

# Lavender Essential Oil Aromatherapy for Anxiety

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Received: October 16, 2019; Published: November 13, 2019

## Abstract

Anxiety disorders are the most common mental illness in the United States with the 12-month prevalence affecting about 10% of the adult population. Afflicted individuals typically exhibit both psychiatric and somatic symptoms with the occurrence of generalized anxiety disorder (GAD) in women being twice that in men.

A variety of prescription medications are used to treat anxiety, depression and other common mental health issues but there are many issues and limitations associated with these drugs. As a result, growing numbers of healthcare professionals and patients are actively exploring complementary and alternative medicine (CAM) treatments for anxiety. In particular, essential oils and aromatherapy are treatment modalities of major and growing importance for the treatment of anxiety, mood-adjustment and insomnia.

This article discusses the effectiveness and mode of action of lavender oil aromatherapy as an anxiolytic agent. In particular, it indicates how the centuries-old CAM therapies for treating anxiety and the plethora of anecdotal reports on the anxiolytic actions of lavender essential oil have now been validated by intense scientific study for over a decade. major and growing importance for the treatment of anxiety, mood-adjustment and insomnia.

Keywords: Lavender Essential Oil; Aromatherapy; Anxiety

## Introduction

Essential oils have been a mainstay of complementary and alternative medicine (CAM) for centuries and there is a wealth of anecdotal and traditional information on their effectiveness in a wide variety of therapeutic applications. As has been discussed elsewhere in detail [1], the essential oil industry and its products is of growing importance to improving health and the overall quality of life for users. Numerous essential oil formulations are manufactured for aromatherapy and for topical applications such as massage therapy and they are mostly safe when used as directed.

There is now strong evidence that nocturnal olfactory stimulation, i.e. aromatherapy, may serve as a low-cost concomitant intervention to improve sleep quality, especially in PTSD sufferers [2]. In fact multiple clinical studies have confirmed the beneficial effects on sleep provided by aromatherapy, particularly with lavender oil, for a wide spectrum of patients and conditions [3-9]. Since impaired sleep is frequently an associated occurrence with anxiety, as discussed below, any harmless, low cost and effective therapy that facilitates sleep is obviously an important facet of CAM therapy. It should be mentioned, however, that the most convenient method of administering essential oils, including lavender, is aerial diffusion using a diffuser or nebulizer.

Overall, essential oils in CAM are recognized as having minimal side effects when used as directed and for short durations. When used in a diffuser, essential oils can be used in addition to prescribed medication with no interactions and they have the great advantage that

*Citation:* R Michael Buch and J Anthony Von Fraunhofer. "Lavender Essential Oil Aromatherapy for Anxiety". *EC Psychology and Psychiatry* 8.12 (2019): 01-09.

they act quickly with no possibility of dependence, tolerance, or withdrawal problems or issues. Nevertheless, as with any CAM therapy, if a potential user has any questions, a primary care provider or pharmacist should be consulted before using essential oils in conjunction with prescription medications.

#### Anxiety

Modern life is stressful and, consequently, most individuals periodically feel a little apprehensive about health and quality of life issues, marital or family problems, finances and work-related issues. These feelings of anxiety, basically worrying about things, is a mental activity than can occupy a person's thoughts from childhood and throughout life. Although the modern obsession with social media improves the ability to connect with others, there is growing evidence that for both teenagers and adults, this ubiquitous and unceasing connectivity is increasingly associated with anxiety, depression and other mental health concerns. The most obvious example of this is the effects on victims of cyber-bullying practiced by school children and teens.

When anxiety, i.e. obsessive worrying, becomes so severe and debilitating that completing even simple and/or mundane tasks is difficult, then the affected individual may be exhibiting signs of generalized anxiety disorder (GAD). The Appendix indicates common signs of generalized anxiety disorder and when these symptoms become severe, then help should be sought from a mental healthcare specialist.

