The Longwood Herbal Task Force (http://www.mcp.edu/herbal/) and The Center for Holistic Pediatric Education and Research (http://www.childrenshospital.org/holistic/) Lavender (Lavandula spp.)

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Principal Proposed Uses: Sedative and anxiolytic; antimicrobial

Other Proposed Uses: Analgesic, anticonvulsant, and antidepressant; cholagogue, antispasmodic and digestive aid; antioxidant; anti-inflammatory; cancer chemopreventative; insecticide; aphrodisiac

Overview

Lavender's essential oil is commonly used in aromatherapy and massage. Its major clinical benefits are on the central nervous system. Many studies conducted on both animals and humans support its use as a sedative, anxiolytic and mood modulator. Lavender oil has *in vitro* antimicrobial activity against bacteria, fungi and some insects. Lavender's essential oil exerts spasmolytic activity in smooth muscle *in vivo*, supporting its historical use as a digestive aid. Particular chemical constituents of lavender have potent anticarcinogenic and analgesic properties; its antioxidant effects are less potent than those of other members of its botanical family such as rosemary and sage. Allergic reactions to lavender have been reported. Because of its potent effects on the central nervous system, people with seizure disorders and those using sedative medications should consult a physician before using lavender. Although lavender has traditionally been used to treat symptoms ranging from restlessness to colic in infants and children, systematic studies have not been conducted to test the efficacy and safety of lavender use in infants and children or during pregnancy or lactation.

Historical and Popular Uses

Perhaps best known for its popular use in the fragrance industry, lavender also has a long history of medicinal use. Many varieties of lavender are cultivated around the world. At least five different species are used medicinally, and each species is believed to have different medicinal properties. Today there is a rekindled interest in lavender for aromatherapy.

The name *lavender* is derived from the Latin "lavare", which means to wash. The fragrant flowers were used in ancient Rome and North Africa to scent public baths and were carried by the Roman army for use as a disinfectant¹. "Lavenders" in Medieval and Renaissance times were used for the storage of laundry. The Ancient Egyptians are said to have used the flower in the mummification process².

In Traditional Chinese Medicine (TCM), lavender is used to treat several conditions including infertility, infection, anxiety, and fever³, ⁴. It has long been used in Arabic medicine to treat stomachaches and kidney problems⁵. Lavender was commonly used as an aphrodisiac in Victorian times⁶. Various folk traditions have used the herb for a variety of other medicinal purposes ranging from giddiness² to hair loss⁷. Preparations from the plant have been used to increase bile flow⁸, treat varicose ulcers⁹, and relieve carpal tunnel syndrome². It has been considered an antidepressant¹⁰; an antispasmodic¹¹, antiflatulent¹², and antiemetic¹⁰; a diuretic¹³; and a general tonic². One variety of lavender has been recommended as a worm remedy and as a topical remedy for insect bites¹, ⁵.

Lavender is commonly used today in perfumes, soaps, bath and talc powders, candles and scented sachets. Small amounts are sometimes used to flavor teas and foods, such as in the French *herbs de Provence*⁶.

The flower's strong and pleasant fragrance has led to its popular use in aromatherapy, where it is considered one of the most versatile and useful essential oils¹⁴. Aromatherapy with lavender oil has been recommended to treat a wide range of ailments including stress, anxiety, depression, fatigue, motion sickness, and hypertension¹³⁻¹⁶. Often administered with massage in Europe, the oil is used to aid in relaxation, treat colic and stimulate the appetite². Massage with a combination of lavender and peppermint essential oils has been recommended to relieve tension headaches¹⁷.

The German Commission E has approved *L. angustifolia* tea to treat restlessness, insomnia and nervous disorders of the intestines.

Botany

- Medicinal species: The genus Lavandula contains at least 28 different species¹. Among the more common species believed to have medicinal value are Lavandula dentata (French lavender), L. angustifolia or officianalis or vera (garden, English, pink, white, or true lavender), L. latifolia or spica (spike, narrow leafed, spikenard, or elf leaf lavender), L. intermedia or hybrida reverchon or hybrida burnamii (lavandin, a hybrid of L. angustifolia and L. latifolia), L. stoechas (Spanish, Italian, or fringed lavender), and L. dhofarensis (Arabic lavender).
- *Common names* are listed above next to each species. There is some confusion in the literature about common names. *L. spica* is sometimes referred to as French lavender, although this is primarily a common name for *L. dentata*. Lavandin oil, made from a hybrid of *L. angustifoli* and *L. latifolia*, is sometimes referred to as true lavender. Because of the inconsistencies, we recommend using the Latin name when referring to a particular species.
 Botanical family: Labiatae (Lamiaceae), the large mint family.
- *Plant description*: The lavenders are evergreen, shrubby plants. They vary from one to three feet high and show a range of leaf and flower shapes. The leaves can be lobed or unlobed and are sometimes present only at the base of the stems. The color of the flowers can range from blue to violet, and the stem and leaves can range from deep bluish grey to green to discolored brown.

The hardy lavenders (*L. angustifolia, L. latifolia, L. intermedia*) do not grow as tall as the tender lavenders (*L. dentata, L. stoechas*) and flower only once a year. They are mostly shrubby plants with narrow, gray leaves that vary in size on different parts of the plants. Some flower spikes are tapered and others are blunt.

The tender lavenders (*L. stoechas*, *L. dentata*) are tall and have showy bracts at the tops of their flower heads. These plants prefer full sun and rich soil; in the right conditions they can grow three feet tall. The weaker, arching stems tend to be more green than grey. *Where it's grown*: Most lavender species are indigenous to the mountain regions of the countries bordering the western Mediterranean, the islands of the Atlantic, Turkey, Pakistan and

India. Native lavender species have also been found in northern and southern Africa,

Micronesia, the Arabian Peninsula, Bulgaria, and Russia¹⁸. Now the plants are extensively cultivated all over the world, particularly in France, Bulgaria, Russia, Italy, Spain, England, the United States, and Australia¹, 9, 19, 20

Biochemistry

The chemical composition of lavender's essential oil depends largely on the species from which it was obtained^{18, 21}. Below, we discuss the potentially active chemical compounds found in four major medicinal species of lavender: *L. dentata, L. angustifolia, L. latifolia,* and *L. hybrida*. The species *L. stoechas*, though also medicinally active, will not be included in this discussion because the chemical composition of this plant is quite different from the traditional varieties²². Within the same species, the biochemical contents of the essential oil found in the flower, stem, or leaves differ significantly depending on where and under what conditions the plant was grown²³⁻²⁶. The presence and concentration of certain chemical constituents also fluctuates according to the season²⁷ and the maturation of the plant²⁸ when harvested. Even the extraction process used to collect the oil introduces variation in the concentrations of biochemical compounds present in the distillate. Steam distilled extracts have a characteristically higher ratio of alpha-terpineol and linalool to linalyl acetate compared to supercritical fluid extracts^{29, 30}. Burning lavender oil does not affect its composition, implying that inhaling smoke from lavender aromatherapy candles may have the same impact as inhaling the vapor of the unheated essential oil³¹.

Lavender: Potentially Active Chemical Constituents

- Monoterpenes: alpha-pinene, beta-pinene, beta-ocimene, camphene, camphor, limonene, pcymene, sabinene, terpinene
- Monoterpene alcohols: alpha-terpineol, borneol, lavandulol, linalool, p-cymen-8-ol, transpivocarveol
- Monoterpene aldehydes: cumin aldehyde
- Monoterpene ethers: 1,8-cineole (eucalyptol)
- Monoterpene esters: linalyl acetate, terpenyl acetate
- Monoterpene ketones: carvone, coumarin, cryptone, fenchone, methylheptenone, n-octanone, nopinone, p-methylacetophenone
- Benzenoids: eugenol, coumarin, cavacrol, hydroxycinnamic acid, rosmarinic acid, thymol
- Sesquiterpenes: caryophyllene, caryophyllene oxide, alpha-photosantanol, alphanorsantalenone, alpha-santalal
- Trace components of many other compounds, such as flavonoids, have been identified²⁸, 32-42.

The biological actions of many of the chemical compounds found in lavender are not well understood. Up to 350 chemical constituents have been detected in the complex essential oil of *L. latifolia Vill*.^{34, 43}. Over 150 compounds have been isolated from the oil of *L. dentata*³⁶; *L. angustifolia* contains at least 38 different compounds, and *L. hybrida* contains at least 50 compounds^{30, 44}. Although the chemical compositions of these oils are complex, the biological activities of some of the major chemical species present have been evaluated.

Linalyl acetate and *linalool* have sedative^{45, 46} and local anesthetic effects⁴⁷; linalool also has antibacterial^{37, 48, 49}, antifungal^{49, 50}, and insecticidal⁵¹⁻⁵⁵ effects. These two compounds are the most prominent chemical constituents in the essential oil of *L. angustifolia*, accounting for up to 90% of the oil by volume^{35, 56}. They also comprise over 70% of the essential oil of *L. hybrida*, a species commonly used by the perfume and pharmaceutical industries^{40, 57, 58}. Relative concentrations of linalyl acetate and linalool are lower in *L. latifolia*⁹, and their concentrations range from five to seventy-five percent in *L. dentata*^{33, 36, 59}.

