Montview Liberty University Journal of Undergraduate Research

Volume 2 | Issue 1 Article 3

2016

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Investigation of the Parasympathetic Effects of Lavender Essential Oil in Humans

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Abstract

The **purpose** of this study will be to investigate the claim that administration of lavender (*Lavandula angustifolia*) essential oil (topically, orally, and/or respiratorily) produces a relaxative effect in human subjects. This investigation will theoretically be conducted in two stages. Stage one will focus primarily on **determining the presence of therapeutic effects and the relative effectiveness of lavender in several application modalities**. Stage two will proceed based on findings from stage one. If significant parasympathetic effects are observed in relation to one or more of the lavender oil modalities described above, a more focused investigation will be conducted in stage two **to ascertain the specific active chemical component(s)** in the oil that stimulate(s) the therapeutic effect.

We hypothesize that application of lavender oil will be accompanied by parasympathetic stimulation, evidenced by a statistically significant ($p<0.01$) depression in vital signs compared to the control group. **We also hypothesize that, in terms of dose volume to therapeutic effect, inhalation will be the most efficient of the three modalities described above.** Lastly, while it is expected that the compounds of the whole lavender oil work together synergistically, with none of the individual components demonstrating the same effectiveness as the whole lavender oil, **we do hypothesize that linalool and linalyl acetate will demonstrate the greatest effect in the focused stage two trials**, as they are the two principal constituent compounds of whole lavender oil, by volume.

Introduction

Therapeutic essential oils are a rapidly growing commodity in the alternative medicine community, touted by many advocates as an effective therapy for maladies ranging from acne to anxiety. Due to **insufficient peer-reviewed research** regarding many of these supposed benefits, the US Food & Drug Administration (FDA) has taken steps to regulate claims made by oil retailers and distributors in the interest of consumer safety and reducing public misinformation until more studies can be done.

One of the most studied essential oils is lavender oil, **derived from various species of the genus *Lavandula*. Lavender essential oil has been tested for its effectiveness (via aromatherapy and ingestion)** in mitigating anxiety, digestive problems, migraines, insomnia, and hypertension; it has been investigated for its antidepressant, sedative, analgesic, antimicrobial, and antifungal qualities, as well as its ability to improve emotional status by promoting calming effects in the autonomic nervous system [1].

Literature Review

In a three month double-blind clinical study, patients with a history of migraines were orally administered lavender extract. The test group was found to suffer from markedly fewer and less severe headaches compared to the placebo control group [1].

In a study in which postoperative patients received lavender aromatherapy to mitigate anxiety after coronary artery bypass surgery, the researchers found no difference between the test and control groups after 3 days [2].

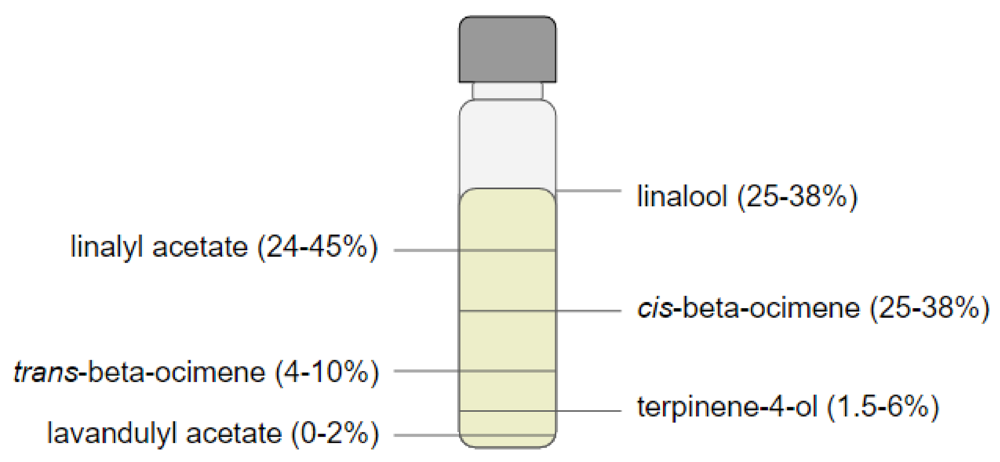
A research team found that lavender essential oil relaxed the carotid artery of rabbit specimens, so further experiments sought to determine the biochemical mechanisms affected by linalyl acetate, a major ingredient of the essential oil, which seems to activate MLC phosphatase. The researchers proposed that the vasodilation property could make the chemical a possible treatment for cardiovascular diseases, including atherosclerosis and hypertension [3].

