

Lemon balm (*Melissa officinalis*): A review of its chemical composition and biological activities

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Article history

Received 16 Nov 2024

Received in revised form 28 Dec 2024

Accepted 09 Jan 2025

Available online 30 Jan 2025

ABSTRACT

Melissa officinalis, better known as lemon balm, has been used historically to treat several medical conditions, including neurology, gastrointestinal issues, and stress management. It contains bioactive components, including rosmarinic acid, flavonoids, and essential oils, which account for its diverse pharmacological effects. Neural rehabilitation combined with GABA-A receptor modulation, antioxidant effects, and acetylcholinesterase activity inhibition improved cognitive function, increased relaxation response, and protected neurons. New clinical evidence indicates that it is helpful in enhancing sleep, alleviating anxiety, and improving overall quality of life, in particular for postmenopausal women. *M. officinalis* may be just as effective as traditional drugs like citalopram and fluoxetine, according to comparative studies, but with better tolerance and fewer side effects. Its effectiveness in lowering acute stress and situational anxiety is further supported by meta-analyses. As an auxiliary or safe, natural substitute. Toxicological assessments indicate that

M. officinalis is generally safe, though high doses of its essential oil may cause liver and kidney toxicity.

Keywords: *Melissa officinalis*, Lemon balm, GABA modulation, Anxiety, Depression, Sleep disorders, Neuroprotection, Lipid metabolism, Traditional medicine, Phytotherapy.

INTRODUCTION

Melissa officinalis (lemon balm) is an herb that has long been used to cure a variety of ailments, including rheumatoid arthritis, neurological disorders, gastrointestinal disorders, and headaches. The plant has been used as a mild hypnotic and sedative, among other things [1]. *Melissa officinalis* (lemon balm) is an herb that has long been used to cure a variety of ailments, including rheumatoid arthritis, neurological disorders, gastrointestinal disorders, and headaches. The plant has been used as a mild hypnotic and sedative, among other things [2]. The father of pharmacology, Dioscorides (40–90 CE), originally described the medicinal qualities of this plant in *De Materia Medica*. Since then, numerous other important medical texts, including Avicenna's *Canon of Medicine* and Zakhireh Kharazmshahi, have referenced the therapeutic qualities of *M. officinalis* [3]. In Portuguese and Cuban traditional medicine, lemon balm has been utilized for its calming and anti-cancer effects. In the US, lemon balm is listed on the FDA's Generally Recognized as Safe (GRAS) list. There have been no reports of any severe negative effects [4]. The leaves are the portion of the plant that is utilized medicinally. They can be ground into powdered or ground herbal material, ethanol liquid extract, tincture, or dry extracts, or they can be used as herbal ingredients in herbal teas. Lemon balm has been licensed by the European Medicines Agency to help with sleep, alleviate minor mental stress symptoms, and treat some gastrointestinal issues [5]. Sleep is essential for sustaining systemic physiology and brain function, and persistent sleep issues may have a major negative influence on human health. Reduced stress resilience, a lower quality of life, mood disorders, and deficiencies in cognition, memory, and performance are all consequences of sleep deprivation. Additionally, it may be a factor in metabolic diseases such as type 2 diabetes mellitus, hypertension, dyslipidemia, and cardiovascular disease [6]. Lemon balm, or *Melissa officinalis* L., is regarded as a heart tonic in traditional medicine and has been shown to

eliminate toxins from the circulation. Thus, the lipid-lowering properties of lemon balm may be explained by its use as a cardiovascular treatment. One important preventive risk factor for atherosclerosis, coronary heart disease, and type 2 diabetes is dyslipidemia [7]. The COVID-19 pandemic has been linked to a 25% rise in the prevalence of depression and anxiety globally. Tricyclic antidepressants (TCAs), monoamine oxidase inhibitors (MAOIs), selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), norepinephrine–dopamine reuptake inhibitors (NDRIs), and serotonin antagonists and reuptake inhibitors (SARIs) are among the conventional drug treatments for depression. For anxiety disorders, the drug therapies include SSRIs, SNRIs, pregabalin, TCAs, buspirone, benzodiazepines (BZDs), and MAOIs. However, according to published data, between 30% and 60% of patients do not take these synthetic antidepressant or anxiolytic drugs as prescribed because of side effects or a noticeable delay in their effectiveness. The study of plant psychopharmacology has gained a lot of attention in recent decades [8].