Following topical application of the essential oil of *L. angustifolia*, linalyl acetate and linalool can be detected in the blood within five minutes, peak at 19 minutes, and are cleared within 90 minutes^{56, 60}. They can also be detected in the blood following inhalation of lavender oil^{46, 61} and in exhaled air following massage⁶².

Lavender oils are often adulterated with synthetic linalool and linalyl acetate, in which case the impurities dehydrolinalool and dihydrolinalool are also present and can be detected³⁶.

Cineole has antispasmodic³³ and antifungal^{49, 50} properties. It comprises over 50% of the essential oil of *L. dentata*^{36, 63}. Cineole has also been detected in *L. angustifolia*, *L. latifolia* and *L. hybrida*, although in much lower concentrations^{34, 35, 58}.

Eugenol also has spasmolytic activity⁶⁴, as well as local anesthetic effects^{47, 64, 65}. The antibacterial properties of *L* angustifolia have also been partially attributed to the actions of eugenol (which is also found in *L*. *latifolia*^{34, 66}) and *rosmarinic* $acid^{38}$ (which has also been detected in *L*. *hybrida*⁶⁷).

Other constituents of lavender with antibacterial effects include *alpha-terpineol* and *terpenen-4-ol* (found in *L. dentate, L. latifolia* and *L. hybrida*^{28, 34, 63}), and *camphor* (present in each, but found in high concentrations in *L. latifolia* compared to the other varieties³⁴) ^{37, 48, 68}. *Rosmarinic acid*, present in *L. angustifolia* and *L. hybrida*, also has antibacterial properties.

Alpha-pinene, *1*,8-*cineole*, *beta-pinene* and *p*-*cymene* have some antifungal activity⁵⁰, 69. *Terpineol*, *alpha-pinene* and *camphene* have anti-lice activity⁵¹.

Rosmarinic acid, hydroxycinnamic acid, 1,8-cineole, and *beta-pinene* may contribute antioxidant activity to *L. angustifolia*³⁹, 67, 70.

Perillyl alcohol, a metabolite of *limonene* found in *L. latifolia* ³⁴ and *L. hybrida*^{28, 40}, and in lower concentrations in *L. angustifolia*⁷¹ as well as in cherries and mint, exerts chemoprotective effects against tumorigenesis *in vitro*⁷². Perillyl alcohol is currently in Phase I clinical trials against breast cancer.

Coumarin (found in *L. angustifolia*, *L. latifolia* and *L. dentata*^{35, 36, 73}) and *caryophyllene oxide* (found in *L. latifolia* and *L. angustifolia*^{35, 36}) have anti-inflammatory effects⁷⁴.

Experimental Studies

Lavender: Potential Clinical Benefits
1. Cardiovascular: <u>Angioprotectant</u>
2. Pulmonary: Expectorant
3. Renal and electrolyte balance: No data
4. Gastrointestinal/hepatic: Effects on hepatic metabolism, cholagogue, antispasmodic/digestive
aid
5. Neuro-psychiatric: Sedative/hypnotic, anxiolytic, anticonvulsant, effects on mood, effects on
cognitive function, analgesic
6. Endocrine: <u>Hypoglycemic effects</u>
7. Hematologic: No data
8. Rheumatologic: Analgesic for arthritis pain
9. Reproductive: Emmenagogue, aphrodisiac, perineal repair
10. Immune modulation: Anti-inflammatory
11. Antimicrobial: Antibacterial, antifungal, insecticide
12. Antineoplastic: Chemoprophylaxis
13. Antioxidant: <u>Antioxidant</u>
14. Skin and mucus membranes: No data
15. Other/miscellaneous: Hair growth stimulant

1. Cardiovascular: Angioprotectant

- i. In vitro data: none
- ii. Animal data: A Russian study on rabbits reported that inhalation of lavender oil reduced aortic cholesterol content and atherosclerotic plaques but did not affect serum cholesterol levels⁷⁵.
- iii. Human data: In a randomized controlled clinical trial on 20 healthy men who performed moderate physical exercise for two minutes, lavender aromatherapy had a tendency to decrease mean diastolic blood pressure, but there were no statistically significant effects on any measure of cardiovascular function⁷⁶. Lavender is not traditionally used for any

cardiovascular conditions and there are no studies evaluating its effect on patients with cardiovascular problems.

2. Pulmonary: Expectorant

- i. In vitro data: none
- ii. Animal data: none
- iii. Human data: In a case series, 40 adults presenting with nasal or sinus congestion inhaled the essential oil of *L. latifolia*. The subjects reported a subjective sense of sinus clearance or expectoration of mucus from the bronchi or lungs which lasted from 20 minutes to two hours. All the patients reported feeling better after the treatment⁷⁷.

3. Renal and electrolyte imbalance: none

4. Gastrointestinal/hepatic: Effects on hepatic metabolism, cholagogue, antispasmodic/digestive aid

- a. Effects on hepatic metabolism
 - i. In vitro data: none
 - ii. Animal data: An Eastern European study on rats reported that inhalation of the essential oil of lavender may be able to restore normal activity of oxidative enzymes involved in normal metabolism⁷⁸.

In rats, prolonged intragastric administration of linalool had a biphasic effect on cytochrome p450 activity. Levels of cytochrome p450 were significantly depressed on day seven, but significantly increased by day 30, compared to controls. Alcohol dehydrogenase also showed a biphasic response; it was significantly depressed on day three and significantly increased by day seven⁷⁹, 80.

iii. Human data: none

b. Cholagogue

- i. In vitro data: none
- ii. Animal data: An Eastern European study reported that lavender oil increased biliary secretion by 118% compared to magnesium sulfate. However, in the same article, the translation reports that lavender oil had far inferior cholecystokinetic effects compared to magnesium sulfate (2.65% activity)⁸¹.
- iii. Human data: none

- c. <u>Antispasmodic/digestive aid</u>: Lavender has traditionally been used as a remedy for upset stomach and indigestion. Lavender oil has spasmolytic effects on smooth muscle *in vitro*.
 - i. *In vitro data*: In isolated rat phrenic nerve-diaphragm preparations, the essential oil of *L. angustifolia* reduced contractions in response to nerve stimulation. The antispasmodic actions of lavender were potentiated by application of a nonspecific phosphodiesterase inhibitor and a stereo-selective type 4 phosphodiesterase inhibitor, suggesting that lavender's effects are mediated through cAMP signalling^{82, 83}. In a separate study on rat-hemidiaphragm preparations, the major constituents linally acetate and linalool and the whole essential oil of *L. angustifolia* each significantly reduced electrically evoked contractions⁴⁷.

In the rat, the essential oil of *L. dentata* showed spasmolytic activity against both acetycholine- and calcium chloride-induced contractions in rat duodenal tissue *in vitro*³³. In the guinea pig, the oil (particularly linalool) exerted spasmolytic activity in smooth muscle, inhibiting the contractile responses to acetylcholine and histamine⁸², 83

- ii. Animal data: none
- iii. Human data: There are no studies in humans on lavender's use as a digestive aid.

A randomized placebo-controlled clinical trial examined the effectiveness of lavender (species unspecified) aromatherapy in recovery from exercise. Twenty men were assigned to receive either ten minutes of lavender inhalation or rest alone following two minutes of moderate exercise. No significant differences were found between groups, however at the end of the rest period, the lavender-treated group had lower systolic and diastolic blood pressures, lower arterial pressures and slower heart rates on average, compared to the control group⁷⁶.

An uncontrolled clinical trial measured the effects of lavender (species unspecified) aroma on muscle torque in six subjects. Lavender inhalation significantly decreased muscle torque with knee flexion at low velocity and non-significantly increased knee extension muscle torque at high velocity⁸⁴.

5. **Neuro-psychiatric:** <u>Sedative/hypnotic, anxiolytic, anticonvulsant; effects on mood, effects on</u> <u>cognitive function, analgesic</u>

a. <u>Sedative/hypnotic</u>

- i. *In vitro data:* In rat cerebral cortex, linalool inhibited glutamate binding in the cerebral cortex⁸⁵.
- ii. *Animal data:* In mice, inhalation of the essential oil of *L. angustifolia* and its major chemical constituents, linalyl acetate and linalool, significantly decreased baseline motility and reduced caffeine-induced hyperactivity in a dose-dependent manner⁴⁶. In rats, injected lavender oil potentiated the sedative effects of alcohol and chloral hydrate and reduced both spontaneous activity levels and caffeine- and amphetamine-induced hyperactivity⁸⁶. In mice and rats, systemic administration of the essential oil of *L. angustifolia* potentiated the effect of pentobarbital on sleep time, but this effect was attenuated over five days in animals given lavender daily^{87, 88}.
- iii. Human data: Although lavender has traditionally been used for its sedative properties, several small case studies have had mixed results. The chemical composition of the essential oil and the patient's baseline mood and activity, hemispheric asymmetries and age may mediate lavender's sedative effects. Studies on the EEG patterns induced by lavender therapy have had conflicting results. Lavender's effects on theta wave EEG activity differ between the left and right hemispheres, and appear to be independent of the subjects' perception of the odor⁸⁹. Several small studies in elderly patients indicate that lavender aromatherapy may improve nighttime sleep.