Lavender aromatherapy was shown to improve the ability to sleep of middle-age women by significantly decreasing heart-rate and improving heart rate variability parameters, which suggests parasympathetic cardiovascular activity [4].

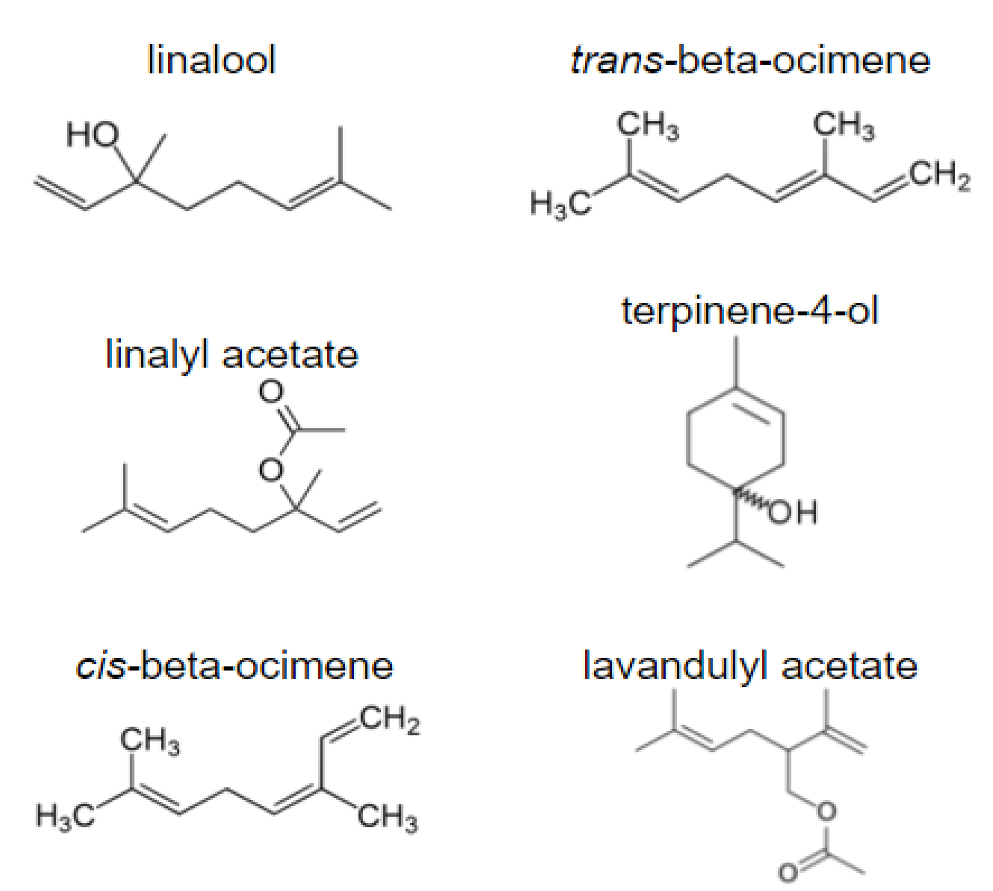
A study of linalool demonstrated the difference between the effects of its two enantiomers. In this study, linalool was determined to constitute 40.9% of the lavender oil, and the enantiomeric ratio of the (*R*)-(−)-isomer was 88.0% ee. After establishing the decrease in heart rate (HR) resulting from the inhalation of lavender odor, a second experiment showed that (*R*)-(−)-linalool alone also similarly decreased HR and subjective indications of negative moods, such as tension and anger. The (*R*)-(−)-isomer, therefore, seems to be a major active ingredient in the volatile lavender essential oil. However, the (*S*)-(+)-linalool administered at the same concentration caused noticeable increases in HR and activity of the sympathetic nervous system, along with an increase in the negative mood scales. The concentrations used were purportedly too low to cause subjective preferences to interfere psychologically; thus, the effects seem to be solely pharmacological [5].