Plant Description



Figure no 1 Lemon balm

Lemon balm is an erect, herbaceous, perennial plant with opposite pairs of serrated, ovate leaves growing on square, branching stems [9]. It is an upright, bushy plant that grows to a height of 60 to 100 cm and has a minimum lifespan of three years. The dark green, heart-

shaped, velvety, hairy leaves measure 2 to 8 cm in length. The fruit of the plant is a little nutlet, the leaf edge is scalloped or toothed, and the leaf surface is coarse and heavily veined. The tiny, two-lipped blossoms of lemon balm can be pale yellow, white, pink, and occasionally purplish or bluish, and they grow in whorled clusters with non-glandular hairs [10]. In Asia Minor, lemon balm grows wild in shaded spots like hedge edges, woods, and cool, uncultivated areas. It is also found in southern Europe and North America. Both the United States and central and western Europe grow it. In late June or early July, the leaves and stems are picked before they flower. There may be a second harvest in late August or early September [11]. The optimum growth and development of lemon balm (*Melissa officinalis*) cuttings was observed in a growing media mix consisting of vermicompost, soil, and farmyard manure (FYM) in a 1:1:1 ratio, according to a study conducted at CIMAP, Research Centre Purara (Uttarakhand). A 36 cm plant height, 6 branches, 38 leaves, 1.95 g fresh weight, 0.98 g dry weight, 6 roots, and 11.2 cm root length were the results of this combination, which also produced an 85% survival rate [12]. Combining biochar, NPK fertilizer, *Trichoderma harzianum*, *Thiobacillus thioparus*, elemental sulfur, and chicken manure compost reduces the negative effects of drought stress on lemon balm (*Melissa officinalis* L.), greatly enhancing its growth and biomass, according to a study. By taking a comprehensive approach, lemon balm becomes more resilient in areas with limited water resources [13].

Taxonomical classification

The taxonomical classification of this plant is as follows [14, 15]

Division	Tracheophyta
Subdivision	Spermatophyta
Class	Magnoliopsida
Superorder	Asteranae;
Order	Lamiales
Family	Lamiaceae
Genus	Melissa
Species	Melissa officinalis L.

Some common names are as follow [11]

Hindi	Billilotan
Urdu	Baranjiboya balm
English name	Balm, lemon Balm

The chemical composition

The leaves of *Melissa officinalis* contain the majority of its active ingredients. These components include polyphenolic chemicals such as rosmarinic acid, caffeic acid, protocatechuic acid, rhamnocitrin, and luteolin, as well as volatile compounds and terpenoids [16]. The essential oil of lemon balm (*Melissa officinalis*) has a lemon scent and contains monoterpene glycosides, polyphenolic chemicals (including rosmarinic acid), and citronellal, neral, and geranial monoterpene aldehydes [14]. Flavonoids are prevalent in lemon balm leaves, making up around 0.5% of their dry weight. Quercitrin, a derivative of quercetin, rhamnocitrin, luteolin, and its different derivatives, including luteolin 7-o- β -d-glucuronopyranoside, luteolin 3'-o- β -d-glucuronopyranoside, apigenin 7-o- β -d-glucopyranoside, and luteolin 7-o- β -d-glucopyranoside-3'-o- β -d-glucuronopyranoside, are the main flavonoids that were found.

The volatile oil content of the plant ranges from 0.1% to 0.5% by weight, with citronellal, geranial, and neral making up approximately 50% to 70% of this oil. Additionally, eugenyl glycoside has been extracted from the leaves of lemon balm. Analysis of lemon balm tea revealed a concentration of 10 mg/L of essential oil, predominantly consisting of 74% citral, along with significant quantities of polyphenolic compounds [17].