EEG recordings of six adults who liked the smell of lavender showed decreases in delta, theta, and beta activity and increases in alpha activity, but in four subjects who disliked lavender, there was a decrease in both alpha and beta activity; all subjects had a slower reaction time when exposed to lavender aroma⁹⁰. In a small study of six healthy adults, lavender fragrance significantly reduced alpha-wave activity ⁹¹. In another study, of 40 healthy adults who received aromatherapy with either lavender or rosemary, those exposed to lavender reported being more relaxed and drowsy, were less depressed and had more beta wave EEG activity and better performance on a mathematics test⁹².

On the other hand, in a within-subjects controlled trial on 16 young women, lavender fragrance was reported as arousing and associated with a significantly increased theta band activity in the left anterior region of the neocortex⁹³. A Japanese study conducted on 16 students was unable to find any effect of lavender on EEG patterns or heart rate⁹⁴. An Eastern European case series reported that when added to baths, lavender oil had no significant sedative effects, although it did exert "harmonizing" properties⁹⁵.

In a randomized controlled clinical trial on 42 students exposed to a psychologically stressful condition, lavender aromatherapy decreased beta and increased theta wave activity compared to controls⁹⁶.

Several studies show that elderly patients receive some benefit from lavender aromatherapy at night. In a pilot study of aromatherapy in two elderly patients with dementia, nighttime aromatherapy with the essential oils of *L. angustifolia* and Anthemis nobilis increased the duration of one patient's nighttime sleep and allowed the other to be taken off of sleep medication⁹⁷. In a case series of three geriatric patients with chronic insomnia, inhalation of ambient lavender oil was an adequate replacement for previous drug therapy. The amount of time spent asleep was the same as under medication and patients reported a better quality sleep. There were no side effects reported⁹⁸. Applying one drop of *L. angustifolia* essential oil to the pillows of nine elderly patients for one week improved wakefulness and alertness in eight of the patients compared with their patterns for a week without the essential oil. Patients also were observed to be more confused in the week without of the oil, compared to with it, and there were no negative side effects reported⁹⁹. In a controlled clinical trial which measured the sleeping conditions of elderly patients receiving treatment for acute medical symptoms over 245 patient-nights, 72% of patients receiving L. angustifolia aromatherapy slept well, compared to 11% of control patients. Seventy-nine percent of the group that received lavender treatment at night reported having a good day, as compared to only 26% of the control group. In a follow up study, each of nine patients who received nighttime lavender aromatherapy for two weeks received some benefit¹⁰⁰.

b. Anxiolytic

i. In vitro data: none

- ii. Animal data: In pigs, lavender straw decreased the incidence and severity of travel sickness but not overall levels of stress, as measured by salivary cortisol concentrations 101.
- iii. Human data: Several studies suggest that lavender aromatherapy decreases subjective anxiety; however, its effect on physiological stress indicators has been inconsistent, partly depending on the species used and the mode of administration.

In a study on 15 adults who inhaled vapors categorized as pleasant or unpleasant, several autonomic nervous system parameters were measured. Skin resistance, skin blood flow and instantaneous heart rate were each significantly decreased when subjects inhaled pleasant odors (including lavender) versus unpleasant odors¹⁰². A Japanese study found that lavender aroma decreased subjects' subjective arousal and stress, but did not influence blood pressure or heart rate⁹⁶. In a randomized, controlled study conducted on 122 critically ill patients in a hospital intensive care unit, subjects who received aromatherapy massage with *L. angustifolia* oil reported a significant improvement in their perceived anxiety compared to patients who received a period of rest or massage without aromatherapy; there were no significant differences in blood pressure, heart rate or respiratory rate between groups¹⁰³.

In a double blind clinical trial, 28 patients recovering from bypass surgery were given two consecutive days of 20-minute aromatherapy massage using the essential oil of one of two different lavender species. Respiratory rates decreased in 20 out of the 24 patients who completed the study. No significant differences were found, but there was a strong trend indicating that the hybrid *L. hybridi*, which has a high camphor content, was better at decreasing anxiety than *L. angustifolia*⁵⁷.

In 14 female chronic hemodialysis patients in Japan, inhalation of lavender essential oil (species unspecified) significantly decreased anxiety as measured by the Hamilton rating scale for anxiety, but had no effect on depression scores¹⁰⁴.

- c. <u>Anticonvulsant</u> (see also <u>Sedative</u> section, above)
 - i. In vitro data: none
 - *Animal data:* In mice, both intraperitoneal injection and inhalation of the essential oil of *L. angustifolia* blocked pentetrazol-, nicotine- and electroshock-induced convulsions in

a dose-dependent fashion¹⁰⁵. In rats, injected lavender oil had anticonvulsive activity against electroshock- and pentetrazole-induced seizures⁸⁶.

iii. *Human data:* There are no studies evaluating the anticonvulsant effects of lavender aromatherapy or assessing potential interactions between anticonvulsant medications and lavender in humans.

d. Effects on mood

- i. In vitro data: none
- ii. Animal data: none
- iii. Human data: In a case series, 20 subjects given three minutes of aromatherapy with lavender oil had a less depressed mood and felt more relaxed when compared to their baseline values⁹². A separate study measured the emotional responses of 15 subjects exposed to a variety of odors in a randomized order. The essential oil of lavender provoked a pleasant mood that correlated with the feeling of "happiness". This experience coincided with transient autonomic nervous system responses including increased skin potential and skin temperature and decreased skin resistance and heart rate¹⁰⁶. In a controlled trial of 72 adults, lavender aromatherapy heightened the subjects' experience of "fun" and "enjoyment" if the subjects were exposed on the first of two sessions. There was no difference, however in the mood of the lavender-treated group compared to controls, as measured by the Depressive Adjective Checklist¹⁰⁷.

In a randomized, controlled study of 94 adults, those exposed to lavender odor reported a more pleasant overall mood than those exposed to dimethyl sulfide. Subjects in the lavender group were more fluent and original in a scented testing environment than in an unscented environment on a different day. They were also in a better mood in the scented environment, as measured by the Semantic Differential Measures of Emotional State questionnaire ¹⁰⁸.

e. <u>Effects on cognitive function</u>

- i. In vitro data: none
- ii. Animal data: none
- iii. *Human data:* Lavender's effects on cognitive function are not clear. If lavender administration does affect cognitive function, its effects are subtle and appear to be

mediated by many factors, including the species and precise chemical constitution of the lavender oil administered as well as the baseline mood, mental activity, and hemispheric preferences of the subject. In most studies, this information is not available.

A Russian case series reported that treatment with a combination of the essential oils of anise, mint and lavender enhanced self-reported alertness in air traffic controllers¹⁰⁹. In a case series of 18 adults who had listened to natural environmental sounds, inhalation of one isomer of linalool but not the other had a tendency to decrease normal beta wave activity compared to both a blank control and pure lavender oil. When these subjects performed a cognitive task, linalool inhalation had a tendency to increase normal beta wave activity.⁴⁵.

In one study on 108 adults, lavender exposure had a positive effect on performance in letter counting and mathematical tests¹¹⁰. In a separate study on 20 subjects, lavender aromatherapy significantly improved math computational skills, compared to treatment with rosemary oil⁹². However, in a study on 72 subjects, lavender aromatherapy resulted in a decreased performance on arithmetic tasks, although this effect did not persist after the first session¹⁰⁷.

The central nervous system effects of lavender stimulation may show hemispheric asymmetry. Each of 30 patients exposed to lavender odor in one nostril at a time systematically showed a greater response amplitude in one hemisphere compared to the other, as measured by electrodermal activity recordings. There was no correlation between handedness and the preferred hemispheric response¹¹¹.

- f. <u>Analgesic</u>: Lavender oil is popularly recommended as a topical massage oil to remedy tension headaches and other aches and pains.
 - i. *In vitro data:* Eugenol, a minor constituent of most lavender oils, exerts membrane stabilizing, topical anesthetic effects^{64, 65}.
 - ii. Animal data: In rabbits, local application of the essential oil of *L. angustifolia* oil and its major chemical constituents, linalyl acetate and linalool, exerted a significant local anesthetic effect, significantly increasing the number of stimuli needed to provoke palpebral closure in a dose-dependent manner⁴⁷.

iii. *Human data:* Studies of topical treatment with lavender have had mixed results in relieving pain.

Among children hospitalized for HIV, massage with a combination of several essential oils including *L. angustifolia* appeared to decrease the need for analgesic medication and entirely relieve the persistent pain of some children¹¹².

