-glucuronopyranoside, and luteolin 7-Obeta-D-glucopyranoside-3'-O-beta-glucuronopyranoside have been isolated [31].

1.4 Other Compounds:

M. officinalis leaves were used to isolate β-sitosterol and palmitic acid [28]. Total phenols (2.9–7.8 mg/mL) and the macro elements under investigation (4.4–11.6, 12.2–1152, and 200– 740 μg/mL for Na, K, and Ca, respectively) were abundant in aqueous ***M. officinalis*** preparations [30]. In conclusion, ***M. officinalis*** is a potential source of phytochemicals that may support the plant's advantageous characteristics.

2. Traditional Uses:

According to historical accounts, lemon balm has the following properties: antiviral and antioxidant activities; antifungal, antiparasitic, and anti-spasmolytic activities; flatulence; asthma; bronchitis; amenorrhea; cardiac failure; arrhythmias; ulcers; and wounds. It also has anti-gas, fever-reducing, antibacterial, spasmolytic,[34] hypotensive, memory-enhancing, menstrual-inducing, and thyroid-related effects.[35],[36] Additionally, it is reported to be helpful in treating a variety of conditions, including headaches, nausea, indigestion, colic, migraines, anaemia, vertigo, syncope, malaise, sleeplessness, epilepsy, melancholy, psychosis, and hysteria.[37].

3. Pharmacological studies:

Numerous biological and physiological benefits, including anxiolytic, antioxidant, depressive, anticancer, antinociceptive, anti-epileptic, anti-angiogenesis, antimicrobial, anti-inflammatory, hypolipidemic, and hypoglycaemic effects, are associated with ***Melissa officinalis***. Fig.3 shows some of the health benefits of Melissa officinalis.