In fact, anxiety disorders are the most common mental illness in the United States (and probably globally), with the 12-month prevalence affecting about 10% of the adult population (i.e. about 6.8 million adults). Afflicted individuals typically exhibit both psychiatric and somatic symptoms (see Appendix), with the occurrence of generalized anxiety disorder (GAD) in women being twice that in men [10-12]. The disorder often starts during adolescence which is understandable given the stresses often experienced during this period in life. Further, the symptoms of GAD tend to magnify and intensify during stressful periods in life.

When a person is anxious<sup>a</sup>, the brain releases neurotransmitters (typically dopamine, serotonin, epinephrine, acetylcholine and histamine) which put the body into a high state of alert, i.e. they prepare the body for the "fight or flight" response to a perceived threat. However, some of the neurotransmitters will enter the digestive tract and disrupt the gut microbiome and can result in nausea. As a result, gastric problems such as nausea and diarrhea are among the most common symptoms of stress and anxiety. The ingress of neurotransmitters into the gut and their effect on the microbiome, is a common and widely recognized cause of peptic ulcer disease.

Unfortunately, a great many mental health patients face problems in receiving proper treatment. The huge treatment gap has led to a global mental health crisis, with up to 90% of people with mental health problems in some countries being unable to receive basic treatment [13]. A survey for the years 2001 - 2005 showed that only 8% of the people with mental illness in China sought professional help and only 5% of them had received psychiatric treatments [14].

#### Anxiolytic medications

A variety of prescription medications have been used as anti-depressants as well as treatments for anxiety but many of these medications have disadvantages, limitations and side-effects. For many years, antidepressants such as benzodiazepines (e.g. Valium, Ativan and Xanax). were commonly used to treat GAD. Unfortunately, these medications are highly addictive, carry a risk of substance abuse and if patients become dependent on them, they can develop additional psychological and physical issues as well as experience severe withdrawal symptoms if they stop taking the medicine. Other antidepressants such as Paxil, Effexor, Prozac, Lexapro and Zoloft have been prescribed over the years to treat chronic anxiety and panic attacks. As with the benzodiazepines, these medications can cause numerous side effects, are slow in the onset of action and often are ineffective [15].

<sup>a</sup>Note that low levels of serotonin give rise to the symptoms of depression and anxiety. Eating foods such as dairy products and nuts (i.e. so-called mood foods) that are rich in tryptophan, which acts as a precursor of several neurotransmitters including serotonin, will raise serotonin levels and reduce anxiety.

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Today's frequently administered anxiolytic medications include selective serotonin reuptake inhibitors<sup>b</sup> (SSRIs), serotoninnorepinephrine reuptake inhibitors<sup>c</sup> (SNRIs) and BuPar (buspirone<sup>d</sup>). Although these medications may be effective in many cases, one issue with them is the delay in onset of action. It is not uncommon, however, that even when anxiolytic agents are used appropriately, they may lack efficacy or only be partially effective in controlling symptoms. Many of the problems and issues identified with prescription medications used to treat depression, anxiety and other common mental health issues are summarized in table 1 [13,15,16].



Table 1: Problems associated with prescription antidepressants and anxiolytics.

Given the problems associated with proper and effective mental healthcare treatment as well as dissatisfaction with available prescription medications, growing numbers of healthcare professionals and lay people are actively exploring and promoting complementary and alternative medicines and treatments (CAMs). In particular, essential oils and aromatherapy are treatment modalities of major and growing importance for the treatment of anxiety, mood-adjustment and insomnia in addition to their antibacterial, anti-inflammatory and analgesic properties [1,17-19].

#### Lavender oil aromatherapy and anxiety

The beneficial effects on mental health and relaxation of inhaling lavender oil, commonly known as aromatherapy, with both humans and their pets have been recognized for centuries [1].

Until comparatively recently, however, most of the reported anxiolytic and relaxational effects associated with essential oils have been anecdotal but this situation has now changed. One development is the wide availability of efficient, effective and reasonably-priced nebulizers/diffusers for vaporization of essential oils dispersed in water. Another major development has been the increasing numbers of scientific and clinical studies on essential oils and aromatherapy reported in the literature every year. One result of this increased scientific interest and scrutiny is that aromatherapy is recognized as an effective and beneficial complementary therapy for people with anxiety symptoms.