In a randomized controlled clinical trial among 100 patients in a critical care unit, lavender aromatherapy combined with massage resulted in a 50% reduction in reported pain and a reduction in heart rate in 90% of participants¹¹³.

In a randomized controlled clinical trial in nine patients with rheumatoid arthritis, those who received massage with *L. angustifolia* aromatherapy reported no reduction in pain levels, but were able to reduce their intake of analgesic medication¹¹⁴.

In a randomized controlled clinical trial in 635 postpartum women, lavender oil baths were no more effective than placebo baths in reducing perineal discomfort following normal childbirth¹¹⁵, 116.

6. Endocrine: <u>Hypoglycemic effects</u>

- i. In vitro data: none
- ii. Animal data: In hyperglycemic and normoglycemic rats, infusions of *L. stoechas*, *L. latifolia* and *L. dentata* exerted hypoglycemic effects. The infusions had significant antidiabetic activity against glucose-induced hyperglycemia measured at 30 minutes and 90 minutes post-administration¹¹⁷, ¹¹⁸. There are no studies evaluating potential hypoglycemic effects with topical administration or aromatherapy.
- iii. Human data: There are no reports of hypoglycemic effects with typical medicinal uses.
- 7. Hematologic: none
- 8. Rheumatologic: <u>Analgesic for arthritis pain</u> (see Neuro-psychiatric: <u>Analgesic</u>)
- 9. **Reproductive:** <u>Emmenagogue</u>, <u>aphrodisiac</u>, <u>perineal repair</u>
 - a. <u>Emmenagogue</u>: Historical use as an emmenagogue (to stimulate menstruation)¹¹⁹; no data.
 - b. Aphrodisiac
 - i. In vitro data: none
 - ii. Animal data: none

- iii. *Human data:* In a widely publicized controlled clinical trial conducted on 31 men wearing masks of varying scents, a combination of the scents of lavender and pumpkin pie was found to increase median blood flow to the penis by 40%, which was significant compared to placebo¹²⁰.
- c. <u>Perineal repair</u>: See Neuro-psychologic: <u>Analgesic</u>

10. Immune modulation: Anti-inflammatory

- i. *In vitro data:* In isolated rat mast cells, pre-incubation with lavender oil (from an unspecified species) significantly reduced IgE-induced histamine release and tumor necrosis factor-alpha in a dose-dependent manner¹²¹.
- ii. Animal data: In both rats and mice, pre-treatment with lavender oil (unspecified species) by topical application or intradermal injection reduced immediate allergic and anaphylactic reactions in a dose-dependent manner, as measured by ear-swelling¹²¹. Caryophyllene oxide, a component of the essential oil of *L. latifolia*, exhibited anti-inflammatory activity in the rat paw model of carageenan-induced edema⁷⁴. In the rabbit, peripheral neutrophil activity following buccal mucosal injury was reduced by application of a wax that contained a mixture of sage, rose, and lavender¹²².
- iii. *Human data:* In a Ukrainian report of adults with chronic bronchitis treated in a health resort, inhalation of the essential oils of lavender and four other medicinal plants was reportedly helpful in reducing inflammation¹²³.

There are no randomized, controlled trials evaluating the effects of lavender as an anti-inflammatory in humans.

11. Antimicrobial: Antibacterial, antifungal; insecticide

- a. Antibacterial
 - In vitro data: Different lavender species have variable antibacterial effects, depending on the concentration of specific chemical constituents⁶⁹. The essential oil of *L. angustifolia* has bacteriostatic and bactericidal activity against methicillin-resistant *Staphylococcus aureus* and vancomycin-resistant *Enterococcus aecium*⁶⁶. Linalool and cineole exhibit antibacterial activity against 17 and 16 out of 18 strains of gram-positive and gram-negative bacteria tested, respectively⁴⁹. In another study, the essential oil of *L. angustifolia* inhibited the growth of *B. megaterium* by 50% as compared to control

cultures; the oil was also found to inhibit the growth of *P. aeruginosa* by 75% and to delay the growth of *S. aureus* and *M. lysodeikticus*¹²⁴. In one study, some clones of *L. angustifolia* showed increases in phenolic content and/or rosmarinic acid synthesis when challenged by a strain of *Pseudomonas*. The authors hypothesized that the upregulation of these metabolites conferred tolerance to the plants against the bacterium³⁸.

In another study, four samples of the essential oil of *L. hybrida* had inhibitory activity against five strains of non-tubercular rapid growth mycobacteria. The samples all had high concentrations of linalool, linalyl acetate, and eucalypto³⁷.

- ii. Animal data: none
- iii. Human data: none

b. Antifungal

In vitro data: Studies measuring lavender's antifungal effects have had mixed results, but most have reported positive effects *in vitro*¹²⁵. In one study, the oil of *L. angustifolia* delayed the sporulation of filamentous fungi and completely inhibited the growth of *T. mentagrophytes*¹²⁴. Similarly, the essential oil of *L. angustifolia* exhibited fungistatic activity against two of three and fungicidal activity against one of three superficial human fungal pathogens; several compounds (p-cymene, limonene, linalool, linalyl acetate, alpha-pinene, beta-pinene, 1,8-cineole and camphor) contributed to this activity⁵⁰. In a third study, cineole and linalool exhibited antifungal activity against 10 and 7 out of 12 strains of fungi tested, respectively⁴⁹. Gaseous contact with the essential oil of lavender alone suppressed the sporulation of four fungal species, suggesting that the active ingredients are highly volatile¹²⁶.

However, another study found that the antimycotic activity of the essential oil of *L. angustifolia* against *Microsporum gypseum* and *M. canis* was only fungistatic at very high doses⁷¹.

Conflicting data exist regarding the activity of lavender oil against yeast. In one study, lavender oil showed marked antifungal action against *C. albicans*¹²⁷. But in

other studies, the essential oil of *L. angustifolia* had only slight inhibitory effects against *C. albicans* and *S. cerevisiae*¹²⁴, 128.

- ii. Animal data: none
- iii. Human data: none

c. Insecticide

i. *In vitro data:* Several chemical components of lavender oil, terpineol, alpha-pinene and camphene all had anti-lice activity when tested *in vitro*⁵¹.

Linalool and D-limonene, two components of lavender oil (see biochemistry section) had rapid insecticidal activity against cat fleas^{52, 53}.

The essential oils of both *L. stoechus* and *L. angustifolia* exhibited insecticidal effects against *Drosophila auraria* flies¹²⁹.

The essential oils of *L. angustifolia* and *L. hybrida* exhibited insecticidal activity against the carmine spider mite, reducing mite fecundity by 78% and 92%, respectively¹³⁰.

The essential oil *L. angustifolia* and its constituents, linalool and coumarin, had miticidal activities against the *Psoroptes cuniculi* mite of the rabbit and the *Psoroptes ovi* mite of the sheep54, 55.

- ii. Animal data: In a case series, fleas were eliminated in cats dipped in linalool oil⁵³.
- iii. *Human data:* In a pilot study of 20 British children with persistent head lice resistant to pharmaceutical treatment, a mixture of six essential oils including lavender was reportedly "fully effective"¹³¹. No controlled trials of lavender as an insecticidal agent have been reported.

12. Antineoplastic: Chemoprophylaxis.

- i. *In vitro data:* Perillyl alcohol (POH) is found in cherries and mint as well as lavender¹³². It blocks cell division, induces apoptosis and, in some cases, induces differentiation.
- ii. Animal data: In rats who received a diet supplemented with POH for 52 weeks, the total incidence of adenocarcinomas in the colon was significantly reduced, and the tumors that did occur exhibited a significantly higher apoptotic index compared to the tumors examined from unsupplemented animals¹³³.

In a randomized trial in mice, those given POH injections prior to administration of a lung carcinogen and three times a week for 22 weeks afterward showed a 22% reduction in tumor incidence and a 58% reduction in tumor multiplicity¹³².

iii. *Human data:* Perillyl alcohol is in Phase I clinical trials for use as a chemoprotective and chemotheraputic agent against advanced breast, ovarian and prostrate cancers^{72, 134}.

13. Antioxidant: Antioxidant

i. *In vitro data:* Many plants in the Labiatae family have known antioxidant effects; these include oregano, sage, thyme and rosemary¹³⁵. Studies on lavender's antioxidant effects have had mixed results, but most support a modest role as an antioxidant, less potent than other members of the Labiatae family.

In one study, none of six different types of extracts from *L. angustifolia* exhibited any antioxidant activity in a beta-carotene bleaching test¹³⁶.

Other studies report that lavender does exhibit antioxidant properties. In one study lavender oil and two of its chemical constituents, cineole and beta-pinene, slowed the normal rate of a hydroxyl radical mediated chemical reaction more than either ethanol and mannitol, known hydroxyl radical scavengers⁷⁰. The essential oil of *L. angustifolia* mildly slowed auto-oxidation in lard¹³⁷. Similarly, a phenolic compound from *L. angustifolia* prevented the development of oxidative rancidity in vegetable oils in a dose dependent manner comparable to 200 ppm BHA and BHT¹³⁸. Finally, extracts of *L. angustifolia* exerted a concentration-dependent inhibition against both enzyme-dependent and enzyme-independent lipid peroxidation³⁹.

