Lemon Balm (Melissa officinalis)

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Principal Proposed Uses: Mild sedative, digestive aid, antiviral
Other Proposed Uses: Anti-inflammatory

Overview

Lemon balm is a lemon-smelling herb native to southern Europe. It has been called an herbal “cure all”, and thought to act as a sedative, carminative, antipyretic, antispasmodic, diaphoretic, hypotensive, aromatic, and emmenagogue. Several clinical studies of an oral lemon balm/valerian combination preparation show promise for lemon balm’s efficacy as a sedative. A topical ointment containing lemon balm extract is widely sold in Europe for the treatment of genital and oral herpes, and open label studies and controlled trials suggest that it may be helpful in speeding recovery from oral and genital Herpes outbreaks. Lemon balm is on the GRAS (generally recognized as safe) list in the US; no serious side effects have been reported.

Historical and Popular Uses

Lemon balm is native to southern Europe and is commonly planted in gardens to attract bees. The name comes from the Greek word “melissa” which means “bee”, and “balm”, a short form of “balsam”\(^1\). Lemon balm’s use has been documented in Ancient Greek and Roman times. Also known by the name "cure-all", it has been used as a sedative, antipyretic, antispasmodic, diaphoretic, antihypertensive, aromatic, emmenagogue, and carminative\(^2, 3\), and a treatment for insomnia, sleep disorders, anxiety, depression, neuralgia, migraine, tension headache, nausea, nervous stomach, anorexia, colic, chronic fatigue, shingles, coughs, irregular menstrual periods, toothache, heart conditions, nervous palpitations and high blood pressure\(^1, 3-7\). It is used as a
treatment for Graves’ disease and other thyroid conditions\textsuperscript{8}. Lemon balm also has a reputation as a memory enhancer\textsuperscript{9}.

Lemon balm is used as a topical treatment for wounds, skin irritations, and insect bites. In Europe it is widely used as a topical antiviral treatment for genital and oral herpes; lemon balm cream is applied at the first sign of a herpes flare-up or regularly for prevention\textsuperscript{1, 3}. In Germany, the essential oil is placed on the temples to relieve headaches or sleeplessness\textsuperscript{5}.

The German Commission E recommends lemon balm for nervous sleep disorders and functional gastrointestinal complaints\textsuperscript{10}. The European Scientific Cooperative On Phytotherapy (ESCOP) recommends it use for tenseness, restlessness and irritability\textsuperscript{1}.

Lemon balm is often combined with other herbs such as valerian (for sleep problems) and peppermint (for dyspepsia).

\textbf{Botany}

\textit{Medicinal species: Melissa officinalis}

\textit{Common names:} Balm, citronellae, cure-all, honey plant, dropsy plant, melissae, melissa, sweet marjoram, sweet balm

\textit{Botanical family:} Lamiaceae

\textit{Plant description:} Lemon balm is a delicate, low-growing (1-2 foot) perennial herb with lemon-smelling, pointed, heart shaped or oval leaves and small white or yellow flowers. The leaves are used medicinally.

\textit{Where it's grown:} Native to the Mediterranean region. Now also grown in western Asia, the USA, and Europe.
Biochemistry

Lemon Balm: Potentially Active Chemical Constituents

- Volatile oil: citronellal, citral a (geranial), citral b (neral), methyl citronellate, ocimene, citronellol, geraniol, nerol, β-caryophyllene, β-caryophyllene oxide, linalool
- Hydroxycinnamic acid derivatives: rosmarinic acid, caffeic acids, chlorogenic acid
- Tannins
- Flavonoids: quercetin, apigen, kaempferol, luteolin
- Monoterpenic glycosides
- Sesquiterpenes: β-caryophyllene, germacrene
- Triterpenic acids: ursolic and oleanolic acids
- Other compounds: melitric acids A and B, eugenylglucoside

Lemon balm contains numerous potentially active compounds. Lemon balm oil is produced by steam distillation from fresh or dried herb.

The volatile oil comprises 0.5-0.1% of the plant by weight, and citronellal, geranial, and nerol constitute about 50-70% of this oil. Volatile oils act in the limbic system, which governs the autonomic nervous system.

