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Lavender Essential Oil as an Adjuvant Therapy for Anxiety Disorders

Zafira Aliya Shafwa Putri Chambali[1], Hafid Algristian[2]
[12]Universitas Nahdlatul Ulama Surabaya, Indonesia
Correspondent: dr.hafid@unusa.ac.id[1]

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ABSTRACT: With more than 301 million sufferers worldwide, anxiety disorders have become one of the most widespread mental health difficulties that frequently seek accessible and effective treatment alternatives. Anxiety results from the brain's response to a stimulus or perceived threat that a person will attempt to avoid. The limitless potential of lavender essential oil (*Lavandula angustifolia*) as an adjuvant therapy for anxiety disorders is investigated in this study, emphasizing the anxiolytic qualities and mechanisms of action of the oil. Data were collected from electronic sources like PubMed, Google Scholar, and Scopus, using a literature review methodology after a thorough literature search, emphasizing studies released in the previous ten years. The results suggest that lavender essential oil regulates the limbic system, especially the amygdala, as a central emotional response. It targets GABA activity and affects monoamine neurotransmitters, mainly through its active components, linalool and linalyl acetate. The most efficient method of delivery was inhalation, which considerably reduced anxiety symptoms with minimum side effects. According to the study, lavender essential oil shows promise as a complementary therapy for anxiety, providing a safe, all-natural substitute for treating anxiety.

Keywords: Anxiety, Lavender Essential Oils, Therapy, Inhalation.

INTRODUCTION

In the past several years, there has been a growing interest in taking advantage of essential oils as an adjuvant therapy for the treatment of anxiety concerns. the most widely used essential oil is lavender *(Lavandula Angustifolia)*. The World Health Organization reports that 4% of people worldwide suffer from an anxiety condition; in 2019, 301 million individuals worldwide suffered from an anxiety disorder, making it the most frequent mental illness. As defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition, anxiety is a state of overwhelming fear that interferes with

day-to-day functioning. Anxiety is a result of the brain's response to a stimulus or perceived threat that a person will attempt to avoid anxiety or the absence of actual risk or a subjective feeling toward the person; anxiety disorder can manifest as disproportionately elevated fear and anxiety. There are several types of anxiety disorders, including separation anxiety, panic disorder, social anxiety, specific phobia, agoraphobia, and generalized anxiety disorder (GAD). These diseases can coexist with other mental health conditions. (Musami et al., 2021). In the United States, approximately 34% of people suffer from anxiety disorders, with the prevalence of panic disorder as low as 2% to 5%, agoraphobia at 2.6%, generalized anxiety disorder at 6%, and social anxiety disorder at 13%. It is thought that 5% to 10% of people have specific phobias, although less than 2% of people have selective mutism. If anxiety is left untreated, it can recur for a long time and cause difficulties in life. (Kothari & Cowan, 2023). According to Riset Kesehatan Dasar (RISKESDAS), in Indonesia, in 2018, 6.1% of Indonesians suffered from anxiety disorders, and by 2023, that number is expected to rise to 16% of the population.

Several studies have researched the beneficial effects of some alternative treatments on reducing anxiety, including music, art therapy, and aromatherapy. Various plant components, among them leaves, bark, flowers, buds, seeds, and peels, are capable of helping to extract essential oils. (Sattayakhom et al., 2023) Aromatherapy uses essential oils extracted by steam distillation from natural plant materials such as flowers, herbs, or trees. Aromatherapy, an adjuvant treatment, is a traditional method of inhaling essential oils to improve mental and physical wellness. Inhaled substances relax the autonomic nervous system, resulting in emotional and physical reactions, and can decrease anxiety symptoms. Through its actions on the limbic system via the olfactory system, particularly the hippocampus and amygdala, lavender produces psychological impacts by increasing GABA (gamma-aminobutyric acid) in the amygdala. Essential oils can be utilized in massages, baths, and inhalations. (Kushee et al., 2021).

Lavandula angustifolia, or lavender, is a common plant-based oil used in the practice of aromatherapy for multiple clinical purposes, including anxiety, depression, headaches, pain, sleeplessness, spasms, and nervousness. (Yoo & Park, 2023). Lavender comprises over 100 distinct chemicals, for example, terpenes like linalool, limonene, triterpenes, linalyl acetate, certain alcohols, ketones, and polyphenols, as well as coumarins, cineole, and flavonoids. Linalool is an important chemical because it is the principal active ingredient. Linalyl acetate is another significant molecule. The two substances act anxiolytically via gamma-aminobutyric acid (GABA-A) receptors. (Bavarsad et al., 2023). This plant contains linalyl acetate and linalool, which may boost the parasympathetic nervous system. Fortunately, linalool has sedative effects, linalyl acetate also possesses anesthetic qualities. (Aisyah et al., 2019). The World Health Organization (WHO), the European Scientific Cooperative on Phytotherapy (ESCOP), and the European Medicines Agency (EMA) have all certified this medicinal plant for treating overwhelming worry, tension, agitation, insomnia, and anxiety. (López et al., 2017).