- ii. Animal data: none
- iii. Human data: none
- 14. Skin and mucus membranes: See Neuro-psychologic: <u>Analgesic</u> section for local anesthetic effects. See Toxicity and Contraindications section below for contact dermatitis.

15. Other/miscellaneous: <u>Hair growth stimulant</u>

- i. In vitro data: none
- ii. Animal data: none
- iii. *Human data:* In a randomized, double blind, controlled clinical trial, 86 patients with alopecia areata (hair loss) were given seven weeks of scalp massage with essential oils

including lavender. Forty-four percent of the experimental group compared with 15% of the control group showed improvement in hair growth as determined by photographic assessment (P = 0.008). The degree of improvement was significant (P=0.05). However, subjects in this study were selected based on demographic variables that indicated they might be responsive to treatment, and there was a higher dropout rate in the control group (eight dropped out of the experimental group and 13 dropped out of the control group). There were no adverse affects associated with the treatment⁷.

Toxicity and Contraindications

All herbal products carry the potential for contamination with other herbal products, pesticides, herbicides, heavy metals, pharmaceuticals, etc. Furthermore, allergic reactions can occur to any natural product in sensitive persons.

Allergic reactions to lavender have been reported. Acute facial allergies have been reported by two adults using lavender facial pillows¹³⁹. Acute airborne contact dermatitis occurred in one man receiving lavender aromatherapy¹⁴⁰. There are several case reports of contact and/or photocontact dermatitis from benzydamine hydrochloride, a topical non-steroidal anti-inflammatory analgesic prepared with lavender fragrance¹⁴¹⁻¹⁵⁰. Allergic reactions have likewise been reported when products containing lavender are repeatedly used by hairdressers¹⁵¹ and in proprietary creams¹⁵² At least four cases of contact dermatitis have been reported in association with use of Madecassol, an herbal extract that contains lavender¹⁵³. Five reports of acute contact dermatitis have been reported from the use of a muscle-relaxant ointment containing lavender oil¹⁵⁴.

People allergic to one member of the mint family may cross-react to lavender. Potentially toxic compounds in lavender: D-limonene, geraniol, linalool and linalyl acetate¹³⁹, 155

Acute toxicity: Although present in teas and as a flavoring in some foods, lavender oil is toxic if ingested in large quantities⁸⁶. Most of the medicinal benefits of lavender can be obtained through its use as an inhalant in aromatherapy or by topical application of the essential oil in massage. Because essential oil preparations are very concentrated, it is easy to overdose. We therefore do not recommend taking the essential oil orally or by direct injection. In one study, cats that licked off products containing the lavender compounds D-limonene and linalool developed signs of acute toxicosis, including hypersalivation, muscle tremors, ataxia, depression and hypothermia¹⁵⁵.

Nausea was reported by some patients who received 20-30 capsules a day of 250mg perrilyl alcohol (POH, a metabolite of limonene) in soy oil as part of a Phase I study evaluating POH as a chemopreventive agent 72, 134.

- *Chronic toxicity:* In rats, ingested linalool is conjugated and rapidly excreted, suggesting that there is no long-term hazard of exposure due to tissue accumulation^{79, 80}.
- *Limitations during other illnesses or in patients with specific organ dysfunction:* Persons with diabetes should not use lavender unless under the supervision of a physician. Infusions of lavender had hypoglycemic activity in rats^{117, 118}.

Because lavender oil is known to affect normal brain activity, epileptics and persons with seizure disorders should use this drug under the guidance of a physician, especially if they are receiving medications that may interact with the herb. In mice and rats, the essential oil of lavender blocks drug-induced seizures⁸⁶, 105.

Interactions with other herbs or pharmaceuticals: Little is known about specific interactions between lavender and other herbs and pharmaceuticals. Any person taking prescription medications should check with their physician or pharmacist for possible drug interactions. The essential oil of lavender may interfere with the activity of drugs that are metabolized by the liver by initially decreasing but then increasing levels of cytochrome p450 and alcohol dehydrogenase⁸⁰.

In rats, the essential oil of lavender has been shown to potentiate the sedative effects of some sedatives and dampen the hyperactivity usually caused by CNS stimulants^{86, 87, 156}. In humans, lavender aromatherapy may potentiate the action of sleep medications^{97, 98}.

Lavender may interact with antiseizure medications. In mice and rats, the essential oil of lavender blocks drug-induced seizures⁸⁶, 105.

Lavender essential oil may interact with analgesic medications. In one small study, lavender aromatherapy reduced patients' need for analgesic medication¹¹⁴.

Safety during pregnancy and/or childhood: Lavender has a historical reputation as an emmenagogue 157, 158; lavender oil has also been shown to affect smooth muscle and should be avoided during pregnancy⁶³, 82, 83.

No formal studies are available to assess the safety of lavender aromatherapy in children, but lavender has been recommended for use to treat childhood illnesses by herbalists¹⁶, 159. A small study of the topical application of lavender oil to treat head lice

in children reported no adverse side effects^{51, 131}. As with adults, allergic reactions to the herb may occur in children.

Typical Dosages

Provision of dosage information dose 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.
Doses may also vary according to the type and severity of the condition treated and individual patient conditions.

Example of typical adult dosages: Typically, the essential oil (distilled from flowers) is used in aromatherapy or combined with massage oils, creams or cosmetics. One or two drops are all one needs for most purposes. For massage aromatherapy, 1-10 mL of the essential oil can be added to 25 mL of a carrier oil. For a bath soak, add ¼-½ cup of dried lavender flowers to the hot bath water. Lavendin oil, lavender absolute (an extract) and spike lavender oil are used in concentrations of up to 1.2% in perfumes. Very small amounts (0.002%-0.004%) are used to flavor food. For tea, 1.5 g (2 tsp) of lavender flowers are added to 12 ounces of boiling water and allowed to steep for 5-10 minutes.

To maximize its sedative effects, herbalists recommend using lavender in combination with other sleep-promoting herbs, such as valerian and chamomile.

- *Pediatric dosages:* Lavender has been recommended for use in children and infants at reduced dosages^{157, 159}, but no formal studies on the safety or efficacy of the use of this herb in these populations have been conducted.
- Availability of standardized preparations: Lavender essential oil is sold in most health food stores and bath shops, however the chemical compositions of these extracts may vary considerably (see **Biochemistry** section). Lavender extracts are components of some prepared sedatives used in Europe: Sedatruw[®], Nervoflux[®], Beruhigungsteev, Salus[®], Nerven-Schlaf-Tee. Also some standardized cholagogue preparations such as Chol-Truw[®] contain lavender essential oil.

Dosages used in herbal combinations: Variable

REFERENCES

- 1. Barrett P. Growing and using lavender. a Storey Country wisdom bulletin. US, 1996.
- 2. Duke JA. CRC handbook of medicinal herbs. Boca Raton: CRC Press, 1985.
- 3. Holmes P. The energetic of western herbs : treatment strategies integrating Western and Oriental herbal medicine. Vol. 1. Boulder, CO: Snow Lotus Press, 1998.
- 4. Kenner D. Using aromatics in clinical practice. California Journal of Oriental Medicine 1998; 9:30-32.
- 5. Ghazanfar SA. Handbook of Arabian medicinal plants. Boca Raton: CRC Press, 1994.
- Szejtli J, Szente L, Kulcsar G, Kernoczy LZ. Beta-cyclodextrin complexes in talc powder compositions. Cosmetics & Toiletries 1986; 101:74-79.
- 7. Hay IC, Jamieson M, Ormerod AD. Randomized trial of aromatherapy : successful treatment for alopecia areata [see comments]. Arch Dermatol 1998; 134:1349-52.
- 8. Weiss RF. Herbal medicine. Gothenburg, Sweden: AB Arcanum, 1988.
- 9. Combest W. Lavender. U.S. Pharmacist 1999; 24:24-33.
- 10. Hoffman D. The complete illustrated holistic herbal. Rockport, MA: Element Books Inc., 1996.
- Schulz V, Hansel R, Tyler VE. Rational phytotherapy : a physician's guide to herbal medicine. Berlin: Springer, 1997:306.
- 12. Fleming T. PDR for herbal medicines. Montvale, NJ: Medical Economics Company, Inc., 1998.
- 13. Peirce A. The American Pharmaceutical Association practical guide to natural medicines. New York: William Morrow and Company, Inc., 1999.
- 14. Welsh C. Three essential oils for the medicine cabinet. Alternative Health Practitioner 1995; 3:11-15.
- 15. Buckle J. Which lavender oil? Complementary therapies. Nurs Times 1992; 88:54-5.
- Kenner D, Requena Y. Botanical medicine : a European professional perspective. Brookline, MA: Paradigm Publications, 1996.
- Anonymous. Staying ahead of headaches: new drugs and approaches offer new ways to manage pain. Drug Topivs 1998; July 6, 1998:46-51.
- Staicov V, Chingova B, Kalaidjiev I. Studies on several lavender varieties. Soap, Perfumery & Cosmetics 1969; 42:883-887.
- 19. Lalande B. Lavender, lavandin and other French oils. Perfumer & Flavorist 1984; 9:117-121.
- 20. Robbers JE, Speedie MK, Tyler VE. Pharmacognosy and pharmacobiotechnology. Baltimore: Williams & Wilkins, 1996:ix, 337.
- Kustrak D, Besic J. Aetheroleum Lavandulae and Aetheroleum Lavandulae hybridae in Pharmacopeia Jugoslavia III. Pharmaceutica Acta Helvetiae 1975; 50:373-378.
- 22. Kokkalou E. The constituents of the essential oil from Lavandula stoechas growing wild in greece. Planta Medica 1988; 54:58-59.