Rosmarinic acid and caffeic acid have significant antioxidant and immune modulating activities. Rosmarinic acid is well absorbed from the gastrointestinal tract and skin. In rats, 31% of oral rosmarinic acid was excreted in urine within 48 hours. After i.v. administration, the absolute bioavailability was 60% after 30 minutes. Rosmarinic acid was detected in brain, heart, liver, lung, muscle, spleen and bone tissue, showing the highest concentration in lung tissue. After topical administration to rats, rosmarinic acid was detected in blood, skin, muscle and bone.

Caffeic acid also appears to have antiviral properties.

Tannins are typically used as herbal astringents and have antiviral properties.
Experimental Studies

**Lemon Balm: Potential Clinical Benefits**

1. Cardiovascular: *Vasodilator*
2. Pulmonary: *Antitussive*
3. Renal and electrolyte balance: none
4. Gastrointestinal/hepatic: Digestive aid (spasmolytic)
5. Neuro-psychiatric: Sedative/hypnotic
6. Endocrine: *Antithyroid*
7. Hematologic: *Antithrombotic*
8. Rheumatologic: none
9. Reproductive: *Emmenagogue*
10. Immune modulation: *Anti-inflammatory*
11. Antimicrobial: Antiviral, antibacterial, antifungal
12. Antineoplastic: none
13. Antioxidant: *Antioxidant*
14. Skin and mucus membranes: See Antimicrobial: Antiviral and Immune modulation: Anti-inflammatory
15. Other/miscellaneous: Inhibition of protein biosynthesis

1. **Cardiovascular: Vasodilator**
   
   i. *In vitro data:* In rabbit aorta, lemon balm essential oil caused vasodilation\(^1\).
   
   ii. *Animal data:* none
   
   iii. *Human data:* none

2. **Pulmonary: Antitussive.** Lemon balm is traditionally used for bronchitis, colds and flu.
   
   i. *In vitro data:* In guinea pig tracheal smooth muscle, lemon balm had a relaxing effect\(^27\).
   
   ii. *Animal data:* none
   
   iii. *Human data:* none

3. **Renal and electrolyte imbalance:** none
4. **Gastrointestinal/hepatic**: Digestive aid (spasmytic)
   
   i. *In vitro data*: *In vitro* studies have shown conflicting results. In guinea pig ileum, rat duodenum, and rabbit jejenum, lemon balm essential oil had spasmytic activity\(^1\), \(^27\). On the other hand, in guinea pig ileum, using histamine and acetylcholine as spasmogens, lemon balm extracts did not show any significant antispasmodic activity\(^28\). In rat duodenum, no spasmytic effects were observed\(^29\).
   
   ii. *Animal data*: none
   
   iii. *Human data*: Despite historical and popular use, there are no clinical trials testing the efficacy of lemon balm as a digestive aid.

5. **Neuro-psychiatric**: Sedative/hypnotic
   
   i. *In vitro data*: In normal brain homogenates, lemon balm extract significantly inhibited cholinesterase enzymes\(^9\).
   
   ii. *Animal data*: In mice, an aqueous alcoholic extract of lemon balm produced dose-dependent sedation; it induced sleep and potentiated subhypnotic and hypnotic doses of pentobarbital. On the other hand, in the same study the *essential oil* of lemon balm had no sedative effect\(^29\), \(^30\). In another study, the oral administration of lemon balm essential oil to mice caused sedative and narcotic effects\(^31\).
   
   iii. *Human data*: Most studies on lemon balm’s sedative effects have used herbal combinations including proven sedatives such as valerian, and have not been published in English. The data presented here are largely drawn from the English abstracts of the German research.

   In a randomized, placebo-controlled, double blind, multicenter study, healthy volunteers were given a valerian/lemon balm combination or placebo to treat minor sleep disorders. No significant changes were seen in regard to laboratory tests, physical examination or rating of well being, but the valerian/lemon balm group had a significantly higher quality of sleep compared to the placebo group. The preparation was well tolerated by the majority of subjects and there was no statistically significant difference in the frequency of adverse events between the valerian/lemon balm and placebo groups; no serious adverse events were reported\(^32\).
In a similar trial, 68 women with DSM-III-R-diagnosed insomnia were given two Euvegal Forte® tablets (160 mg valerian root extract and 80 mg lemon balm extract) or a placebo twice daily for 14 days. Sleep quality improved during and after the trial for those taking the Euvegal Forte. Additionally, a significant improvement in the “feeling of well being” for the Euvegal Forte group occurred during and after the trial compared to the placebo group. The severity of insomnia was reduced 60% in those taking the valerian/lemon balm combination, as compared with only 20% in those taking the placebo. Mild side effects such as nausea, headache, stomach upset and calf cramps were similar for the herb and placebo group\textsuperscript{33, 34}.