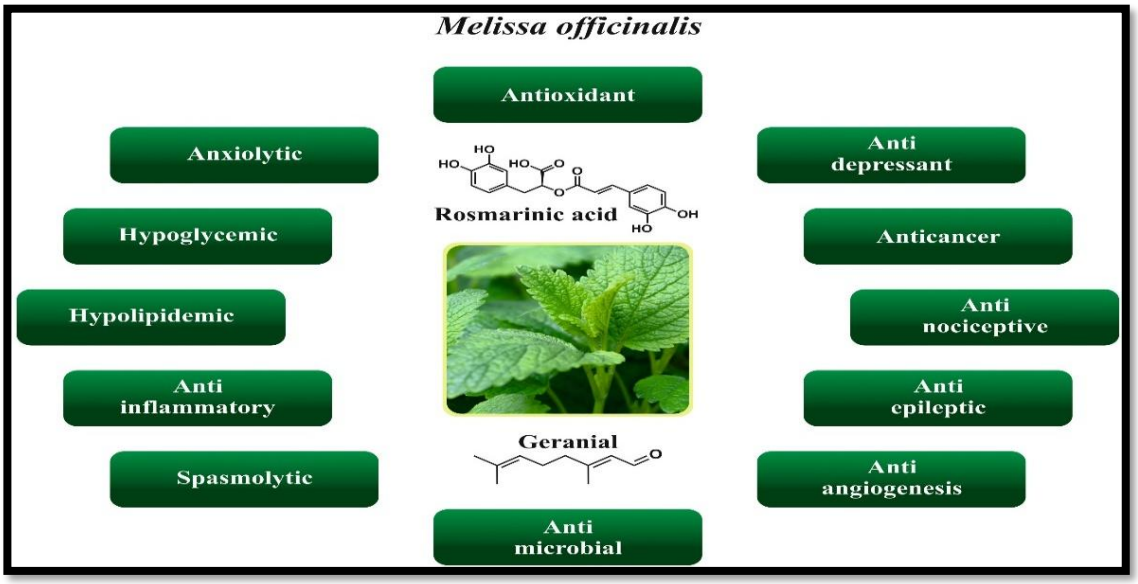

Figure 3. Various health properties of the ***Melissa officinalis***

3.1 Antibacterial activity:

Aromatic plants typically contain high concentrations of essential oils that have strong antibacterial qualities. The essential oils isolated from ***M. officinalis*** were found to include citronellal (37.33%), thymol (11.96%), citral (10.10%), and β-caryophyllene (7.27%) according to GC-MS analysis. Strong antibacterial activities of the oils against Salmonella typhimorium, Escherichia coli, Listeria monocytogenes, and Staphylococcus aureus were observed, as per the disk diffusion agar assay and micro-dilution method [38]. The most susceptible bacterium, S. aureus, had the lowest MIC value (0.12 mg/mL), according to the results [38]. High sensitivity to the essential oil of ***Melissa officinalis*** was demonstrated by E. Coli ATCC 25922 and the multiresistant strain of Shigella sonei IPH-MR [39]. With MICs ranging from 1.65 to 191.40 µg/mL, the petroleum ether extract of ***M. officinalis*** showed variable inhibitory potencies against Gram-positive bacteria, specifically Staphylococcus aureus and Pseudomonas aeruginosa [40]. However, no antibacterial effect was observed against Escherichia coli and Klebsiella pneumonia. Gram-negative bacteria like E. coli were less implicated in the results of the hydro-alcoholic extract of ***M. officinalis***, which shown intriguing antibacterial action against S. aureus and Staphylococcus epidermidis [41]. Notably, but not always, essential oils demonstrated strong antifungal activity. When comparing the M. officinalis essential oil to the antimycotic medication bifonazole, the essential oil's low MIC and MFC against Trichophyton tonsurans stood out [39]. Additionally, with MICs of 0.30–345.10 g/mL, the crude petroleum ether

extract and its derivative fractions showed impressive antifungal activity against Candida albicans, Candida krusei, and Candida glabrata [40].

3.2 Neuroprotective Properties:

Globally, there has been a recent rise in the number of people with neurological conditions, including neurodegenerative diseases and psychiatric problems [42]. Because ***M. officinalis*** possesses higher concentrations of tocopherols and phenolic chemicals, it has historically been utilized for its effects on the neurological system [39]. Acetylcholinesterase was inhibited by ***M. officinalis*** crude ethanol extract and its fractions both in vitro and in vivo [43,44,45]. Similarly, attributable mostly to monoamine oxidase inhibition, methanol and aqueous extracts of ***M. officinalis*** exhibited a strong protective effect against hydrogen peroxide-induced toxicity in PC12 cells [46]. Furthermore, as a prospective model of epilepsy, the effects of an ethanol extract of ***M. officinalis*** were examined in the hippocampus of rats treated with pilocarpine [47]. Specifically, the extract's antioxidative and anti-inflammatory properties at 250 mg/kg had a positive effect on the Nrf2/HO-1 signaling pathway, Na+/K+-ATPase activity, and GABA. Meanwhile, glutamate and acetylcholine decreased and decreased neuronal loss. These findings add a new potential benefit (anti-epileptic) to the many uses of ***M. officinalis***.

According to Hassanzadeh et al. [48], ***M. officinalis*** aqueous extract may have neuroprotective benefits in hippocampus primary culture against ecstasy-induced neurotoxicity. Furthermore, Yoo and associates demonstrated that oral administration of ***M. officinalis*** could increase cell proliferation and differentiation by increasing GABA levels in the mouse dentate gyrus and decreasing serum cortisol levels [49]. The effect of ***M. officinalis*** on hypoxia-induced neuronal death in a cortical neuronal culture system was tested both in vitro and in transient hippocampal ischemia in vivo models [50]. Cytotoxicity assays showed significant protection of M. officinalis against hypoxia in cultured neurons by decreasing caspase3 activity and TUNEL-positive cells significantly. ***M. officinalis*** oil was found to inhibit malondialdehyde levels and attenuate the decrease of the antioxidant capacity in the hippocampus. Pro-inflammatory cytokines TNF- α, IL-1β, and HIF-1αmRNA levels and HIF-1α gene expression were highly decreased by the treatment with the plant [50]. The main constituent of ***M. officinalis***, rosmarinic acid, showed cytotoxic effects on rat glioblastoma C6 cells by causing necrosis and inhibiting cell division [51]. When it came to glioblastoma cells, extracts made with 70% ethanol were the most effective since they caused apoptosis and necrosis as well as started the production of intracellular ROS [51]. Because spinal cord injury (SCI) causes damage to the motor, sensory, and autonomic nerve systems, the pathophysiology of SCI usually has a poor prognosis and can result in severe impairments [52]. Hosseini et al. [53] demonstrated that ***M. officinalis*** combined with human umbilical cord blood stem cells produced neuroprotective benefits in the SCI model on adult male rats. Researchers looked at how M. officinalis extracts affected rats' scopolamine-induced memory impairment through their behavioral mechanism of action [44, 54]. While some research revealed that ***M. officinalis*** extract was absolutely inert [54], other studies found that ***M. officinalis*** extract significantly improved rats' learning and memory, hence mitigating the scopolamine-induced learning deficit [44,54]. The frontal cortex's AChE mRNA level was shown to be 52% lower in the ***M. officinalis*** extract, accompanied by a significant inhibition of BACE1 mRNA transcription [55]. A model of anxiety-related illnesses was explored using ***M. officinalis*** oil at a concentration of 1 μg/mL in isolated mouse ileum and atria tissues in a recent study [56]. The study found that the oil could halt both induced and spontaneous ileum contractions, but it only marginally decreased AChE activity, indicating that ***M. officinalis*** may have alternative effects through different mechanisms, such as voltage-gated Ca2+ channels or muscarinic receptors.