- Lopez-Carbonell M, Alegre L, Pastor A, Prinsen E, Van Onckelen H. Variation in abscisic acid, indole-3acetic acid and zeatin riboside concentrations in two Mediterranean shrubs subjected to water stress. Plant Growth Regulation 1996; 20:271-277.
- 24. Maffei M, Peracino V. Fatty acids from some Lavandula hybrids growing spontaneously in north west Italy. Phytochemistry 1993; 33:373-376.
- 25. Guillen M, D., Cabo N, Burillo J. Characterisation of the essential oils of some cultivated aromatic plants of industrial interest. Journal of the Science of Food & Agriculture 1996; 70:359-363.
- 26. Lappin GJ, Stride JD, Tampion J. Biotransformation of monoterpenoids by suspension cultures of Lavandula angustifolia. Phytochemistry 1987; 26:995-998.
- 27. Figueiredo AC, Barroso JG, Pedro LG, et al. Composition of the essential oil of Lavandula pinnata L. fil. var. pinnata grown on Madeira. Flavour & Fragrance Journal 1995; 10:93-96.
- 28. Mastelic JM, Kustrak D. Essential oil and glycosidically bound volatiles in aromatic plants : I. Lavandin (Lavandula hybrida reverchon). Acta Pharmaceutica 1997; 47:133-138.
- 29. Oszagyan M, Simandi B, Sawinsky J, Kery A, Lemberkovics E, Fekete J. Supercritical fluid extraction of volatile comp ounds from lavandin and thyme. Flavour & Fragrance Journal 1996; 11:157-165.
- 30. Reverchon E, Della Porta G, Senatore F. Supercritical CO-2 extraction and fractionation of lavender essential oil and waxes. Journal of Agricultural & Food Chemistry 1995; 43:1654-1658.
- 31. Buchbauer G, Jirovetz L, Wasicky M, Nikiforov A. Volatiles of cold and burning fragrance candles with lavender and apple aromas. Flavour & Fragrance Journal 1995; 10:233-237.
- 32. Lawrence BM. Progress in essential oils. Perfumer & Flavorist 1996; 21:55-68.
- Gamez M, Jimenez J, Navarro C, Zarzuelo A. Study of the essential oil of Lavandula dentata L. Pharmazie 1990; 45:69-70.
- Wobben HJ, ter Heide R, Rimmer R. Investigation into the composition of Spanish spike lavender oil. Soap, Perfumery & Cosmetics 1969; 42:739-740.
- 35. Bissett NG. Herbal drugs and phytopharmaceuticals. Stuttgart: MedPharm CRC Press, 1994:566.
- Agnel R, Teisseire P. Essential oil of French lavender--its composition and its adulteration. Perfumer & Flavorist 1984; 9:53-56.
- Gabbrielli G, Loggini G, Cioni P, Giannaccini B, Mancuso E. Activity of lavandino essential oil against nontubercular opportunistic rapid grown mycobacteria. Pharmacological Research Communications 1988; 20 Suppl V.
- 38. Al-Amier H, Mansour BMM, Toaima N, Korus RA, Shetty K. Tissue culture based screening for selection of high biomass and phenolic producing clonal lines of lavender using Pseudomonas and azetidine-2carboxylate. Journal of Agricultural & Food Chemistry 1999; 47:2937-2943.
- 39. Hohmann J, Zupko I, Redei D, et al. Protective effects of the aerial parts of Salvia officinalis, Melissa officinalis and Lavandula angustifolia and their constituents against enzyme-dependent and enzyme-independent lipid peroxidation [letter]. Planta Med 1999; 65:576-8.

- 40. Marotti M, Piccaglia R, Galletti C. Characterization of essential oils From Lavandula hybrida Rev. in northern Italy. Herba Hungarica 1989; 28:37-44.
- 41. Kaiser R, Lamparsky D. New carbonyl compounds in the high-boiling fraction of lavender Lavandula officinalis oil 3. Helvetica Chimica Acta 1984; 67:1184-1197.
- 42. Ferreres F, Barberan FAT, Tomas F. Flavonoids From Lavandula dentata. Fitoterapia 1986; 57:199-200.
- 43. Boelens MH. Essential oil of spike lavender, Lavendula latifolia Vill. (L. spica D.C.). Perfumer & Flavorist 1986; 11:43-54.
- 44. Pascual Teresa J, Ovejero J, Caballero E, Caballero MC, Anaya J, Pastrana ID. Contribution to the study of lavandin and the lavender oils. Anales de Quimica 1991; 87:402-404.
- 45. Sugawara Y, Hara C, Tamura K, et al. Sedative effect on humans of inhalation of essential oil of linalool : sensory evaluation and physiological measurements using optically active linalools. Analytica Chimica Acta 1998; 365:293-299.
- 46. Buchbauer G, Jirovetz L, Jager W, Dietrich H, Plank C. Aromatherapy: evidence for sedative effects of the essential oil of lavender after inhalation. Z Naturforsch [C] 1991; 46:1067-72.
- 47. Ghelardini C, Galeotti N, Salvatore G, Mazzanti G. Local anaesthetic activity of the essential oil of Lavandula angustifolia. Planta Med 1999; 65:700-3.
- 48. Cosentino S, Tuberoso CI, Pisano B, et al. In -vitro antimicrobial activity and chemical composition of Sardinian Thymus essential oils. Lett Appl Microbiol 1999; 29:130-5.
- 49. Pattnaik S, Subramanyam. Antibacterial and antifungal activity of aromatic constituents of essentail oils. Microbios 1997; 89:39-46.
- 50. Adam K, Sivropoulou A, Kokkini S, Lanaras T, Arsenakis M. Antifungal activities of Origanum vulgare subsp. hirtum, Mentha spicata, Lavandula angustifolia, and Salvia fruticosa essential oils against human pathogenic fungi. Journal of Agricultural & Food Chemistry 1998; 46:1739-1745.
- 51. Yarnell E. Essential oils against lice. Quarterly Review of Natural Medicine 1998; 3:177-184.
- 52. Hink W, Fee J. Toxicity of D-limonene, the major component of citrus peel oil, to all stages of the cat flea, *Ctenocephalides felis*. J. Med. Entomol. 1986; 23:400-404.
- 53. Hink W, Liberati T. Toxicity of linalool to life stages of the cat flea, Ctenocephalides felta (Siphonaptera Pulicidae) and its eficacy in capres and on animals. Journal of Medical Entymology 1988; 25:1-4.
- 54. Perrucci S, Cioni PL, Flamini G, Morelli I, Macchioni G. Acaricidal agents of natural origin against Psoroptes cuniculi. Parassitologia 1994; 36:269-71.
- 55. O'Brien DJ. Treatment of psoroptic mange with reference to epidemiology and history. Vet Parasitol 1999; 83:177-85.
- Jager W, Buchbauer G, Jirovetz L, Fritzer M. Percutaneous absorption of lavender oil from a massage oil. Journal of the Society of Cosmetic Chemists 1992; 43:49-54.
- 57. Buckle J. Aromatherapy. Nurs Times 1993; 89:32-5.
- 58. Peracino V, Caramiello R, Maffei M. Essential oils from same Lavandula hybrids growing spontaneously in North West Italy. Flavour & Fragrance Journal 1994; 9:11-17.