<sup>c</sup>Serotonin-norepinephrine reuptake Inhibitors (SNRIs), also known as selective serotonin-norepinephrine reuptake Inhibitors (SSNRIs), are effective in treating depression, anxiety disorders and long-term (chronic) pain, especially nerve pain. Their action is to increase levels of serotonin and norepinephrine in the brain by blocking or delaying their reuptake by neurons.

<sup>d</sup>Buspirone is an anxiolytic that affects chemicals in the brain that may be out of balance for people with anxiety. It is used to treat anxiety disorders or the symptoms of anxiety, such as tension, irritability, fear, dizziness, accelerated heartbeat and other physical symptoms.

<sup>&</sup>lt;sup>b</sup>Selective serotonin reuptake inhibitors (SSRIs) are the most commonly prescribed antidepressants to treat the symptoms of moderate to severe depression and anxiety disorders. They are relatively safe and typically cause fewer side effects than other antidepressants. They treat depression by increasing serotonin levels in the brain and block the reabsorption (reuptake) of serotonin into neurons.

Several years ago, there was a review of 16 randomized controlled clinical trials reported in the literature from 1990 to 2010 on the use of aromatherapy for people suffering from anxiety or exhibiting anxiety symptoms. Most of the reviewed studies indicated positive effects in controlling anxiety with no adverse events being reported [20]. These findings were supported by those of another review of clinical trials studying the anxiolytic effects of lavender ingestion [21]. Likewise, a review [22] of several clinical studies suggested a positive effect of lavender aromatherapy in reducing women's anxiety during the first stage of labor. It has also been found that lavender oil aromatherapy reduced anxiety when administered to women before undergoing breast surgery [23].

Two studies have been performed that evaluated the anti-anxiety properties of a proprietary lavender oil preparation called Silexan that is taken orally [24,25]. It was found that this lavender oil capsule was equal in effectiveness in alleviating anxiety as lorazepam (Ativan) and paroxetine (Paxil) in patients with GAD.

The growing body of scientific research reported in the literature clearly indicates that lavender oil aromatherapy has a significant and well-documented anxiolytic action in patients suffering from anxiety [26]. This evidence-based validation of the safety and effectiveness of aromatherapy is of growing importance given that the limitations and risks associated with existing pharmacotherapies for treating anxiety disorders. There is, however, the open question of how lavender oil aromatherapy exerts its anxiolytic effect.

In recent years, there has been a growing trend for medical and dental offices and practices to place aromatherapy diffusers containing lavender oil within waiting rooms to help alleviate patient anxiety. Since the latter is very common for virtually all patients regardless of the nature of the proposed treatment and even patient-doctor consultations, elevated blood pressures and anxiety are common occurrences. Numerous anecdotal reports indicate that this application of lavender oil aromatherapy has a pronounced anxiety-reducing influence on patients.

#### Mode of action

Traditionally, lavender oil aromatherapy was believed to be a nonspecific CAM modality that produced anxiolytic effects. Research studies over the past few years, however, clearly indicate that lavender oil produces its potent anxiolytic effect through inhibition of voltage-gated calcium channels (VOCCs), reduction of 5-HT serotonin receptor<sup>e</sup> activity and increased parasympathetic tone [27-28]. These effects are now ascribed to the principal components of lavender oil, namely the monoterpene alcohols linalool and (+)-borneol as well as linalool oxide (the oxidation/biotransformation product of linalool) [20,29-35]. The mechanism of action of essential oils with regard to curbing anxiety, however, may be determined in part by the pathway through which they act. On the other hand, it should be noted that most neurological anxiety studies reported in the literature have been performed on rodents and may have limitations when the experimental findings and conclusions are extended to humans.