Linalool has been studied for its sedative, anxiolytic, anticonvulsant, anesthetic, analgesic, anti-inflammatory, antitumoral, antimicrobial, and antioxidant properties The alcohol can cause skin sensitization, an allergic reaction involving irritation or dermatitis, as a side effect in some individuals [6].

Chemical Constituents of Lavender Essential Oil



According to AFNOR standards, therapeutic-grade lavender essential oil contains compounds in these proportions [7].



Aromatherapy: Evidence for sedative effects of the essential oil of lavender after inhalation

[8] Buchbauer, G, Jirovetz, L, Jäger, W, Dietrich, H,Plank, C. (1991). Aromatherapy: Evidence for sedative effects of the essential oil of lavender after inhalation. Zeitschrift Für Naturforschung.C, Journal of Biosciences, 46(11-12), 1067-1072.

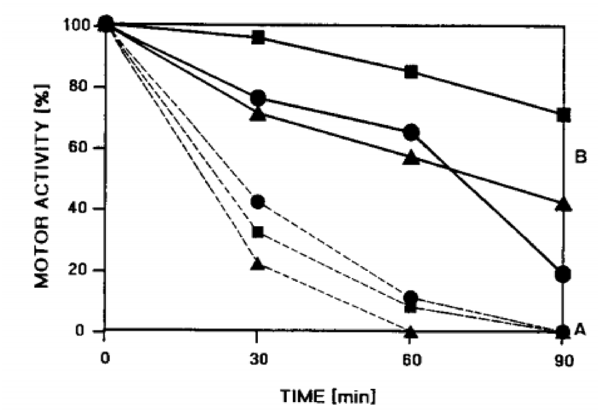


Fig. 2. Decrease of motor activity of 6−8 week old mice (A) and 6 month old mice (B) after inhalation of lavender oil (▲), linalool (■) and linalyl acetate (●). Motor activity values of untreated control animals was arbitrarily fixed as 100%. The motor activity was found 30 min after inhalative exposure to lavender oil: 22%/71%, linalool: 32%/96%, linalyl acetate: 42%/76%. 60 min after exposure to lavender oil: 0%/57%, linalool: 8%/85%, linalyl acetate: 11%/65%. 90 min after exposure to lavender oil: 0%/42%, linalool: 0%/71%, linalyl acetate: 0%/19%. The sample volume of each fragrance compound: 1.5 ml.

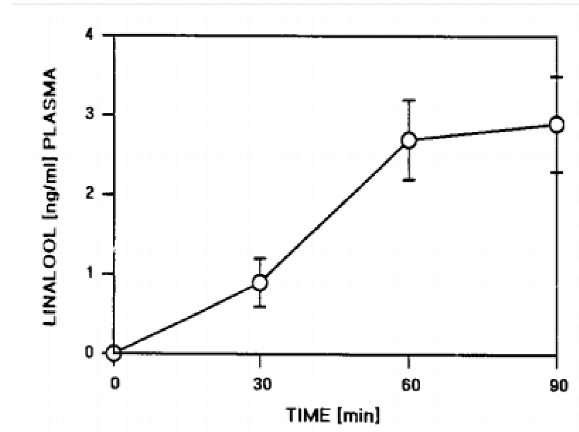


Fig. 3. The plasma levels of linalool in mice after the inhalation of this monoterpenic alcohol. (Means: ± S.E.M.; $n = 4$).

Table I. Additional activity after caffeine injection and exposure of the animals to the fragrance compounds 1 h after the administration of the excitant.

Caffeine:	+ 60%
Caffeine + lavender oil:	+ 5%
Caffein + linalool:	+ 26%
Caffein + linalyl acetate:	+ 32%