In clinical practice, Anxiety can be managed by modifications to the lifestyle, with or without consuming medicine such as cognitive-behavioral therapy (CBT), selective serotonin reuptake inhibitors (SSRIs), or serotonin-norepinephrine reuptake inhibitors (SNRIs). Mental illness, especially

anxiety, can also be addressed with alternative therapies; one of them involves using essential oils as an agent. Essential oils have gained immense popularity for their remarkable ability to alleviate anxiety symptoms, offering a simple yet effective solution for those seeking relief. Their effectiveness depends on how they are applied; the best method is through the nasal-brain route. Based on this background, the researcher will review literature articles, such as "Lavender essential oil as an adjuvant therapy for anxiety disorders."anxiety disorders."

METHOD

This study employs a comprehensive literature review methodology, integrating data from several credible sources, including published clinical trials and meta-analyses, and synthesizing findings from peer-reviewed journals of the current body of literature. The data for this assessment had been collected through a comprehensive investigation of electronic databases ranging from PubMed, Google Scholar, ScienceDirect, and Scopus. The databases of materials incorporated research publications, journal articles, and review papers. These databases are selected for their comprehensive coverage of literature on health care and medical themes. Lavender essential oil's impact on anxiety symptoms is one of the leading data sources. The primary focus of the inclusion criteria was relevance to research impact that explored the psychological impacts of lavender essential oil on the neural system, and the effectiveness of treatment for anxiety symptoms; the studies should have been published in less than ten years. The exclusion criteria are studies published before 2015 andirrelevant research that has not focused on the beneficial effect of lavender essential oils regarding anxiety symptoms.

RESULTS AND DISCUSSION

Anxiety Disorders

The brain's response to a stimulus or threat that a person will intentionally seek to avoid is anxiety. Anxiety disorders are higher in the female population in comparison to the male population in all demographics; the reason why females experience more anxiety disorders than males is unclear, while some ideas have pointed to gonadal steroids. According to additional studies, women exhibit a broader range of life events perceived as stressful compared to men, who tend to respond to a narrower array of stressful situations. particularly those that impact them or close family members. (Musami et al., 2021) Anxiety was defined as an awareness of future dangers; it is not intended to be associated with fear, which is defined as the psychological and behavioral aspects of worrying. (Crocq, 2015). Anxiety, recognized as the pathological counterpart to normal fear, is characterized by variations in mood, cognition, behavior, and physiologic processes. According to the current theory, anxiety disorders are caused by a combination of environmental variables, such as stress, trauma, 25% of first-degree blood relatives demonstrate generalized anxiety disorder, medical conditions, or adversity in childhood, and genetic background, which shows up as neuropsychological and neurobiological dysfunctions. There

seems to be a stronger hereditary basis for some anxiety disorders than others, such as panic disorder. Stressful life situations are the primary cause of other anxiety disorders. Psychological processes, particularly individuals' interpretations of stressful experiences, are crucial in the etiology of anxiety. (Bandelow et al., 2017).

This incident often occurs during adolescence to early adulthood, but it can also start in adulthood or occur in childhood, with effects that continue into adulthood. It enhances the secretion of hormones, including cortisol, noradrenaline, and adrenaline, by influencing the mechanism of sympathetic nerve interactions. Stress activates the paraventricular nucleus (PVN) to secrete corticotropin-releasing hormone (CRH). The response of the brain's central nervous system (CNS) to anxiety is regulated by the receptive vagus nerve, the sympathetic nervous system (SN), and the hypothalamic-pituitary-adrenal (HPA) axis. This operates in the hypothalamus, resulting in the pituitary gland creating and releasing increased levels of adrenocorticotropic hormone (ACTH). Moreover, stressors activate your sympathetic nervous system's inflammation-promoting response, leading to the release of noradrenaline (NA) and adrenaline (AD) from the sympathetic nervous system's response and adrenal glands.(Lizarraga-Valderrama, 2021).

According to the Diagnostic and Statistical Manual of Mental Disorders (DSM-5), anxiety disorders are frequent non-psychotic mental disorders. Anxiety is an overwhelming sense of worry that impairs an individual's regular activities. (Donelli et al., 2019). The most recent version of the International Classification of Diseases and Related Health Issues (ICD-10) and the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), Anxiety disorders can be separated as generalized anxiety disorder (GAD), phobias, social anxiety disorder (SAD), selective mutism (SM), posttraumatic stress disorder (PTSD), panic disorder (PD) accompanied or absent agoraphobia, obsessive-compulsive disorder (OCD), and various problems classed under the general heading "anxiety disorders without further criteria." (Sartori & Singewald, 2019). Most research indicates that the incidence of social phobia, separation anxiety, and generalized anxiety is low, but the prevalence of specific phobias is higher. Post-traumatic stress disorder has the lowest prevalence, whereas obsessive-compulsive disorder has even lower rates. Anxiety disorders are defined as signs that refer to physiological manifestations, including palpitations, dyspnea, and vertigo, alongside anticipated anxiousness and avoidant attitudes, as well as extreme worry, social and behavioral apprehensions, and unanticipated or induced panic attacks. (Szuhany & Simon, 2022).