#### Inhalation

After inhalation of lavender, the odor molecules combine with olfactory receptors located on the nasal olfactory epithelium which, in turn, transmit signals from the olfactory tracts to the olfactory bulbs and then to higher brain areas. It appears that most olfactory sensory neurons (OSNs) are specifically "tuned" to detect subsets of odorants with related structures. Odorants appear to activate a unique set of OSNs, usually two or more in combination. The postulated olfactory pathways have been used to explain how a 5 min exposure of essential oils can work quickly and significantly in mice [36]. Further, in both rats and humans, odor intensity grows systematically with the concentration, but the effect rapidly decreases due to adaptation. It has been postulated that this is the reason for chronic inhalation of essential oils not showing a greater effect than acute inhalation [20].

<sup>&</sup>lt;sup>e</sup>The serotonin receptors, 5-hydroxytryptamine or 5-HT receptors, are a group of G-protein-coupled receptors (G-protein-coupled receptors or GPCRs mediate most of the physiological responses to hormones, neurotransmitters and environmental stimulants) found in the central and peripheral nervous systems. These receptors mediate both excitatory and inhibitory neurotransmissions.

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Research studies indicate that inhalation of lavender oil paralleled the effects of chlordiazepoxide<sup>f</sup> (CDP) in up-regulating synthesis of serotonin in the pre-frontal cortex of rats. It was also noted that the co-administration of chlordiazepoxide with lavender oil tended to augment the effect of CDP on serotonin in the rat pre-frontal cortex and striatum [28].

#### **Neurotransmitter System**

In addition to the olfactory signal pathway, essential oils can be absorbed into the body and then into the blood through absorption by the lungs and nasal mucosa, with odor molecules being detected in the blood or brain tissues after topical administration and inhalation of essential oils [16]. This theory has been confirmed by several studies using anosmia<sup>g</sup> models with mice whose nasal cavities were treated such that they became anosmic. It was found that although anosmia did not interfere with the anxiolytic effect of lavender essential oil [37], linalool has no anxiolytic effect in anosmic mice [31]. The latter finding suggests that the anxiolytic effect of linalool is triggered only by olfactory input whereas the effects of lavender oil might be activated by entering the blood circulation, i.e. anxiolysis involves neurotransmitters. This indicates that anxiolytic effects do not rely solely on inhalation of essential oils, a finding that gives support to the efficacy of aroma massage therapy [1].

The neurotransmitters 5-HT, dopamine (DA), glutamic acid and GABA in the limbic system<sup>h</sup> are thought to be involved in the regulation of anxiety, with 5-HT being the most closely related to anxiety although dopamine has an important role in fear response. In particular, when the aversive/fright response reaction occurs, the dopamine level within the limbic system increases significantly. Likewise, GABA shows stress-related changes and there appears to be a balance between glutamate and GABA in the central nervous system (CNS).

Many studies have shown that the effects of essential oils on the CNS are related to these neurotransmitters. The anxiolytic effect of lavender essential oil was closely related to the 5-HT system, notably increasing the level of 5-HT in the rat striatum<sup>1</sup> and pre-frontal cortex [28].

#### The brain-gut connection

Over the past 15 years, the number of research studies performed on the gut microbiome has virtually exploded and one of the most important findings is the strong connection between gut microbes and brain health. One of the more exciting and certainly very interesting recent studies has been the finding that in mice, the bacterial species *Akkermansia muciniphilia* in the gut released higher levels of the metabolite nicotinamide, a form of vitamin B-3 [38,39]. Interestingly, it was noted that people with ALS (commonly known as Lou Gehrig's disease) have different gut microbiomes to those without the disease and the former had less nicotinamide in their cerebrospinal fluid than the latter. It was postulated that nicotinamide reduced oxidative stress in the nervous system, improved motor function and reduced the symptoms of ALS. The study supports the idea that ALS is influenced as much by the environment (and presumably diet) as genetics. It is also known that nicotinamide has a role in neuronal health and that of the central nervous system [40].