In a German double blind, controlled study, 20 adults with insomnia were randomized to take a) a valerian/lemon balm preparation (2 tablets of valerian root 160 mg and lemon balm 80 mg), b) triazolam (0.125 mg), or c) placebo at bedtime for nine days. The subjects with less severe insomnia who received valerian/lemon balm showed significant reductions in REM sleep and duration of the first REM phase, compared to the placebo group. Those with more severe insomnia showed significant increases in their sleep efficiency and amount of deep sleep. Subjects receiving valerian/lemon balm demonstrated better focus on a concentration-performance test than the placebo group. Both active treatments were significantly better than placebo and not significantly different from each other. The herbal combination caused less daytime sedation and impaired mental functioning than triazolam\textsuperscript{34, 35}.

In a placebo-controlled assessment of the effects of aromatherapy using the essential oil of lemon balm (combined with lavender), a small number of patients with dementia were reported to improve on measures of independence and “general functioning” in comparison with the placebo group exposed to culinary vegetable oil\textsuperscript{9, 36}.

6. **Endocrine: Antithyroid**

   i. *In vitro data:* Freeze-dried extracts of lemon balm inhibited the binding of bovine TSH to human thyroid plasma membranes and adenylate cyclase. In rat liver microsomes, lemon balm aqueous extract inhibited both the extrathyroidal enzymatic T4-5'-deiodination to T3 and T4-5'-deiodination\textsuperscript{37}.
The thyroid-stimulating immunoglobulin G (IgG) found in patients with Graves’ disease resembles TSH in its ability to bind to the thyroid plasma membrane and to activate the thyroid gland. Freeze-dried extracts of lemon balm exhibited antithyrotropic activity by forming adducts with TSH that bound weakly, if at all, to the TSH receptor. When Graves-IgG was incubated with extracts of lemon balm, there was a dose-dependent decrease in the TSH-binding inhibitory activity. As a result, adenylate cyclase activity was stimulated (thyroid-stimulating Ig activity) and thyroid iodine release was enhanced in the McKenzie assay system.

Cinnamic acid inhibited the binding of TSH to human thyroid membranes.

ii. Animal data: In euthyroid rats, the administration of freeze dried extracts of lemon balm reduced pituitary and serum TSH concentrations.

iii. Human data: There are no clinical trials evaluating the antithyroid effects of lemon balm in humans.

7. Hematologic: Antithrombotic
   i. In vitro data: none
   ii. Animal data: In rats, rosmarinic acid inhibited venous thrombosis approximately 50% at dosages of 50 and 100 mg/kg; it also suppressed blood platelet aggregation by 30% and 40% at doses of 100 and 150 mg/kg respectively.
   iii. Human data: There are no clinical trials testing the efficacy of lemon balm as antithrombotic agent or evaluating its potential synergistic effects with anticoagulant medications or herbs.

8. Rheumatologic: none

9. Reproductive: Emmenagogue. Lemon balm has historically been used as to stimulate menstruation.
   i. In vitro data: Freeze dried extracts of lemon balm inhibited binding of 125I hCG to rat testis membranes.
   ii. Animal data: In rats, prolactin serum levels and hypophyseal stores were reduced by 40 mg/100g of a freeze dried extract of lemon balm.
   iii. Human data: There are no clinical trials testing the efficacy of lemon balm as an emmenagogue or with lactating women.
10. **Immune modulation:** Anti-inflammatory

i. *In vitro data:* Rosmarinic acid has inhibitory effects on both the classical pathway convertase and the alternative pathway convertase. It inhibited 70% of the immunohemolysis of antibody-coated sheep erythrocytes by guinea pig serum via possible inhibition of the C3-convertase of the classical complement pathway. However, higher concentrations of rosmarinic acid were less effective\(^4\). Rosmarinic acid (1 mM) also inhibited C5 convertase in the classical pathway\(^4\). Rosmarinic acid impaired *in vivo* activation of mouse macrophages by heat-killed *Corynebacterium parvum*, as measured by the decreased capacity of the activated macrophages to undergo the oxidative burst\(^4\).

