Lavender (Lavandula angustifolia Miller)

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Lavender (*Lavandula angustifolia* Miller)

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ABSTRACT. An evidence-based systematic review including scientific evidence, expert opinion, folkloric precedent, history, pharmacology, kinetics/dynamics, interactions, adverse effects, toxicology, and dosing. [Article copies available for a fee from The Haworth Document Delivery Service: 1-800-HAWORTH. E-mail address: <docdelivery@haworthpress.com> Website: <http://www.HaworthPress.com>]

KEYWORDS. Lavender, Lavandula angustifolia Miller, limonene, perillyl alcohol, POH

SYNONYMS/COMMON NAMES/RELATED SUBSTANCES


CLINICAL BOTTOM LINE/EFFECTIVENESS

Brief Background

Lavender is native to the Mediterranean, the Arabian Peninsula, Russia, and Africa. It has been used cosmetically and medicinally throughout history. In modern times, lavender is cultivated around the world and the fragrant oils of its flowers are used in aromatherapy, baked goods, candles, cosmetics, detergents, jellies, massage oils, perfumes, powders, shampoo, soaps, and tea. English lavender (L. angustifolia) is the most common species of lavender used, although other species are in use, including Lavandula burnamii, L. dentate, L. dhofarensis, L. latifolia, and L. stoechas.
Many people find lavender aromatherapy to be relaxing, and it has been reported to have anxiolytic effects in several small, methodologically flawed trials. Overall, the weight of the evidence suggests a small positive effect, although additional data from well-designed studies are required before the evidence can be considered strong.

Lavender aromatherapy is also used as a hypnotic, although there is insufficient evidence in support of this use.

Small phase I human trials of the lavender constituent perillyl alcohol (POH) for cancer have suggested safety and tolerability (up to 1200 mg/m² four times/day), although efficacy has not been demonstrated.

**Scientific Evidence for Common/Studied Uses**

<table>
<thead>
<tr>
<th>Indication</th>
<th>Evidence Grade</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety (aromatherapy)</td>
<td>B</td>
</tr>
<tr>
<td>Hypnotic/Sleep (aromatherapy)</td>
<td>C</td>
</tr>
<tr>
<td>Perineal discomfort following childbirth (bathing)</td>
<td>C</td>
</tr>
<tr>
<td>Spasmolytic (oral)</td>
<td>C</td>
</tr>
<tr>
<td>Antibiotic (topical)</td>
<td>C</td>
</tr>
<tr>
<td>Cancer (oral perillyl alcohol [POH])</td>
<td>C</td>
</tr>
</tbody>
</table>

**Historical or Theoretical Uses that Lack Sufficient Evidence**

Acne, alopecia, analgesia, angioprotectant, anticolic, anticonvulsant, antidepressant, antiflatulant, antifungal, anti-inflammatory,¹ antimicrobial,² antioxidant,³ antipyretic, antiseptic, anxiety, appetite stimulant, asthma, balenotherapy (functional circulatory disorders), chalagogue, choleretic, chronic bronchitis, ciatrizing, cordial, diabetes,⁴ diuretic, douche, emmenagogue, exercise recovery, gas, hangovers, hyptension, infertility, insect repellent, insomnia,⁵ lice, migraine, non-tubercular mycobacteria (NTM),⁶ parasitic infection, psychosis, rheumatism, Roehmheld’s syndrome, rubefacient, toothache, varicose veins, vomiting.

**Expert Opinion and Historic Precedent**

Lavender is rich in volatile oils and has been used for centuries both as a fragrance and medicinal herb. Linen bags containing lavender flowers were commonly placed under pillows for their alleged soporific properties.

Lavender is thought by some experts to possess antibacterial properties. Currently, lavender oil is often used as an aromatherapeutic anxio-
lytic and hypnotic, including in the hospital setting. Infusions of lavender flowers have been used for similar indications.

**Brief Safety Summary**

*Likely Safe:* When consumed in amounts commonly found in foods and beverages (received Generally Recognized as Safe [GRAS] status for food use in the United States), or when used in recommended oral/topical doses.