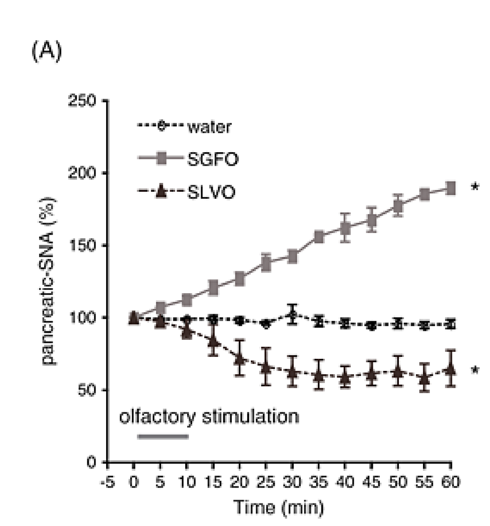
In an experiment designed to test the sedative effect of lavender oil and its principal compounds, linalool and linalyl acetate, mice were measured for their motility rates. Mice in the control group were significantly more active than those who inhaled lavender oil, linalool, or linalyl acetate. Furthermore, the whole oil caused a greater decrease in activity versus the samples of the individual compounds, either linalool or linalyl acetate (Figure 2). To ensure that the chemical was being absorbed into the bloodstream of the animals, plasma was tested at four time intervals for linalool content. The amount of linalool in the plasma was directly correlated to the length of time that the mice inhaled the linalool (Figure 3).

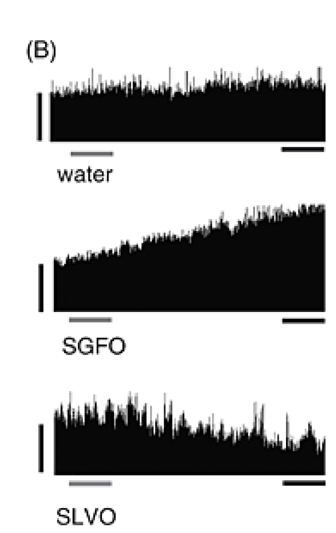
In a subsequent experiment, mice received intraperitoneal caffeine injections to induce hyperactivity. The control group became dramatically more active, while the test groups, exposed to the volatile compounds (either lavender oil proper, linalool, or linalyl acetate), became only slightly more active than before receiving either the caffeine or the fragrant chemicals (Table I). Lavender aromatherapy, therefore, not only causes a soporific effect, it also counteracts the excitatory effect of caffeine.

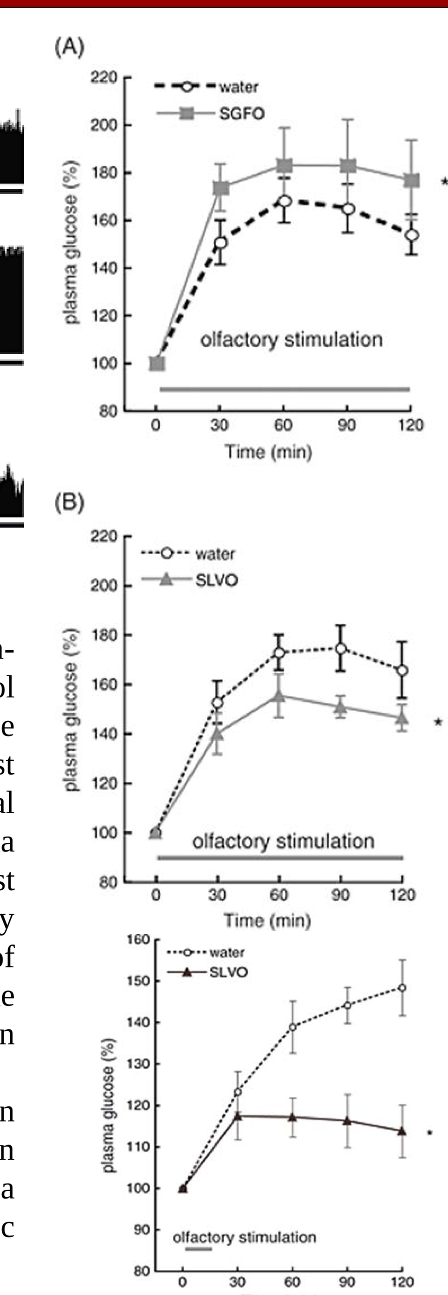
These experiments suggest the speed and efficacy of inhalation as a means of receiving the chemicals as compared to topically or orally. Lower doses are sufficient for this modality compared to ingestion. The researchers suggested two possible reasons for the effectiveness of inhalation: first, the nasal mucosa demonstrates a rapid absorption rate, resulting in a serum concentration similar to that from an intravenous injection; second, pulmonary absorption may be an effective route for the chemicals.