Chlorogenic acid and rosmarinic acid had antiallergic activities *in vitro*\(^4\).

In human polymorphonuclear leukocytes, rosmarinic acid inhibited the chemiluminescence induced by preopsonized Zymosan or phorbol myristate. Rosmarinic acid also inhibited the opsonization of *E. coli* by inhibiting complement activation. No direct effects of rosmarinic acid on the killing mechanisms of PMNL were observed\(^4\).

ii. *Animal data:* Rosmarinic acid reduced paw edema induced by cobra venom factor in the rat, and inhibited passive cutaneous anaphylaxis in rats at doses of 1-100 mg/kg p.o. Rosmarinic acid did not inhibit t-butyl hydroperoxide-induced paw edema in the rat, indicating selectivity for complement-dependent processes\(^4\). In rat ears, there was a statistically significant reduction in TPA-induced edema with pretreatment with lemon balm\(^4\).

In rhesus monkeys, three weeks of topically applied rosmarinic acid (5%) lowered gingivitis plaques compared to placebo\(^4\).

iii. *Human data:* There are no clinical trials testing the effects of lemon balm as an immunomodulator.

11. **Antimicrobial:** Antiviral, antibacterial, antifungal

a. **Antiviral:** Numerous studies have demonstrated lemon balm’s antiviral properties\(^2\), \(^4\)\(^9\)-\(^5\)\(^1\)

i. *In vitro data:* An aqueous extract of lemon balm containing polyphenolic substances, including caffeic acid and its derivatives, inhibited HSV-1 and HSV-2\(^5\)\(^2\). Aqueous extracts of lemon balm have antiviral effects against Newcastle disease virus, Semliki
forest virus, influenza virus, myxoviruses, vaccinia, and herpes simplex virus\textsuperscript{1, 26, 27, 49, 53, 54}. Lemon balm extract and rosmarinic acid have antiviral properties against HIV\textsuperscript{55-57}.

ii. \textit{Animal data:} none

iii. \textit{Human data:} In open studies, topical lemon balm extracts reduce the duration and severity of genital and oral herpes symptoms. In a multicenter open study, 115 adults with cold sores (symptoms for less than 72 hours), were given cream containing 1\% dried lemon balm extract, to apply as needed up to five times daily until the lesion resolved (maximum 14 days). Healing was completed in 60\% of the patients by the fourth day, 87\% by the sixth day, and 96\% by the eighth day\textsuperscript{58}.

In a double blind, placebo controlled trial, 116 patients received either a five-day course of topical Lomahephan\textsuperscript{®} (1\% dried lemon balm extract) or placebo. Both the physicians and patients judged the herbal cream significantly superior to placebo. There was a statistically significant difference in time to complete recovery between the two groups. No severe side effects were reported\textsuperscript{58}.

In a double-blind, placebo-controlled, randomized trial, 66 patients with a history of recurrent herpes labialis (at least four episodes per year) were treated topically on the affected area four times daily for five days with Lomahephan\textsuperscript{®}, a dried extract of \textit{Melissa officinalis} L. leaves (70:1) or placebo. The patients were instructed to start the application within four hours of prodromal symptoms. There was a significant difference in combined symptom score, favoring the lemon balm group\textsuperscript{59}.

\begin{enumerate}
\item[b.] \textbf{Antibacterial}
\begin{enumerate}
\item \textit{In vitro data:} The essential oil of lemon balm showed inhibitory activity against \textit{Listeria monocytogenes} and \textit{Mycobacterium tuberculosis}\textsuperscript{60, 61}. Alpha-citral (geranial) and beta-citral (neral) have antibacterial effects against both Gram-negative and Gram-positive organisms\textsuperscript{62}.
\item \textit{Animal data:} none
\item \textit{Human data:} There are no clinical trials testing the efficacy of lemon balm as an antibacterial in humans.
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c. **Antifungal**
   i. *In vitro data:* Lemon balm and citral demonstrate antifungal activity\(^{63-65}\). Lemon balm essential oil had antifungal activity against *Microsporum gypseum*, *Trichophyton equinum*, *T. rubrum*, *Colletotrichum* species, and *Trichoderma viridae*\(^{63}\).
   ii. *Animal data:* none
   iii. *Human data:* There are no clinical trials testing the efficacy of lemon balm as an antifungal in humans.