*Possibly Unsafe:* When used concomitantly with central nervous system depressants, due to potential additive effects.

**DOSING TOXICOLOGY**

**General**

Recommended doses are based on those most commonly used in available trials, or on historical practice. These doses have not necessarily been shown effective. Anecdotal dosing regimens are based on traditional health practice patterns and/or expert opinion. With natural products it is often not clear what the optimal doses are to balance efficacy and safety. Preparation of products may vary from manufacturer to manufacturer, and from batch to batch within one manufacturer. Because it is often not clear what are the active components of a product, standardization may not be possible, and the clinical effects of different brands may not be comparable.

**Standardization**

- Lavender products are not standardized in the United States.
- Each species of lavender has unique chemical constituents and activity.
- The flowers are the part of lavender most often used medicinally.

**Adult Dosing (18 Years and Older)**

**Oral**

*Tea:* One to two teaspoons of the herb taken as a tea (based on anecdote and expert opinion). The tea can be made by steeping 2 U.S. teaspoons (10 grams) of leaves in 250 mL (1 cup) boiling water for 15 minutes.
Oral Perillyl Alcohol (POH): In preliminary (phase I) cancer trials, doses between 800-1200 mg/m² four times/day in a 50:50 POH:soybean oil preparation were tolerated with minimal adverse effects (efficacy has not been demonstrated).11,12

Inhalation (Aromatherapy)

Aromatherapy: Two to four drops in 2-3 cups boiling water; inhale vapors. Aromatherapy can be administered intermittently or daily as needed (based on anecdote and expert opinion).

Topical/Infusion

Bath Additive: For perianal discomfort after childbirth, 6 drops of lavender oil has been studied as a bath additive (no specific brand).13 Those wishing to use the whole flower may add 1/4 to 1/2 cup of dried lavender flowers to hot bath water (based on anecdote and expert opinion).

Massage Therapy: One to four drops per tablespoon of base oil (based on anecdote and expert opinion).

Pediatric Dosing (Younger Than 18 Years)

Insufficient data available.

Toxicology

There have been rare reports of sensitization after topical use of lavender.14,15

Lavender has been reported to exert ‘narcotic-like’ effects in both animals8,9 and humans.5

PRECAUTIONS/CONTRAINDICATIONS

Allergy

Caution should be exercised in patients with known allergy/hypersensitivity to lavender. Persons with allergy to lavender may experience mild local skin reactions after topical use of lavender oil.14,16

Adverse Effects

General: In recommended doses, lavender is generally considered to be well-tolerated, with minimal adverse effects.7,13,17
Dermatologic: There have been case reports of mild dermatitis following the use of topical lavender oil.\(^{18}\) One individual developed an itchy dermatitis on his face after using lavender oil on his pillow.\(^{16}\) Patch testing subsequently confirmed a positive allergy to lavender. There have been reports of photosensitization and changes in skin pigmentation after the use of topical products containing lavender oil.\(^{19,14}\)

Neurologic/CNS: Central nervous system depression has rarely been reported with aromatherapy,\(^{5,11}\) and additive narcotic effects have been noted in rats when taken orally concomitantly with barbiturates or chloral hydrate.\(^{9,20}\)

Hematologic: Reversible neutropenia has been noted after high oral doses of perillyl alcohol (POH), a monoterpenic constituent of lavender, in patients with untreatable malignancies (on multiple chemotherapy regimens).\(^{11}\)

Gastrointestinal: Nausea, vomiting and anorexia have been reported after large oral doses of lavender (>5.0 g/day),\(^{21,22}\) and after large doses of the lavender constituent perillyl alcohol (POH).\(^{12}\)

Precautions/Warnings/Contraindications

Avoid in patients with a known allergy/hypersensitivity to lavender, based on several case reports of dermatitis in patients with lavender allergy.\(^{16,19}\)

Use cautiously in patients who are currently taking drugs that depress the central nervous system, because concomitant use of lavender may exacerbate sedation.\(^{5,9,10}\)

Pregnancy and Lactation

Not recommended due to lack of sufficient data.

Due to its purported properties as an emmenagogue, excessive internal use should be avoided during pregnancy. However, there is no definitive evidence in this area.