Effect of grapefruit and lavender essential oil scents on pancreatic sympathetic nerve activity and plasma glucose in rats

[9] Horii, Y., Maeda, K., Shen, J., Fujisaki, Y., & Nagai, K. (2015). Effect of grapefruit and lavender essential oil scents on pancreatic sympathetic nerve activity and plasma glucose in rats. *Flavour and Fragrance Journal*, *30*(4), 282-287.







In the first of a set of experiments exploring the effects on the ANS of grapefruit and lavender oil scents, rats exposed to grapefruit oil scent demonstrated increased stimulation of the efferent sympathetic nerve of the pancreas, while the scent of lavender oil induced a decrease in activity of the nerve (Graphs A and B above).

In rats with hyperglycemia caused by intracranial injection of 2-deoxy-D-glucose (2DG), the scent of grapefruit oil resulted in a greater increase in blood plasma glucose levels when compared to the control group (Graph A right). By contrast, the lavender oil scent resulted in a lesser increase in blood plasma glucose levels than observed in the control group (Graph B right). Therefore, olfactory stimulation of grapefruit oil seems to heighten the hyperglycemic effect of 2DG on glucose levels, whereas olfactory stimulation of lavender oil counteracts the effect of 2DG.

In the third experiment, streptozotocin-diabetic (non-insulin secreting) rats received glucose orally. The control group, which received water, underwent a steady increase in plasma glucose levels over time; conversely, the test group exposed to lavender oil scent showed an initial increase, followed by a gradual decrease in the plasma glucose levels (Graph lower right). These data suggest that the hypoglycemic effect of lavender aromatherapy may not involve insulin, but rather a suppression of activity of the pancreatic sympathetic nerve and the adrenal sympathetic nerve, lessening release of glucagon and adrenaline.

This set of experiments reveals the connection between olfactory stimulation by lavender and inhibition of the SNS. The scent of lavender oil correlates to a decrease in activity of the efferent pancreatic sympathetic nerve and a hypoglycemic response.

Methods

Stage one will be a double-blind study involving seven separate trial groups. All subjects, regardless of group, will be allowed to sit in a position of comfort for ten minutes to allow the body to acclimate to a resting state. A pre-intervention set of vital signs (blood pressure, heart rate, and respiratory rate) will be taken at this point to provide a baseline. After this ten minute pre-intervention phase has been completed, three of the groups will receive lavender oil:

- *Group 1*-lavender oil (3 drops, neat, applied topically to the wrists)
- *Group 2*-lavender oil (1 drop, neat, oral ingestion)
- *Group 3*-lavender oil (6 deep breaths through the nose, direct inhalation)

In order to prevent subjects in Group 1 from simultaneously inhaling the volatile oil, they will have their lower arms covered to prevent smelling the oil. For comparison, groups 4-6 will be given a placebo (a non-volatile oil such as oleic acid):

- *Group 4*-placebo oil (3 drops applied topically to the wrists)
- *Group 5*-placebo oil (1 drop, oral ingestion)
- *Group 6*-placebo oil (6 deep breaths through the nose, direct inhalation)
- *Group 7* will receive no intervention and will function as a control.

Four sets of vital signs (blood pressure, respiratory rate, and heart rate) will be taken in the duration of the experiment: first an initial baseline measurement, recorded prior to the intervention, followed by three response measurements, recorded post-intervention at 10 minute time intervals. Data from the intervention groups will be compared to data from the control group **to ascertain whether or not any parasympathetic responses were associated with each of the intervention modalities**, and the data from those modalities that are found to produce a response will be further compared to assess their relative effectiveness in comparison to each other.

In **stage two** of the experiment, isolated samples of each major constituent compound will be procured and administered to the subjects in the same concentrations found in whole lavender oil. Protocol for obtaining vital signs will be identical to stage one. The method of administration will be whichever method was found most effective in the previous experiments of stage one. Data will be analyzed following the trials **to determine which of the individual constituent compounds produced a parasympathetic response**, and the extent of these responses will be compared quantitatively to determine which constituents contribute most to the overall parasympathetic effect of the complete lavender oil.

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Chemical Structure Images: http://www.wikipedia.org

Acknowledgements:
The Student Research Society of Liberty University for Poster Funding
The Department of Biology and Chemistry, Liberty University
Patricia Greenhalgh for essential oil resources