<sup>f</sup>Chlordiazepoxide (Librium) is used to treat anxiety and acute alcohol withdrawal as well as to relieve fear and anxiety before surgery through its effect on the brain and central nervous system. Its mechanism of action is thought to be through enhancement of the action of GABA (gamma-aminobutyric acid), the principal inhibitory neurotransmitter in the mature central nervous system.

<sup>g</sup>Anosmia is the term for the total or partial loss of the sense of smell. It may be caused by head injury, infection, blockage of the nose or the result of chemical and medicinal effects.

<sup>b</sup>The limbic system is a set of brain structures located on top of the brainstem that are involved in many human emotions and motivations, particularly those that are related to survival such as fear and anger. A part of the limbic system is the hippocampus which helps in the formation and retention of memories,

<sup>t</sup>The cluster of neurons known as the striatum are a critical component of the motor and reward systems, coordinating many aspects of cognition such as action planning, motivation, decision-making and reward-perception.

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There is increasing evidence that gut microbes interact with drugs and may affect both safety and efficacy [41]. A specific example of this is the use of levodopa (in combination with other drugs) for the treatment of Parkinson's disease, notably to control tremors and shakiness. Unfortunately, levodopa works inconsistently and this inconsistent action tentatively has been ascribed to the possible involvement of gut microbes and their enzymes.

As previously mentioned, the anxiolytic effects of lavender oil may be initiated by entering the blood circulation and these effects are found regardless of whether administered by oral, intraperitoneal injection or inhalation routes. Further, it was discussed earlier that the brain releases neurotransmitters into the gut following intake of essential oils with anxiolytic properties. In this context, the recent finding that serotonin assists bacteria to survive and colonize the gut is interesting and potentially highly significant [42]. These observations suggest that effective anxiety treatment may rely, at least in part, on the patient having a balanced and healthy gut microbiome. It also raises the question of whether regular ingestion of prebiotics and probiotics could be a useful adjunct in the prevention and treatment of GAD.

### Conclusion

The centuries-old CAM therapies for treating anxiety and the plethora of anecdotal reports of the anxiolytic actions of lavender essential oil have now been validated by intense scientific study for over a decade. An important finding was that the benefits of lavender essential oil, notably its anxiolytic effect, may operate regardless of whether it has been inhaled, ingested orally or applied topically through massage therapy. Although there is no evidence of any adverse reactions resulting from inhalation of lavender essential oil, caution should be exercised with regard to oral administration.

Interestingly, it appears that chronic inhalation of essential oils does not exert a superior anxiolytic effect to acute inhalation, but this may be the result of adaptation or habituation to the undiluted essential oil. Reduced efficacy, however, may not be an issue with lavender oil distributed aerially with a diffuser. Further, inhalation of lavender essential oil together with water vapor will have a beneficial effect on the nasal cavities and sinuses.

A final word of caution is that only 100% pure and unadulterated lavender essential oil should be used in a diffuser. Lower cost essential oils usually contain various solvents and diluents which, as the recent alarming rise in deaths and lung problems related to vaping show, may have untoward effects on the respiratory and neurological systems.

## Appendix

Common signs of anxiety include:

- 1. Nausea, indigestion and diarrhea.
- 2. Stomach cramps.
- 3. Loss of appetite or unnatural hunger.
- 4. Irritable bowel syndrome (IBS).
- 5. Peptic ulcers.
- 6. Constant feelings of worry and tension.
- 7. Excessive concern over simple, everyday tasks.
- 8. Feeling of constantly being "on edge" or easily startled.
- 9. Irritability and mood swings.
- 10. Inability to relax.
- 11. Lightheadedness or shortness of breath.

- 12. Restlessness.
- 13. Unrealistic view of problems.
- 14. Difficulty in concentrating.
- 15. Perpetual tiredness.
- 16. Difficulty falling asleep or staying asleep.
- 17. Frequent headaches.
- 18. Depression symptoms.
- 19. Muscle tension, aches and body pains.
- 20. Trembling or twitching.
- 21. Difficulty swallowing.
- 22. Sweating.
- 23. Frequent urges to urinate and/or have a bowel movement.
- 24. Panic attacks.
- 25. Intense separation anxiety.
- 26. Alcohol and substance abuse.