INTERACTIONS

Lavender/Drug Interactions

Sedating Drugs: In rats, concomitant use of lavender and pentobarbital or chloral hydrate has significantly increased sleeping time and narcotic ef-
Concurrent use with other sedative or hypnotic agents theoretically may act in an additive or synergistic fashion.

Anticoagulants, NSAIDs, Anti-Platelet Agents: Lavender contains varying amounts of coumarins and may therefore theoretically increase the effect of anticoagulant medications.

Anti-Seizure Medications: Lavender enhances GABA effects and may therefore intensify the sedative effects of GABA-dependent antiepileptics.

HMG-CoA Reductase Inhibitors, Niacin, Cholesterol Lowering Agents; Theoretical Positive Interaction: Lavender may act in an additive fashion with cholesterol-lowering agents: Cineole, a cyclic monoterpene found in lavender, lowers cholesterol in rats via inhibition of the HMG-CoA enzyme; the lavender constituent perillyl alcohol (POH) has been shown to inhibit the conversion of lanosterol to cholesterol.23,24

Lavender/Herb/Supplement Interactions

Sedating Agents: Lavender has been found to have sedative effects in animal models, and acts additively with sedatives including pentobarbital and chloral hydrate.9,20 In theory, it may intensify the effects of other sedative agents such as kava or valerian root.

Anticoagulant Herbs/Supplements: Lavender contains varying amounts of coumarins and may therefore theoretically increase the effect of anticoagulant medications.

Lavender/Food Interactions

Insufficient available evidence.

Lavender/Lab Interactions

Low Density Lipoprotein (LDL), Total Cholesterol, High Density Lipoprotein (HDL): Based on animal studies, oral lavender may act similarly to HMG-CoA reductase inhibitors and lower total cholesterol/LDL while raising HDL.23,24

MECHANISM OF ACTION

Pharmacology

Lavender is comprised of over 100 constituents, including linalool, perillyl alcohol, linalyl acetate, camphor, limonene, tannins, triterpenes, coumarins, cineole, and flavonoids.

Linalool has been shown to reduce motor activity in mice due to a
dose-related binding to glutamate, a primary excitatory neurotransmitter of the central nervous system, and it has been suggested that hypnotic and anticonvulsant effects of lavender may be due to the potentiation of the neurotransmitter GABA.\textsuperscript{25}

The mechanism of lavender’s spasmolytic activity has not been fully elucidated. Gamez et al. studied the antispasmodic effect of \textit{L. dentate} (a lavender species) \textit{in vitro}.\textsuperscript{26} An observed antagonism of acetylcholine-induced muscle contractions was attributed largely to cineole. Lis-Balchin et al. observed that the linalool and linalyl acetate in \textit{L. angustifolia} oil can induce cAMP-mediated relaxation of guinea pig ileum smooth muscle.\textsuperscript{27} The authors postulated a cAMP-based mechanism for lavender’s purported physiological effects on sympathetic nervous system activity.

Components of lavender appear to have cytotoxic properties. Fulton et al. demonstrated cell proliferating effects of perillyl alcohol (POH) on smooth muscle cell cultures.\textsuperscript{28} Both limonene and POH have been shown to inhibit tumor growth in rats by blocking initiation and by promoting apoptosis.\textsuperscript{29,30,31} One \textit{in vitro} study evaluated the effects of POH in lung carcinogenesis, and described an inhibitory effect on farnesylation, a step towards activation of the oncogene K-ras.\textsuperscript{32}

The lipid-lowering effect of lavender has been attributed to the constituent cineole, a cyclic monoterpene which lowers cholesterol in rats via inhibition of the HMG-CoA enzyme.\textsuperscript{23} The lavender constituent perillyl alcohol (POH) has been shown to inhibit the conversion of lathesterol to cholesterol.\textsuperscript{24}

Caffeic acid, a constituent of lavender, has been demonstrated to possess antioxidant effects \textit{in vitro}.\textsuperscript{33}