3.3 Anti-inflammatory Effects:

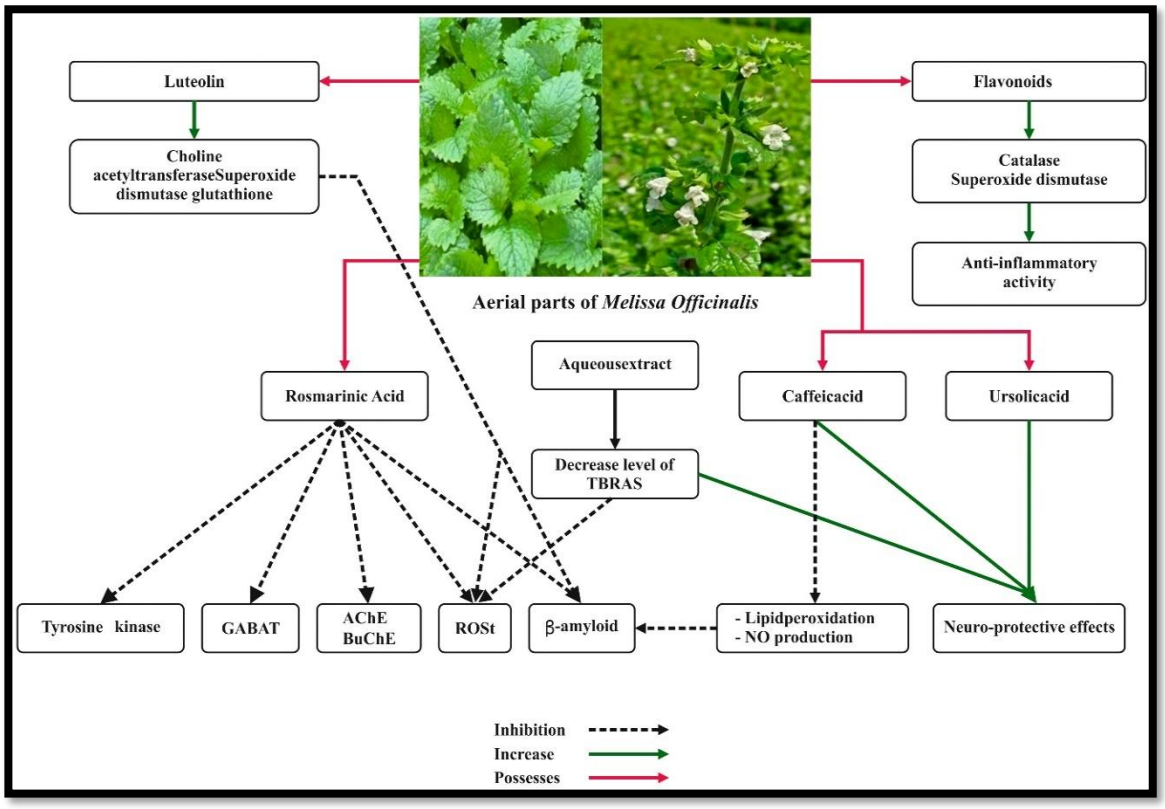

Figure 4. Anti-inflammatory property and neuroprotective effects of ***Melissa officinalis L.***