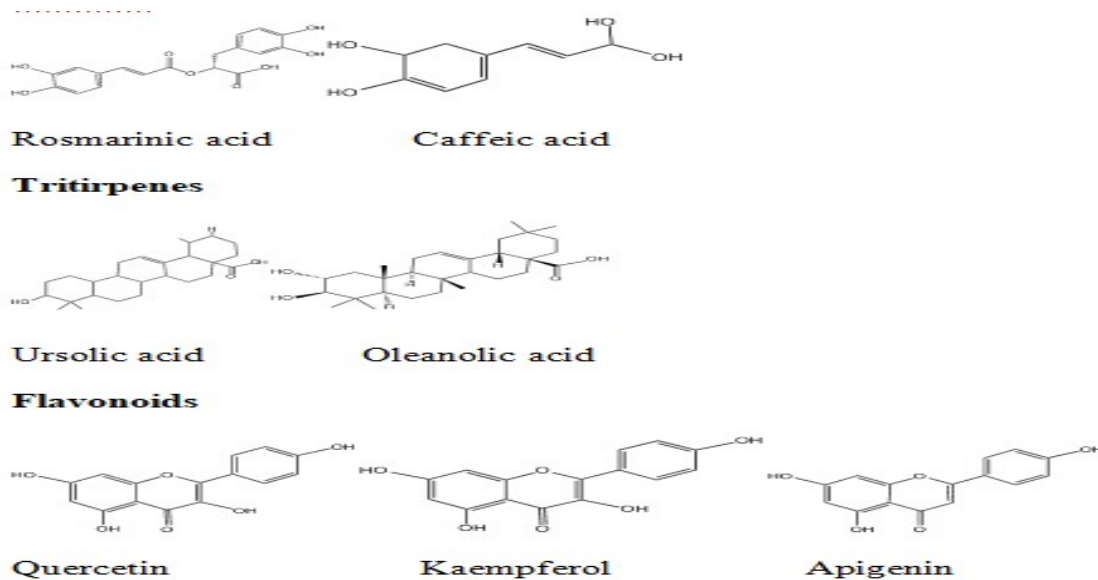


Figure no 2. The primary active ingredients found in *Melissa Officinalis* L. (lemon balm) include triterpenes [19], flavonoids [20], phenolic acids [18], essential oils [21], and secondary metabolites [23].

Phenolic acids

Essential oil



Secondary metabolites

1. tannins
- 2 Coumarins
3. Polysaccharides

Mechanism of lemon balm in Sleeping disorder

Because lemon balm includes rosmarinic, ursolic, and oleanolic acids, a methanolic extract of the plant inhibits GABA-T. At 100 µg/ml of rosmarinic acid, 40% inhibition takes place. The latter is present in the methanol extract at this concentration, indicating that it is the source of the observed inhibitory activity. Ursolic acid inhibits GABA-T by 13% and oleanolic acid by 20% at 10 µg/ml. The action that was seen [25].

The nootropic effects of lemon balm are caused by a variety of methods [24, 25].

Action	Mechanism of operation
Changes to GABA-A receptors	Rosmarinic acid and other compounds found in lemon balm bind to GABA-A receptors, enhancing GABA's effects and promoting relaxation.
Inhibition of AChE	Act By blocking the enzymes that break down acetylcholine, Rosmarinic acid and other compounds found in lemon balm bind to GABA-A receptors, enhancing GABA's effects and promoting relaxation.
Antioxidant and neuroprotective effects	Lemon balm's strong rosmarinic acid and other antioxidant content shields brain cells from inflammation and oxidative damage.

Clinical Studies

Study on Postmenopausal Women (in 2020)

For some women, the menopause is one of the most critical times in their lives [26]. Sleep disorders are among the most prevalent issues facing women at this time.

A double-blind randomized clinical trial of 110 postmenopausal women was done to determine the effects of lemon balm extract on sleep quality. The participants were separated into two groups: intervention and control. The intervention group received lemon balm capsules with 250mg of extract. The study found that the intervention group had significantly higher sleep quality scores than the control group, showing that lemon balm extract can improve sleep quality in postmenopausal women [27].

One hundred women with sleep disturbances who were menopausal were split into two groups for this triple-blind randomized control clinical experiment. For a month, the control group was given placebo capsules, while the intervention group was given daily capsules containing 160 mg of Valerian and 80 mg of Lemon Balm. Sleep quality was evaluated using the Pittsburgh Sleep Quality Index (PSQI). A 36% improvement in sleep quality in the experimental group compared to 8% in the placebo group indicates that the combination of Valerian and Lemon Balm considerably improves sleep quality in menopausal women, according to the study's findings [28].

The Effectiveness of Melissa Officinalis L. versus Citalopram on the Quality of Life of Menopausal Women with Sleep Disorders

Study type: Double-Blind Clinical Trial

Citalopram and a placebo were found to be less beneficial than Melissa officinalis L. (lemon balm) in enhancing quality of life, particularly in the vasomotor, physical, psychomotor-social, and sexual domains. Perhaps because lemon balm raises GABA levels in the brain, it showed anxiolytic benefits and enhanced sleep quality. Furthermore, it was well tolerated and did not cause any serious side effects, in contrast to citalopram, which had anxiety and insomnia as side effects [29].