\textbf{Pharmacodynamics/Kinetics}

\textit{Topical}: Lavender oil is quickly absorbed by the skin. The constituents linalool and linalyl acetate are detectable in the blood five minutes after topical application, peak at 19 minutes, and largely disappear from the blood within 90 minutes.\textsuperscript{34}

\textit{Oral}: The constituents limonene and perillyl alcohol (POH) are metabolized into perillic acid (PA) and dihydroperillic acid (DHPA). In rats fed a diet containing POH or limonene, peak levels of PA can be seen at 1-2.5 hours, peak levels of DHPA are noted at 2-3.5 hours, and half-lives for each metabolite are 1-2 hours.\textsuperscript{30} POH, PA, and DHPA are detectable in subjects’ urine following high doses of POH ingestion. Approximately 9% of the total dose can be recovered in the first 24 hours. PA is the major metabolite found, with <1% of recovered POH.
The absorption of POH does not appear to be affected by concomitant ingestion of foods.\textsuperscript{11,12}

**HISTORY**

The name lavender is derived from the Latin *lavare*, meaning to wash. In ancient Greece, Persia and Rome, it was used as a perfume in baths and laundry, and as an antiseptic. Ancient Egyptians created mummification casts by soaking linen in oil of lavender containing asphalt, then wrapping the bodies with these and drying them in the sun until the casts were hard. Lavender has been renowned as a ‘healing agent’ in India and Tibet. In Tibetan Buddhist medicine, lavender is still used to treat insanity and psychoses. Today, in Europe and the Americas, lavender is often used as an anxiolytic and sleep aid.

**EVIDENCE TABLE**

<table>
<thead>
<tr>
<th>Condition</th>
<th>Study Design</th>
<th>Author, Year</th>
<th>N</th>
<th>Statistically Significant?</th>
<th>Quality of Study</th>
<th>Magnitude of Benefit</th>
<th>ARR</th>
<th>NNT</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety</td>
<td>Not randomized, controlled</td>
<td>Saeki, 2000</td>
<td>10</td>
<td>Yes</td>
<td>1</td>
<td>Small</td>
<td>NA</td>
<td>NA</td>
<td>Poor description of methodology, unclear blinding or randomization.</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Randomized, controlled</td>
<td>Dunn, 1995</td>
<td>12</td>
<td>2</td>
<td>Yes</td>
<td>Small</td>
<td>NA</td>
<td>NA</td>
<td>Initial benefit dissipated after first session.</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Not randomized, controlled</td>
<td>Motomura, 1998</td>
<td>42</td>
<td>Yes</td>
<td>0</td>
<td>Large</td>
<td>NA</td>
<td>NA</td>
<td>Small study, results unclear due to lack of randomization.</td>
</tr>
<tr>
<td>Anxiety</td>
<td>Case series</td>
<td>Itai, 2000</td>
<td>14</td>
<td>Yes</td>
<td>NA</td>
<td>Large</td>
<td>NA</td>
<td>NA</td>
<td>No significant difference compared to odorless smell.</td>
</tr>
<tr>
<td>Hypnotic</td>
<td>Case series</td>
<td>Hardy, 1995</td>
<td>4</td>
<td>NA</td>
<td>NA</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>Small series using aromatherapy.</td>
</tr>
<tr>
<td>Perineal relief following childbirth</td>
<td>Double-blind, randomized, controlled</td>
<td>Dale, 1994</td>
<td>63</td>
<td>No</td>
<td>3</td>
<td>None</td>
<td>NA</td>
<td>NA</td>
<td>Subjective outcome measure, incomplete data, no difference found.</td>
</tr>
<tr>
<td>Tumor regression (phase I clinical trial)</td>
<td>Case series</td>
<td>Ripple, 1998</td>
<td>18</td>
<td>NA</td>
<td>1</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>Uncontrolled trial using perillyl alcohol (POH).</td>
</tr>
</tbody>
</table>
EVIDENCE DISCUSSION

Anxiety (Aromatherapy)

Summary: In general, the evidence supporting lavender aromatherapy as an anxiolytic is weak. There are conflicting results from methodologically flawed studies, with some showing lack of effect. However, overall, the weight of the evidence suggests a small positive effect in relieving anxiety. Further study through well-designed randomized trials would strengthen this case. However, there are inherent difficulties involved with designing blinding or placebo control for study of an olfactory therapy. These difficulties must be overcome before compelling results can be generated.