## Bibliography

- 1. von Fraunhofer JA. "Essential oils from the ground up". LifeRich Publishing, Bloomington, IN (2019).
- 2. Schäfer L., *et al.* "Nocturnal olfactory stimulation for improvement of sleep quality in patients with posttraumatic stress disorder: A randomized exploratory intervention trial". *Journal of Traumatic Stress* 32.1 (2019): 130-140.
- Goel N., *et al.* "An olfactory stimulus modifies nighttime sleep in young men and women". *Chronobiology International* 22.5 (2005): 889-904.
- Hirokawa K., et al. "Effects of lavender aroma on sleep quality in healthy Japanese students". Perceptual and Motor Skills 114.1 (2012): 111-122.
- 5. Lytle J., *et al.* "Effect of lavender aromatherapy on vital signs and perceived quality of sleep in the intermediate care unit: a pilot study". *American Journal of Critical Care* 23.1 (2014): 24-29.
- 6. Lillehei AS and Halcon LL. "A systematic review of the effect of inhaled essential oils on sleep". *Journal of Alternative and Complementary Medicine* 20.6 (2014): 441-451.
- 7. Keshavarz Afshar M., *et al.* "Lavender fragrance essential oil and the quality of sleep in postpartum women". *Iranian Red Crescent Medical Journal* 17.4 (2015): e25880.
- 8. Dyer J., *et al.* "The use of aromasticks to help with sleep problems: A patient experience survey". *Complementary Therapies in Clinical Practice* 22 (2016): 51-58.
- 9. Roozbeh N., *et al.* "Effect of lavender on sleep, sexual desire, vasomotor, psychological and physical symptom among menopausal and elderly women: A systematic review". *Journal of Menopausal Medicine* 25.2 (2019): 88-93.

- 10. American Psychiatric Association. Diagnostic and statistical manual of mental disorders. 5<sup>th</sup> edition American Psychiatric Association, Arlington, VA (2013).
- 11. Kessler RC., *et al.* "The global burden of mental disorders: an update from the WHO World Mental Health (WMH) Surveys". *Social Psychiatry and Psychiatric Epidemiology* 18.1 (2009): 23-33.
- 12. McLean CP, *et al.* "Gender differences in anxiety disorders: prevalence, course of illness, comorbidity and burden of illness". *Journal of Psychiatric Research* 45.8 (2011): 1027-1035.
- 13. Phillips MR. "Can China's new mental health law substantially reduce the burden of illness attributable to mental disorders?". *Lancet* 381.9882 (2013): 1964-1966.
- 14. Phillips MR., *et al.* "Prevalence, treatment and associated disability of mental disorders in four provinces in China during 2001-05: An epidemiological survey". *Lancet* 373.9680 (2009): 2041-2053.
- 15. Kirsch I., *et al.* "Initial Severity and Antidepressant Benefits: A Meta-Analysis of Data Submitted to the Food and Drug Administration". *PLOS Medicine* 5.2 (2008): e45: 260-268.
- 16. Zhang N and Yao L. "Anxiolytic effect of essential oils and their constituents: A review". *Journal of Agricultural and Food Chemistry* 10 (2019): 1021-1040.
- 17. Lee MS., et al. "Aromatherapy for health care: An overview of systematic reviews". Maturitas 71.3 (2012): 257-260.
- 18. Bakkali F., et al. "Biological effects of essential oils A review". Food and Chemical Toxicology 46.2 (2008): 446-475.
- 19. Raut JS and Karuppayil SM. "A status review on the medicinal properties of essential oils". *Industrial Crops and Products* 62 (2014): 250-264.
- 20. Lee YL., *et al.* "A systematic review on the anxiolytic effects of aromatherapy in people with anxiety symptoms". *Journal of Alternative and Complementary Medicine* 17.2 (2011): 101-108.
- Perry R., et al. "Is lavender an anxiolytic drug? A systematic review of randomised clinical trials". Phytomedicine 19.8-9 (2012): 825-835.
- 22. Ghiasi A., et al. "A Systematic Review on the Anxiolytic Effect of Aromatherapy during the First Stage of Labor". Journal of Caring Sciences 8.1 (2019): 51-60.
- 23. Franco L, *et al.* "Both lavender fleur oil and unscented oil aromatherapy reduce preoperative anxiety in breast surgery patients: a randomized trial". *Journal of Clinical Anesthesia* 33 (2016): 243-249.
- 24. Woelk H and Schläfke S. "A multi-center, double-blind, randomised study of the Lavender oil preparation Silexan in comparison to Lorazepam for generalized anxiety disorder". *Phytomedicine* 17.2 (2010): 94-99.
- 25. Kasper S., et al. "Silexan in anxiety disorders: Clinical data and pharmacological background". The World Journal of Biological Psychiatry 19.6 (2018): 412-420.
- Malcolm BJ and Tallian K. "Essential oil of lavender in anxiety disorders: Ready for prime time?". Mental Health Clinician 7.4 (2018): 147-155.