Comparison of Lemon balm with Fluoxetine

Scientists conducted a study to compare how well lavender and lemon balm work against depression, measuring them up to fluoxetine. They set up the test so neither the researchers nor the participants knew who got what treatment. The results showed that both herbs worked just as well as fluoxetine. What's more, they caused fewer problems and were less likely to make people dependent on them. Other research backs up the idea that these plants can help with depression. This work points to the possibility of using these natural options instead of regular antidepressant drugs [30].

Meta Analysis (2021)

A meta-analysis of randomized clinical trials conducted in 2021 found that lemon balm significantly reduces anxiety. Lemon balm may be more useful at treating immediate or situational (acute) anxiety than long-term (chronic) anxiety. According to studies, it greatly reduces acute anxiety in hospitalized patients and adolescent girls suffering from PMS, as

well as moderately alleviating chronic worry in office workers and patients with stable angina [31].

Study Type: Human clinical intervention trial

18 healthy participants participated in a human clinical intervention experiment to see if lemon balm could lessen acute stress. Single doses of 300 mg or 600 mg of lemon balm or a placebo were given in this double-blind, placebo-controlled, randomized, balanced, crossover study, which had a seven-day washout period. Both before and after a 20-minute stress test, the subjects' moods were evaluated.

Dosage	Results
300 mg	Improved test speed without loss of accuracy.
600 mg	Alleviated negative mood and significantly increased calmness.

Conclusion: Melissa officinalis has the ability to lessen the negative impacts of stress [32]

Toxicity

The essential oil of lemon balm (*Melissa officinalis*) was found to be mildly hazardous in a study involving BALB/c mice, with an oral LD50 of 2.57 g/kg. Geranial, neral, and citronellal are important constituents. It resulted in liver and renal damage and behavioral abnormalities at doses greater than 1 g/kg [33]. A study also indicated that the aqueous extract of *Melissa officinalis* (lemon balm) is safe for use as a food additive because it is non-genotoxic and did not cause any negative effects in rats over a 90-day period at high doses [34]. In the study of 21 BALB/c, hydroalcoholic extract damages the liver in a dose-dependent manner without changing the levels of creatinine and urea. Because of the mild to severe histopathological alterations in the liver and renal tissues, high dosages should be avoided [35]. Lemonbalm or *Melissa officinalis*, is well-known for its antimicrobial and soothing qualities. 21 male mice were used in the investigation; three groups were given hydroalcoholic lemon balm extract at 0.450 g/kg and 1.350 g/kg each day for two weeks, while the control group was given saline. Changes in liver and kidney tissues' histopathology and blood analysis revealed variations in enzyme levels, suggesting possible toxicity at high dosages [36].

The highly potent essential oil of lemon balm might be harmful if left undiluted. It contains substances including citral, eugenol, and linalool that can depress the central nervous

system or cause irritation. Drowsiness, muscle weakness, and even breathing problems can result from overdoses (e.g., more than 2 grams daily) [37].

DISCUSSION

There is a lot of promise in balm. In order to produce sedative and anxiolytic effects, its active ingredients—oleanolic acid, ursolic acid, and rosmarinic acid—primarily function by blocking GABA transaminase, altering GABA activity, and leveraging antioxidant activities. Together, these traits improve sleep, promote relaxation, and prevent brain damage brought on by stress. Clinical studies have consistently demonstrated the benefits of lemon balm for a range of people. Menopausal women report significantly improved sleep, particularly when taking Valerian alongside it. Comparative studies have demonstrated that lemon balm is a safer alternative to drugs like citalopram and fluoxetine, with equivalent efficacy and fewer side effects. Studies on acute stress and anxiety have also shown that stress can be lessened.

CONCLUSION

Melissa officinalis has GABAergic and antioxidant properties and is thus a safe and effective natural remedy for stress, anxiety, and sleep problems. Clinical studies indicate that this treatment may be effective both alone and in combination with other therapies, and it produces minimal side effects. Furthermore, another therapeutic potential is the cardioprotective quality; though it may seem promising, further work needs to be done on standardization of dosing and on the assessments of the long-term effects. Thus, lemon balm may eventually be better regarded as an all-purpose enhancer of mental wellness and sleep.

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