Evidence: Saeki et al. attempted to demonstrate that lavender aromatherapy via footbath produced anxiolytic effects compared to placebo. This “before and after” study, which consisted of 10 subjects, concluded that a hot footbath with lavender oil is associated with small but significant changes in autonomic activity. However, the incomplete description of methodology and analysis make results difficult to interpret.

Dunn et al. conducted a randomized, single-blind study in 122 intensive care unit patients, allocated to one of three groups: body massage with grapeseed oil, body massage with lavender oil, or undisturbed rest. Psychological endpoints were assessed using an arbitrary 4-point scale, and physiological endpoints included blood pressure, heart rate, and breaths-per-minute. Treatment ranged from one to three 30-minute sessions, 24 hours apart. All patients received at least one session; 66 patients completed three sessions. After the first session, patients who had received a massage with lavender oil had significantly less anxiety than the group who rested. This difference was not maintained in the following sessions. It is not clear to what extent the lack of double-blinding, or the high dropout rate, affected results.

Motomura et al. conducted an experiment in which 42 students were divided into three groups: Group 1 experienced a “stressful condition;” group 2 experienced a “stressful condition” with the addition of lavender odor; group 3 experienced a “non-stressful condition.” Stress was evaluated based on a Japanese version of Cox and Mackay’s stress/arousal adjective checklist. The experiment found that scores in the lavender group were significantly lower than the group who was stressed and did not receive lavender therapy. However, blinding and randomization were not clearly described.

In a case series consisting of 14 female, chronic renal failure patients on hemodialysis, Itai et al. evaluated the effect of lavender oil on mood...
using the Hamilton rating scale for depression (HAMD) and the Hamilton rating scale for Anxiety (HAMA). \(^3\) Compared to natural smell (baseline), lavender was observed to decrease anxiety as evidenced by the HAMA scale (\(P = 0.05\)). Lavender did not significantly alter patients’ HAMD scores from baseline. When lavender was compared to odorless conditions, the difference in HAMA and HAMD scores was minimal.

Buckle compared therapeutic benefits of oils from two different species of lavender (\(L.\) angustifolia and \(L.\) burnatti) applied by massage to 28 hospitalized patients.\(^3\) A semi-structured interview to collect qualitative, subjective data was used several days after treatment. The study reported that \(L.\) burnatti had significantly more relaxing effects than its counterpart. However, further details of statistical analysis or methodology were incomplete, thus raising question about the results.

**Hypnotic/Sleep (Aromatherapy)**

**Summary:** Many experts and patients believe that lavender aromatherapy is an effective hypnotic. Although preliminary evidence suggests some hypnotic effects of lavender, there are no randomized trials in the available literature. Without further study, the current evidence can only be considered equivocal. However, there are inherent difficulties involved with designing blinding or placebo control for study of an olfactory therapy. These difficulties must be overcome before compelling results can be generated.

**Evidence:** Hardy et al. evaluated aromatherapeutic lavender as an alternative to conventional hypnotics in four geriatric patients.\(^5\) Sleep hours were monitored during three two-week phases. During phase I, subjects continued their current hypnotic (temazepam, promazine, chloromethiazole). Phase II involved a withdrawal and washout period. During phase III, lavender oil was introduced into the patients’ sleeping quarters via an odor diffuser. The results demonstrated that hours asleep were comparable to the number of hours asleep during phase I of the trial for all four participants. However, without controls or blinding, results can only be considered preliminary.

Diego et al. demonstrated the effects of three-minute aromatherapy sessions using a 10% lavender oil concentration on participants’ brain waves via electroencephalogram (EEG).\(^3\) The EEG reading was recorded prior, during, and after sessions. Alpha and beta activity were found to increase after the inhalation of lavender. Notably, increased frontal alpha and beta activity have been associated with increased drowsiness, which provides mechanistic supportive evidence for this purported indication.
Perineal Discomfort Following Childbirth (Baths)

**Summary:** There is insufficient scientific evidence regarding the use of lavender oil baths for the relief of postpartum perineal discomfort.