- 27. Schuwald AM., *et al.* "Lavender oil-potent anxiolytic properties via modulating voltage dependent calcium channels". *PLOS One* 8.4 (2013): e59998.
- 28. Tsang HWH., *et al.* "Neurophysiological and behavioural effects of lavender oil in rats with experimentally induced anxiety". *Flavour and Fragrance Journal* 28.3 (2013): 168-173.
- 29. Linck VM., *et al.* "Effects of inhaled linalool in anxiety, social interaction and aggressive behavior in mice". *Phytomedicine* 17.8-9 (2010): 679-683.
- Caputo L., *et al.* "Lavandula angustifolia essential oil and linalool counteract social aversion induced by social defeat". *Molecules* 23.10 (2018): 2694.
- 31. Harada H., et al. "Linalool odor-induced anxiolytic effects in mice". Frontiers in Behavioral Neuroscience 12 (2018): 241.
- 32. Cline M., *et al.* "Investigation of the anxiolytic effects of linalool, a lavender extract, in the male Sprague-Dawley rat". *AANA Journal* 76.1 (2008): 47-52.
- 33. Souto-Maior FN., *et al.* "Anxiolytic-like effects of inhaled linalool oxide in experimental mouse anxiety models". *Pharmacology Biochemistry and Behavior* 100.2 (2011): 259-263.
- 34. Umezu T., *et al.* "Anticonflict effects of lavender oil and identification of its active constituents". *Pharmacology Biochemistry and Behavior* 85.4 (2006): 713-721.
- 35. Cao B., *et al.* "(+)-Borneol suppresses conditioned fear recall and anxiety-like behaviors in mice". *Biochemical and Biophysical Research Communications* 495.2 (2018): 1588-1593.
- Chioca LR., *et al.* "Anxiolytic-like effect of lavender essential oil inhalation in mice: Participation of serotonergic but not GABAA/ benzodiazepine neurotransmission". *Journal of Ethnopharmacology* 147.2 (2013): 412-418.
- 37. Shaw D., et al. "Anxiolytic effects of lavender oil inhalation on open-field behaviour in rats". Phytomedicine 14.9 (2007): 613-620.
- 38. Blacher E., et al. "Potential roles of gut microbiome and metabolites in modulating ALS in mice". Nature 572.7770 (2019): 474-480.
- 39. Satyanarayana M. "Gut microbes implicated in ALS development". Chemical and Engineering News 97.30 (2019): 3.
- 40. Williams AC and Hill LJ. "Nicotinamide's Ups and Downs: Consequences for Fertility, Development, Longevity and Diseases of Poverty and Affluence". *International Journal of Tryptophan Research* 11 (2018): 1178646918802289.
- 41. Satyanarayana M. "Gut microbes digest our medicines". Chemical and Engineering News 97.34 (2019): 22-25.
- 42. Fung TC., et al. "Intestinal serotonin and fluoxetine exposure modulate bacterial colonization in the gut". Nature Microbiology (2019).

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