Many studies have looked into the anti-inflammatory properties of M***. officinalis*** leaves. The essential oil's anti-inflammatory properties were demonstrated by the results, confirming its traditional use in a variety of pain- and inflammation-related disorders [57]. According to recent research, ***M. officinalis*** extracts interact with muscarinic and nicotinic receptors as well as the L-arginine-nitric oxide pathway, which are linked to terpenoids, flavonoids, and RA. This results in anti-inflammatory and antinociceptive actions [58]. It is well established that RA and flavonoids inhibit a variety of inflammatory-processing enzymes, including lipoxygenase, cyclooxygenase, and monooxygenase [59]. Owing to these anti-inflammatory characteristics, ***M. officinalis*** extract was found to be effective in reducing atopic dermatitis symptoms [59]. Fig. 4 illustrates ***M. officinalis's*** anti-inflammatory ability. The effects of ***M. officinalis*** extract and its RA content on skin cells under oxidative stress and in normal conditions were studied by Ramanauskien et al. [51]. According to research on human keratinocyte cells, RA reduced intracellular ROS by roughly 28% under oxidative stress conditions, increased cell viability by 10%–24% (at a dosage of 0.25–0.5 mg/mL), and shielded the cells from H2O2 damage [51]. The histamine- and carrageenan-induced paw oedema tests in rats and mice were used to examine the anti-inflammatory and antinociceptive properties of ***M. officinalis***. Pretreatment with ***M. officinalis*** aqueous extract was reported to significantly reduce the nociceptive response in mice and the amount of paw oedema in rats generated by inflammagen [60]. An aqueous extract of ***M. officinalis*** was evaluated by Müzell and colleagues for its anti-inflammatory properties in acetaminophen-induced hepatic and renal lesions in animal models [68]. The extract showed nephroprotective activity against acetaminophen lesions and an anti-inflammatory effect on carrageenan-induced pleurisy, even if it was not hepatoprotective [61]. ***M. officinalis*** was also found to be a good source of chemopreventive agents. Its extracts demonstrated cytotoxicity in breast cancer cells (MDAMB- 231) even at low concentrations (100 µg/mL), with also a pronounced impact on cell migration and proliferation, while resulting in poorly toxic for HaCat cells (500 and 1000 µg/mL). Differently, stem extracts resulted highly cytotoxic (>100 µg/mL) [62].

❖ **Tulsi *(Ocimum tenuiflorum):***


Scientific classification:[63]
Kingdom: Plantae
(Unranked): Angiosperms
(Unranked): Eudicots
(Unranked): Asterids
Division: Magnoliophyta
Order: Lamiales
Family: Lamiaceae
Genus: Ocimum
Species: teinufolium

Ocimum tenuiflorum, also referred to as Ocimum sanctum, holy basil, or tulasi, is a fragrant member of the Lamiaceae family of plants that is native to the Indian Subcontinent and widely grown as a garden plant across the tropical regions of Southeast Asia. [64] It is a 30–60 cm tall, erect, heavily branched subshrub with hairy stems and simple, opposite, intensely scented green or purple leaves. Petioles are present on oval, up to 5 cm long leaves that are typically somewhat serrated. The tight whorls of elongate racemes with violet blooms [65]. The two primary morphotypes grown in India and Nepal are the purple-leaved (Krishna tulasi) and green-leaved (Sri or Lakshmi tulasi). [66]. Ocimum tenuiflorum, commonly referred to as Ocimum sanctum L. (tulsi), is an upright, heavily branching sub-shrub that grows to a height of 30 to 60 cm. It has hairy stems and straightforward, opposite, intensely scented green or purple leaves. Petioles are present on oval, up to 5 cm long leaves that are typically somewhat serrated. Close whorls of elongated racemes with purplish flowers are seen [67].

1. Pharmacological studies:

1.1 Antifungal activity

The essential oil that is obtained by steam-distilling the aerial portions of Oryza gratissimum at a concentration of 1.1% w/v has antifungal properties. According to Prabuseenivasan et al. (β006), the findings demonstrated that the essential oil inhibited the growth of every type of fungus examined, including two strains of Alternaria sp., Botryospaeria rhodina, and phytopathogens. Colletotrichum species isolated from spoiled tomatoes were evaluated against ethanolic, hot water, and cold water extracts of O. gratissimum. The hot water extract had the highest zone of inhibition, followed by the ethanolic extract and the cold water extract with the lowest (Orji et al., β015) [68]. Antifungal properties against Trichophyton rubrum, Microsporum canis, M. gypseum, and T. mentagrophytes. Research on Trichophyton rubrum, the most prevalent dermatophyte in Brazil, revealed that eugenol and O. gratissimum hexane extract are highly efficient against the dermatophyte (Silva et al., β010) [69].