**Evidence:** Dale and Cornwell examined the effect of lavender oils baths on perineal discomfort in 635 postpartum women in a randomized trial. Subjects were divided into three groups: Group 1 added a natural lavender oil extract to baths, group 2 added a synthetic lavender oil to baths, and the third group used an unspecified control substance that had U.S. “Generally Recognized As Safe” status. The control was reported to be distinguishable from the other two oils by smell, and in efforts to compensate for this, patients were informed that the trial was testing “different bath additives.” To evaluate discomfort, women were asked to complete visual analogue scales (VAS), a subjective questionnaire used to evaluate the degree of discomfort over the 10 days of the experiment. Data were obtained from ~60% (n = 386) of participants. Although this trial found no significant differences in perineal relief between the groups, the large dropout rate and lack of information about the control substance (which could have been active) raise doubts about the validity of results.

Spasmolytic (Oral)

**Summary:** Preliminary data from animal and in vitro studies indicate a potential spasmolytic effect of lavender oil inhalation. However, human evidence is lacking.

**Animal Data:** A variety of lavender species have demonstrated an ability to inhibit stimulated muscle contractions in the ileum and conjunctiva of animal models.

Antibiotic (Topical)

**Summary:** Preliminary data from in vitro studies suggest that lavender oils possess antibiotic activity. However, this has not been tested in animal or human studies, and results cannot be considered clinically relevant.

**In Vitro Data:** Gabbrigieli et al. demonstrated in vitro activity of lavender oil (L. angustifolia and L. latifolia) against various strains of non-tubercular Mycobacterium. Nelson et al. found documented activity of 2% to 0.12% (v/v) lavender oils against both methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococci (VRE).
Cancer (Oral)

Summary: Preliminary data from animal studies suggest an antineoplastic effect of oral perillyl alcohol (POH) and other monoterpenes found in lavender. Studies have focused on cancers of the pancreas, breast, and intestine. Small phase I studies have been conducted in humans, suggesting safety and tolerability of POH (up to 1200 mg/m² four times/day), but efficacy has not been established.

Animal Data: Elegbede et al. and Haag et al. demonstrated regression of primary mammary tumors in rats after supplementing diets with limonene and POH (lavender constituents).²⁹,³⁰ Burke et al. documented inhibition of pancreatic adenocarcinoma growth in hamsters using a similar diet.⁴² Reddy et al. found a significant chemoprotective effect of oral POH on carcinogenesis of the large and small intestines in rats.⁴³

Human Evidence: In a phase I clinical trial, Ripple et al. examined the potential of POH to suppress tumor growth in humans.¹¹ This study consisted of 18 patients with advanced malignancies of various origins, refractory to standard therapies. POH was formulated in gelatin capsules containing 250 mg of POH and 250 mg of soybean oil. Prior to receiving POH, as a washout, patients did not receive hormonal or immunological therapy for two weeks, or chemotherapy/radiation for four weeks. Patients were divided into three groups: 800 mg/m²/dose; 1600 mg/m²/dose; or 2400 mg/m²/dose, three times/day. Although no objective tumor responses were noted, disease stabilization was noted in several patients for up to six months. POH was generally well tolerated, although dose-dependent gastrointestinal side effects (nausea, early satiety) and fatigue led to withdrawal of one patient from the study.

In a second case series, the same authors examined the effects of more frequent administration at slightly lower doses.¹² Nineteen patients with various malignancies, refractory to standard treatment, were treated at the following doses: 800 mg/m²/dose; 1200 mg/m²/dose; or 1600 mg/m²/dose, four times/day. The maximum tolerated dose of POH given continuously four times/day was 1200 mg/m²/dose. Patterns of disease progression similar to the initial trial were observed at all doses. Although promising, these results must be further evaluated through controlled studies before a recommendation can be made. Nonetheless, these small studies suggest safety and tolerability of POH at doses up to 1200 mg/m² four times/day.
REFERENCES