- 59. Hassan MM, Habib AA, Muhtadi FJ. Investgation of the volatile oil of Saudi Lavandula dentata. Pharmazie 1976; 31:650-1.
- 60. Opdyke D. Linalool. Food Cosmet. Toxicology 1975; 13(suppl):827-832.
- 61. Jirovetz L, Buchbauer G, Jager W, Raverdino V, Nikiforov A. Determination of lavender oil fragrance compounds in blood samples. Fre. J. Anal.Chem 1990; 338:922-923.
- 62. Jirovetz L, Buchbauer G, Jager W, W.Balba. A simple and efficient trapping-system for the investigation of exhalation-samples. Fres. J. Anal. Chem 1991; 340:785-786.
- 63. Gamez MJ, Jimenez J, Navarro C, Zarzuelo A. Study of the essential oil of Lavandula dentata L. Pharmazie 1990; 45:69-70.
- 64. Brodin P, Roed A. Effects of eugenol on rat phrenic nerve and phrenic nerve-diaphragm preparations. Arch Oral Biol 1984; 29:611-615.
- 65. Skoglund L, Jorkjed L. Postoperative pain experience after gingivectomies using different combinations of local anaesthetic agents and periodontal dressings. J Clin Periodontol 1991; 18:204-209.
- 66. Nelson RRS. In -vitro activities of five plant essential oils against methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus faecium. Journal of Antimicrobial Chemotherapy 1997; 40:305-306.
- 67. Lopez-Arnaldos T, Lopez-Serrano M, Ros Barcelo A, Calderon AA, Zapata JM. Tentative evidence of a rosmarinic acid peroxidase in cell cultures from lavandin (Lavandula x intermedia) flowers. Biochemistry & Molecular Biology International 1994; 34:809-16.
- Jedlickov'a Z, Mottl O, Ser'y V. Antibacterial properties of the Vietnamese cajeput oil and ocimum oil in combination with antibacterial agents. Journal of Hygiene, Epidemiology, Microbiology and Immunology 1992; 36:303-9.
- 69. Lis-Balchin M, Deans Stanley G, Eaglesham E. Relationship between bioactivity and chemical composition of commercial essential oils. Flavour & Fragrance Journal 1998; 13:98-104.
- Billany MR, Denman S, Jameel S, Sugden JK. Topical antirheumatic agents as hydroxyl radical scavengers. International Journal of Pharmaceutics 1995; 124:279-283.
- Perrucci S, Mancianti F, Cioni PL, Flamini G, Morelli I, Macchioni G. In vitro antifungal activity of essential oils against some isolates of Microsporum canis and Microsporum gypseum. Planta Medica 1994; 60:184-186.
- 72. Zhang Z, Chen H, Chan KK, Budd T, Ganapathi R. Gas chromatographic-mass spectrometric analysis of perillyl alcohol and metabolites in plasma. J Chromatogr B Biomed Sci Appl 1999; 728:85-95.
- 73. Khalil AM, Ashy MA, El Tawil BAH, Tawfiq NI. Constituents of local plants: 5. The coumarin and triterpenoid constituents of Lavandula dentata plant. Pharmazie 1979; 34:564-565.
- Shimizu M, Shogawa H, Matsuzawa T, et al. Anti-inflammatory constituents of topically applied crude drugs.
 IV. Constituents and anti-inflammatory effect of Paraguayan crude drug "alhucema" (Lavandula latifolia
 Vill.). Chemical & Pharmaceutical Bulletin 1990; 38:2283-4.
- 75. Nikolaevskii VV, Kononova NS, Pertsovskii AI, Shinkarchuk IF. Effect of essential oils on the course of experimental atherosclerosis. Patologicheskaia Fiziologiia i Eksperimentalnaia Terapiia 1990; 5:52-53.

- Romine IJ, Bush AM, Geist CR. Lavender aromatherapy in recovery from exercise. Percept Mot Skills 1999; 88:756-8.
- 77. Charron JM. Use of Lavandula latifolia as an expectorant [letter]. J Altern Complement Med 1997; 3:211.
- 78. Yurkova O. Vegetable aromatic substances influence on oxidative-retoration enzymes state in chronic experimen with animals. Fiziol Zh 1999; 45:40-43.
- 79. Parke D, Rhaman K, Walker R. The absorption, distribution and excretion of linalool in the rat. Biochemical Society Transactions: 54th Meeting, London 1974; 2:612-615.
- Parke D, Rahman K, Walker R. Effect of linalool on hepatic drug-metabolizing enzymes in the rat. Biochemical Society Transactions 1974; 2:615-618.
- Gruncharov V. [Clinico-experimental study on the choleretic and cholagogic action of Bulgarian lavender oil].
 Vutr Boles 1973; 12:90-6.
- Lis-Balchin M, Hart S. A preliminary study of the effect of essential oils on skeletal and smooth muscle in vitro. J Ethnopharmacol 1997; 58:183-7.
- Lis-Balchin M, Hart S. Studies on the mode of action of the essential oil of lavender (Lavandula angustifolia P. Miller). Phytother Res 1999; 13:540-2.
- Harada H, Hamabe H, Koizumi K. "Study of effect on muscle torque by aroma". Bulletin of the Nippon Veterinary & Animal Science University 1998; 0:16-20.
- 85. Elizabetsky E, al MJe. Effects of linalool on glutamatergic system in the rat cerebral cortex. Neurochemical Research 1995; 20:461-465.
- Atanassova-Shopova S, Roussinov KS. On certain central neurotropic effects of lavender essential oil. Izv Inst Fiziol 1970; 13:69-77.
- Guillemain J, Rousseau A, Delaveau P. Neurosedative effects of essential oil of lavandula angustifolia Mill.
 Annales Pharmaceutiques Francaises 1989; 47:337-343.
- Delaveau P, Guillemain J, Narcisse G, Rousseau A. Neurodepressant effects of lavender essential oil. C R Seances Soc Biol Ses Fil 1989; 183:342-348.
- Lorig TS, Schwartz GE. Brain and odor : I. Alteration of human EEG by odor administration. Psychobiology 1988; 16:281-284.
- Yagyu T. Neurophysiological findings on the effects of fragrance: Lavender and jasmine. Integrative Psychiatry 1994; 10:62-67.
- 91. Lee CF, Katsuura T, Shibata S, et al. [Responses of electroencephalogram to different odors]. Ann Physiol Anthropol 1994; 13:281-91.
- Diego M, Jones N, et al. Aromatherapy positively affects mood, EEG patterns of math computations. International Journal of Neuroscience 1998; 96:217-224.
- Klemm WR, Lutes SD, Hendrix DV, Warrenburg S. Topographical EEG maps of human responses to odors. Chemical Senses 1992; 17:347-361.
- 94. Honda Y, Kawagoe Y, Nishimura T, Yonemura Ki. A study of the effects of fragrances on EEG and heart rate. Memoirs of the Faculty of Education Kumamoto University Natural Science 1995; 0:253-262.

- 95. Uehleke B. Phytobalneology. Zeitschrift fur Phytotherapie 1996; 17:26-43.
- 96. Motomura N, Sakurai A, Yotsuya Y. A psychophysiological study of lavender odorant. Memoirs of Osaka Kyoiku University Series III Natural Science & Applied Science 1999; 47:281-287.
- 97. Wolfe N, Herzberg J. Can aromatherapy oils promote sleep in severely demented patients? [2]. International Journal of Geriatric Psychiatry 1996; 11:926-927.
- 98. Hardy M, Kirk-Smith MD, Stretch DD. Replacement of drug treatment for insomnia by ambient odor. Lancet 1995; 346.
- 99. Hudson R. Use of lavender in a long-term elderly ward. Nursing Times 1995; 91:12.
- Hudson R. Nursing : The value of lavender for rest and activity in the elderly patient. Complementary Therapies in Medicine 1996; 4:52-57.
- Bradshaw RH, Marchant JN, Meredith MJ, Broom DM. Effects of lavender straw on stress and travel sickness in pigs. J Altern Complement Med 1998; 4:271-5.
- 102. Alaoui-Ismaili O, Vernet-Maury E, Dittmar A, Delhomme G, Chanel J. Odor hedonics: connection with emotional response estimated by autonomic parameters. Chem Senses 1997; 22:237-48.
- 103. Dunn C, Sleep J, Collett D. Sensing an improvement: an experimental study to evaluate the use of aromatherapy, massage and periods of rest in an intensive care unit. J Adv Nurs 1995; 21:34-40.
- 104. Itai T, Amayasu H, Kuribayashi M, et al. Psychological effects of aromatherapy on chronic hemodialysis patients. Psychiatry & Clinical Neurosciences 2000; 54:393-7.
- Yamada K, Mimaki Y, Sashida Y. Anticonvulsive effects of inhaling lavender oil vapour. Biol Pharm Bull 1994; 17:359-60.
- 106. Vernet-Maury E, Alaoui-Ismaili O, Dittmar A, Delhomme G, Chanel J. Basic emotions induced by odorants: a new approach based on autonomic pattern results. J Auton Nerv Syst 1999; 75:176-83.
- 107. Ludvigson HW, Rottman TR. Effects of ambient odors of lavender and cloves on cognition, memory, affect and mood. Chemical Senses 1989; 14:525-536.
- 108. Knasko SC. Ambient odor's effect on creativity, mood, and perceived health. Chemical Senses 1992; 17:27-35.
- 109. Leshchinskaia I, Makarchuk NM, Lebeda AF, Krivenko VV, Sgibnev AK. [Effect of phytoncides on the dynamics of the cerebral circulation in flight controllers during their occupational activity]. Kosm Biol Aviakosm Med 1983; 17:80-3.
- 110. Degel J, Koster EP. Odors: implicit memory and performance effects. Chem Senses 1999; 24:317-25.
- 111. Brand G, Millot JL, Henquell D. Olfaction and hemispheric asymmetry: unilateral stimulation and bilateral electrodermal recordings. Neuropsychobiology 1999; 39:160-4.
- 112. Styles J. The use of aromatherapy in hospitalized children with HIV. Complement Ther Nurs 1997; 3:16-20.
- 113. Woolfson A, Hewitt D. Intensive aromacare. Int J Aroma 1992; 4:12-14.
- 114. Brownfield A. Aromatherapy in arthritis: a study. Nurs Stand 1998; 13:34-35.
- 115. Cornwell S, Dale A. Lavender oil and perineal repair. Mod Midwife 1995; 5:31-3.