1.2 Anxiety activity

The idea of mixed anxiety and depressive disorders (MADD) was first presented in recent research. The efficacy of ***Ocimum sanctum***, a well-known medicinal herb, against anxiety and depressive disorders was assessed in this study using an ethanol leaf extract**.** ***Ocimum sanctum*** extracts have both antidepressant and antianxiety qualities at the same dosage, suggesting that they may be a useful treatment for mixed anxiety and depressive syndrome [70].

1.3 Antistress activity

Everybody has experienced stress at some point in their lives. The definition of stress is the "non-specific effect of any exertion on the body." Stress can manifest as both physical and psychological symptoms, depending on where the stress is coming from. You should deal with stress since it can be detrimental to the health if it becomes out of control[71]. This category includes immunosuppression, depression, anxiety, and endocrine illnesses such as ulcerative colitis (UC), diabetic mellitus (DM), male impotence (IM), cognitive dysfunction (CDD), and male impotence (IM). Tulsi can help you remember things better and reduce both physical and mental stress. When exposed to anoxic stress, tulsi has an anti-hypoxic impact and lengthens life. Studies have revealed that Tulsi may help reduce oxidative stress in rabbits.

One interpretation of tulsi leaves is as a "adaptogen," or anti-stress agent. Recent research indicates that the leaves offer significant relief from stress. Tulsi can be used to provide sedative effects by consuming it twice a day. Long-term stress can alleviate gastrointestinal problems, anxiety, and insomnia in yoga. It has been shown that using Tulsi leaf extracts reduces an acute increase in corticosterone levels[72].

1.4 Antiviral activity

A virus is a tiny infectious agent that can only reproduce in the living cell of its host and has no independent metabolism. Following the identification of the first tobacco mosaic virus, many of viruses have been found; each ecosystem contains millions of them. Traditionally, medicinal plants have been used to cure a variety of illnesses, and the need for drugs to combat infectious diseases is growing. The study showed that extracts of ***Ocimum sanctum L***., ***Ocimum basilicum L***., and ***Ocimum americanum L***. had anti-herpes simplex virus properties in dichloromethane and methanol. ***Ocimum sanctum L***., ***Ocimum basilicum L***., and ***Ocimum americanum L***. extracts in dichloromethane and methanol demonstrated anti-HSV activity at different stages of the viral replication cycle [73].

2. Traditional Uses:

In dental care, basil, also known as tulsi, has been used to treat respiratory conditions, fever, asthma, lung conditions, heart illnesses, and stress[74]. Tulsi leaves are regarded as an anti-stress or "adaptogen." According to recent studies, leaves provide a substantial level of resistance against stress. Chewing 10-12 tulsi leaves twice or three times a day can help prevent stress in healthy individuals. It helps to avoid various common diseases and purifies blood[81]. Chewing on the leaves helps treat the flu and cold. In the event of influenza, a decoction made of the leaves, cloves, and regular salt also provides fast relief[75]. According to a review of the literature, plant extracts help albino rats' sorbitol dehydrogenase assay (SDH) levels, which indicates their anti-stress activity[76].

Results:

1. *Melissa officinalis* (Lemon Balm)

• **Chemical Composition**: Rich in citral, citronellal, and geraniol, the essential oils found in ***Melissa officinalis*** have been demonstrated to have anxiolytic properties. Furthermore, substances like rosmarinic acid support its ability to reduce stress.

• **Clinical Evidence**: Numerous research suggest that lemon balm helps lessen anxiety symptoms. Clinical research, for example, have shown that it is effective in reducing anxiety ratings and elevating

mood. Participants utilizing lemon balm extract shown significant increases in cognitive performance and reductions in anxiety symptoms in a double-blind, placebo-controlled experiment.

• **Mechanism of Action**: Because of its ability to control GABAergic activity in the brain, ***Melissa officinalis*** is claimed to have anxiolytic characteristics. This action is comparable to that of benzodiazepines but without the unpleasant side effects.