12. **Antineoplastic:** none

13. **Antioxidant:** Antioxidant
   i. *In vitro data:* Lemon balm and rosmarinic acid are both antioxidants *in vitro*\(^{15, 66-69}\). Lemon balm extract prevented oxidation in sunflower oil and a sunflower oil-in-water emulsion\(^{70}\). Hydroalcoholic lemon balm extract and rosmarinic acid showed significant antioxidant activities via a free radical scavenger effect\(^{19}\).
   ii. *Animal data:* none
   iii. *Human data:* There are no human studies testing the efficacy of lemon balm as an antioxidant.

14. **Skin and mucus membranes:** See **Anti-inflammatory** and **Antiviral**

15. **Other/miscellaneous:** Inhibition of protein biosynthesis. Caffeic acid from an extract of *Melissa officinalis* leaves inhibited protein biosynthesis due to a direct interaction with elongation factor EF-1 and EF-2, and the blocking of the binding reaction of EF-2 with ribosomes inhibited the incorporation of labeled amino acids into proteins\(^{71, 72}\).
Toxicity and Contraindications

All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, pharmaceuticals, etc.

This is particularly concerning with imports from developing countries.

Furthermore, allergic reactions can occur to any natural product in sensitive persons.

Allergic reactions to lemon balm: Contact dermatitis has been reported\textsuperscript{73}. Lemon balm extract had a weak sensitizing effect in guinea pigs\textsuperscript{74}.

Potentially toxic compounds in lemon balm: None known.

Acute toxicity: None reported. Lemon balm is on the FDA’s generally recognized as safe (GRAS) list. Lemon balm leaf tincture (1:5 in 70\% ethanol) had no mutagenic effects in the standard Ames test\textsuperscript{75}. Citral, a component of the essential oil of lemon balm, has been shown to elevate intraocular pressure in monkeys\textsuperscript{76}; there are no reports of this effect in humans.

Chronic toxicity: None known

Limitations during other illnesses or in patients with specific organ dysfunction: People with thyroid problems such as Graves’ disease should use lemon balm with caution because it may inhibit certain thyroid hormones\textsuperscript{39, 40, 77}

Interactions with other herbs or pharmaceuticals: There are no human studies evaluating potential interactions of lemon balm with anticoagulants or sedatives. In animal studies, lemon balm increased the hypnotic effects of barbiturates\textsuperscript{77, 78}. A combination of lemon balm and \textit{Valeriana officinalis} (valerian) root extracts did not show any additive effects with ethanol in impairing healthy volunteers' driving ability\textsuperscript{79}.

Safety during pregnancy and/or childhood: There are no clinical studies that assess the safety of lemon balm in pregnancy, lactation, or childhood.
Typical Dosages

Provision of dosage information does NOT constitute a recommendation or endorsement, but rather indicates the range of doses commonly used in herbal practice.

Doses are given for single herb use and must be adjusted when using herbs in combinations.

Typical adult dosages:

Oral use:

Dried herb: 1.5 to 4.5 g. daily\(^\text{10}\).

Infusion: 2-3 g. of dried herb, steeped in water, 2-3 times daily

Tincture (1:5 in 45% alcohol): 2-6 ml three times daily\(^\text{1}\).

Topical use:

For treatment of active viral herpes flares: Cream containing 1% of a standardized 70:1 extract, topically four times daily.

For preventative treatment of viral herpes flares: Cream containing 1% of a standardized 70:1 extract, topically twice daily.

Pediatric dosages: Infusion for insomnia or functional gastrointestinal disorders: 1 tablespoon cut up lemon balm leaf steeped in 150 ml of boiling water and infused for 10 minutes, cooled and strained\(^\text{6}\). Or 1.5-4.5 grams (2-3 tsp) herb per cup of tea several times daily.

Availability of standardized preparations: Lomaherpan\(^\text{®}\), is a topical lemon balm extract sold in Europe that is standardized by bioassay. Herpilyn\(^\text{®}\), a topical preparation with equivalent standardization to the European products, is sold in the US.

Dosages used in herbal combinations: Variable

See Also:

Lemon Balm Clinician Information Summary:
http://www.mcp.edu/herbal/lemonbalm/lemonbalm.cis.pdf

Lemon Balm Patient Fact Sheet: http://www.mcp.edu/herbal/lemonbalm/lemonbalm.ph.pdf
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