- 116. Dale A, Cornwell S. The role of lavender oil in relieving perineal discomfort following childbirth: a blind randomized clinical trial. J Adv Nurs 1994; 19:89-96.
- Gamez MJ, Jimenez J, Risco S, Zarzuelo A. Hypoglycemic activity in various species of the genus Lavandula.
 Part 1: Lavandula stoechas L. and Lavandula multifida L. Pharmazie 1987; 42:706-7.
- Gamez MJ, Zarzuelo A, Risco S, Utrilla P, Jimenez J. Hypoglycemic activity in various species of the genus Lavandula. Part 2: Lavandula dentata and Lavandula latifolia. Pharmazie 1988; 43:441-2.
- 119. Duke JA. Green pharmacy. Emmaus, PA: Rodale Press, 1997:507.
- Hirsch A, Gruss J. Human male sexual response to olfactory stimuli. J Neurol Orthop Med Surg 1999; 19:14 19.
- 121. Kim HM, Cho SH. Lavender oil inhibits immediate-type allergic reaction in mice and rats. J Pharm Pharmacol 1999; 51:221-6.
- 122. Sysoev NP. [The effect of waxes from essential-oil plants on the dehydrogenase activity of the blood neutrophils in mucosal trauma of the mouth]. Stomatologiia (Mosk) 1991; 70:12-3.
- 123. Shubina LP, Siurin SA, Savchenko VM. [Inhalations of essential oils in the combined treatment of patients with chronic bronchitis]. Vrachebnoe Delo 1990:66-7.
- Larrondo JV, Agut M, Calvo-Torras MA. Antimicrobial activity of essences from labiates. Microbios 1995; 82:171-2.
- 125. Zambonelli A, D'Aulerio AZ, Bianchi A, Albasini A. Effects of essential oils on phytopathogenic fungi in vitro. Journal of Phytopathology 1996; 144:491-494.
- 126. Inouye S, Watanabe M, Nishiyama Y, Takeo K, Akao M, Yamaguchi H. Antisporulating and respirationinhibitory effects of essential oils on filamentous fungi. Mycoses 1998; 41:403-10.
- 127. Prokopchuk AF, Khanin ML, Perova TV, Prokopchuk Yu A, Nikolaeva LA. Antifungal action of carbon dioxide-extracts of spicy and medicinal-aromatic plant raw material on Candida albicans. Izvestiya Severo Kavkazskogo Nauchnogo Tsentra Vysshei Shkoly Estestvennye Nauki 1979; 4:81-83.
- Larrondo JV, Calvo MA. Effect of essential oils on Candida albicans : a scanning electron microscope study. Biomedical Letters 1991; 46:269-272.
- 129. Konstantopoulou I, Vassilopoulou L, Mavragani Tsipidou P, Scouras ZG. Insecticidal effects of essential oils : a study of the effect of essential oils extracted from eleven Greek aromatic plants on Drosophila auraria. Experientia 1992; 48:616-619.
- 130. Mansour F, Ravid U, Putievsky E. Studies of the effects of essential oils isolated from 14 species of Labiatae on the carmine spider mite Tetranychus cinnabarinus. Phytoparasitica 1986; 14:137-142.
- 131. Weston S, Burgess I, Williamson E. Evaluation of essential oils and some of their component terpenoids as pediculicides for the treatment of human lice. J. Pharm. Pharmacol. 1997; 49:120.
- 132. Lantry LE, Zhang Z, Gao F, et al. Chemopreventive effect of perillyl alcohol on 4-(methylnitrosamino)-1- (3-pyridyl)-1-butanone induced tumorigenesis in (C3H/HeJ X A/J)F1 mouse lung. J Cell Biochem Suppl 1997; 27:20-5.

- Reddy BS, Wang CX, Samaha H, et al. Chemoprevention of colon carcinogenesis by dietary perillyl alcohol. Cancer Res 1997; 57:420-5.
- Ziegler J. Raloxifene, retinoids, and lavender: "me too" tamoxifen alternatives under study [news]. J Natl Cancer Inst 1996; 88:1100-2.
- 135. Cuppett SL, Hall CA, 3rd. Antioxidant activity of the Labiatae. Adv Food Nutr Res 1998; 42:245-71.
- 136. Dapkevicius A, Venskutonis R, Van Beek TA, Linssen JPH. Antioxidant activity of extracts obtained by different isolation procedures from same aromatic herbs grown in Lithuania. Journal of the Science of Food & Agriculture 1998; 77:140-146.
- Economou KD, Oreopoulou V, Thomopoulos CD. Antioxidant activity of some plant extracts of the family Labiatae. Journal of the American Oil Chemists Society 1991; 68:109-113.
- Amr A, Yousef M. A natural antioxidant from lavender (Lavandula officinalis Chaix). Dirasat Series B Pure & Applied Sciences 1995; 22:1271-1288.
- 139. Coulson IH, Khan AS. Facial 'pillow' dermatitis due to lavender oil allergy. Contact Dermatitis 1999; 41:111.
- Schaller M, Korting HC. Allergic airborne contact dermatitis from essential oils used in aromatherapy. Clin Exp Dermatol 1995; 20:143-5.
- Rademaker M. Allergic contact dermatitis from lavender fragrance in Difflam gel. Contact Dermatitis 1994;
 31:58-9.
- 142. Corres F. Photodermatitis from benzydamine. Contact Dermatitis 1980; 6:285.
- 143. Bruynzeel D. Contact allergy to benzy damine. Contact Dermatitis 1986; 14:313-314.
- 144. Balato N, Lembo G, C. Patruno ea. Contact dermatitis from benzydamine hydrochloride. Contact Dermatitis 1986; 15:105.
- 145. Christopherson J. Allergic contact dermatitis to benzydamine. Contact Dermatitis 1987; 16:106-107.
- 146. Motley R, Reynolds A. Photodermatitis from benzydamine cream. Contact Dermatitis 1988; 19:66.
- 147. Vincenzi C, Cameli N, M. Tardio ea. Contact and photocontact dermatitis due to benzydamine hydrochloride.
 Contact Dermatitis 1990; 23:125-126.
- 148. Foti C, Vena G, Angelini G. Occupational contact allergy to benzydamine hydrochloride. Contact Dermatitis 1992; 27:328-329.
- 149. Bujan JJG, Ilardia-Lorentzen R, Arachavala RS. Allergic contact dermatitis from benydamine with probable cross-reaction to indomethacin. Contact Dermatitis 1993; 28:111-112.
- 150. Cockayne SE, Gawkrodger DJ. Occupational contact dermatitis in an aromatherapist. Contact Dermatitis 1997; 37:306-307.
- 151. Calnan C. Oil of cloves, laurel, lavender, peppermint. Contact Dermatitis Newsletter 1970; 7:148.
- 152. Rudzki E, Grzywa Z, Brno S. Sensitivity to 35 essential oils. Contact Dermatitis 1976; 2:196-200.
- 153. Eun H, Lee A. Contact dermatitis due to Madecassol. Contact Dermatitis 1985; 13:310-313.
- 154. Degreef H, Bonamie A, Van Derheyden D, Dooms-Goossens A. Mephenesin contact dermatitis with erythema multiforme features. Contact Dermatitis 1984; 10:220-223.

- 155. Hooser S. Toxicology of selecteed pesticides, drugs, and chiemicals. D-limonen, linalool, and crude citrus oil extracts. Veterinary Clinics of North America. Small Animal Practice. 1990; 20:383-385.
- 156. Komori T, Tanida M, Kikuchi A, Shoji K, Nakamura S, Nomura J. Effects of odorant inhalation on pentobarbital-induced sleep time in rats [1]. Human Psychopharmacology 1997; 12.
- 157. Ody P. The Complete Medicinal Herbal. Boston: Dorling-Kindersley, 1993:192.
- 158. Brinker FJ. Herb contraindications and drug interactions : with appendices addressing specific conditions and medicines. Sandy, OR: Eclectic Institute, 1997:146.
- 159. Schilcher H. Phytotherapy in paediatrics : handbook for physicians and pharmacists : with reference to commission E monographs of the Federal Department of Health in Germany : includes 100 commission E monographs and and 15 ESCOP monographs. Stuttgart: medpharm Scientific Publishers, 1997:181.