2. *Ocimum tenuiflorum* (Holy Basil/Tulsi)

• **Chemical Composition**: Essential oils including methyl eugenol, caryophyllene, and eugenol are abundant in ***Ocimum tenuiflorum***. These substances have shown anxiolytic and adaptogenic qualities.

• **Clinical Evidence**: holy basil has been shown in studies to be useful in lowering tension and anxiety. ***Ocimum tenuiflorum*** extracts have been demonstrated in randomized controlled trials to effectively reduce cortisol levels, a biomarker of stress, and alleviate symptoms associated with stress.

• **Mechanism of Action*: Ocimum tenuiflorum*** is thought to have adaptogenic qualities because of its influence on the hypothalamic-pituitary-adrenal (HPA) axis and capacity to strengthen the body's resilience to stress.

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Discussion:

1. Comparative Efficacy

• ***Melissa officinalis vs. Ocimum tenuiflorum***: Both plants demonstrate significant potential in alleviating stress and anxiety, but they operate through different mechanisms. ***Melissa officinalis*** primarily affects GABAergic neurotransmission, leading to a calming effect on the central nervous system. In contrast, ***Ocimum tenuiflorum*** exerts its effects through its adaptogenic properties, helping the body to manage and resist stress more effectively.

• **Synergistic Potential**: The combined use of these herbs could potentially offer complementary benefits. For example, ***Melissa officinalis*** could be used for acute anxiety relief while ***Ocimum tenuiflorum*** might be more suited for long-term stress management.

2. Safety and Side Effects

• ***Melissa officinalis***: Though some people may experience modest side effects including nausea or allergic reactions, the medication is generally thought to be safe. Caution is warranted due to its interaction with sedative drugs.

• ***Ocimum tenuiflorum***: Also well-tolerated, with rare complaints of stomach discomfort or allergic responses. Because it may affect thyroid function, it should be used carefully, as with any adaptogen, in people with thyroid diseases.

3. Practical Applicatons

• **Dosage and Administration**: Studies indicate that 300–600 mg of ***Melissa officinalis*** extract or 500–1000 mg of ***Ocimum tenuiflorum*** extract daily may be helpful, while effective dosages vary. Nonetheless, further investigation is required to develop uniform dosage recommendations.

• **Formulations**: There are other ways to consume these herbs, such as tinctures, teas, and capsules. User preference and bioavailability should be taken into account while selecting a formulation.

4. Future Research Directions

• **Long-term Studies**: Long-term clinical trials are necessary to gain a better understanding of ***Ocimum tenuiflorum*** and ***Melissa officinalis's*** safety profiles and long-term effects.

• **Mechanistic Studies**: Deeper understanding of the precise mechanisms of action and possible drug interactions would come from additional study into these drugs' safety and efficacy.

• **Population Studies**: It might be possible to customize the use of these herbs to meet the demands of each individual by conducting research on various demographic groups and stress levels.

Conclusion:

In conclusion, Ocimum tenuiflorum, or holy basil, and Melissa officinalis, or lemon balm, have both become well-known natural stress and anxiety relievers. Each herb has special advantages that are backed by research that demonstrates its safety and effectiveness.

Melissa officinalis's impact on GABAergic neurotransmission has shown promise as a substantial anxiolytic. It can be a good alternative for acute anxiety alleviation because clinical studies have shown that it can effectively reduce anxiety symptoms and improve cognitive function. Its ease of usage and comparatively low frequency of adverse effects bolster its efficaciousness in the management of anxiety.

Conversely, ***Ocimum tenuiflorum*** exhibits potent adaptogenic properties, supporting the body in the regulation of ongoing stress and augmenting total stress tolerance. Research suggests that it is a good option for long-term stress management because it successfully reduces cortisol levels and eases symptoms associated with stress. It is a potential option for promoting mental and emotional well-being due to its adaptogenic qualities and overall safety.

Given these herbs' complementary qualities, using them together may have synergistic effects that help with both acute and chronic stressors. To maximize their therapeutic utility, more research and standardized dose guidelines are required.

All things considered, ***Ocimum tenuiflorum*** and ***Melissa officinalis*** are beneficial supplements to natural methods of reducing stress and anxiety. Subsequent investigations ought to concentrate on enduring consequences, mechanistic perspectives, and varied demographic analyses to augment our comprehension and use of these herbal treatments.

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