People with generalized anxiety disorder (GAD) spend months worrying excessively Concerning daily tasks, avoiding or looking for comfort in circumstances when the result is unknown, and worrying about potential problems. GAD often occurs as a co-morbid with other psychiatric disorders. Panic disorder is differentiated by unexpected episodes of panic or anxiety (generally short-lived, but can be so intense that the person fears they may collapse or die), worry about the attacks happening again, avoiding stressful circumstances, brief episodes of acute anxiousness, accompanied by a perception of imminent tragedy, along with physiological manifestations include respiratory discomfort, dizziness, and dyspnea are the things that commonly felt in a person with panic disorder. Social anxiety disorder (SAD) is defined by a person's fear of being the center of attention, their worry of saying or doing

something embarrassing, and their fear that others will notice and scrutinize them. Alternatively, it can be felt as anxiety and worry in social settings that cause people to shun social interaction. Likewise, studies show that those with SAD and GAD are particularly vulnerable to experience persistent or recurrent anxiety symptoms, particularly if these people also suffer from along concerned depressive illness. (Andrews et al., 2018). In contrast, specific phobia is typified by identical signs and actions but is brought on by a particular thing or circumstance. For example, a dread of specific creatures (most notably dogs, rats, and snakes); birds, insects (most notably spiders, wasps, or hornets); higher places, lifts, flight; things like driving, water, storms, the blood, and injections. (Jbireal & Azab, 2019)

After experiencing a traumatic incident, a patient could develop anxiety disorders such as post-traumatic stress disorder (PTSD) or acute stress disorder (ASD), enduring immediate physiological arousal in response to stimuli that trigger memories of the traumatic incident, and feeling as though they are returning to that moment. The former describes a more chronic type of the condition, whereas the latter happens in the short term. Based on frequent behaviors—compulsions—obsessive-compulsive disorder (OCD) helps to lower anxiety related to uncomfortable, intrusive ideas. Frequently seen actions include washing or cleaning in reaction to contamination worries or constantly ensuring that the flame is turned off in order to address fire safety concerns. Some people with compulsive self-doubt constantly review their work or seek excessive reassurance. (Jbireal & Azab, 2019)

The diagnostic criteria include trouble regulating worrying and extreme anxiety, and worry for a minimum period of six months. For six months, anxiety has been linked to three or more of the following symptoms.: anxiousness, tension or worried sensations, easily becoming exhausted, difficulty focusing or losing focus, irritability, muscular tension, poor sleep, and mood swings. These symptoms, which tend to be chronic, can range from faint, moderate or severe. Anxiety disorders frequently co-exist with other anxiety disorders, major depressive illness, physical symptom disorders, personality disorders, and the effects of drug disorders. Many anxiety disorders have a subjective sense of stress, as well as difficulties in sleep, focused attention, and social and/or job-related functioning. (Jbireal & Azab, 2019). To establish a psychiatric diagnosis, a person should have 6 of the 18 symptoms of anxiety, which are Motor Tension, muscle twitching or trembling, tense/stiff/sore muscles, inability to stay still, and quickly tired. Autonomic Hyperactivity: shortness of breath / feels heavy, heart palpitations, wet-cold palms, dry mouth, dizziness / floating sensation, nausea, diarrhea, stomach feels unwell, hot face/body shivers, urinating more often, difficulty swallowing/feels blocked. Hypervigilance and Reduced Perception: Feeling too sensitive, easily surprised/shocked, having difficulty concentrating, sleeping, and being easily irritated. The brain's chemical substances implicated in this condition comprise serotonin (5-HT), norepinephrine (NE), dopamine (DA), histamine (H), acetylcholine (ACh), and GABA. (Bavarsad et al., 2023).

According to an intriguing new line of research, worry activates various neurocircuits. The hippocampus and the amygdala, two important regulatory areas located in the brain's cerebral hemispheres, are brought to prominence by this line of inquiry. These locations are thought to activate the hypothalamic-pituitary-adrenocortical (HPA) axis. Among other things, the hippocampus and

amygdala regulate emotions and memory storage, respectively. The hippocampus is a vital organ in the process of memory, particularly when it comes to the time and location of events that have strong emotional overtones, meanwhile amygdala is critical to fear processing. The core region of the amygdala connects to many brain systems that are implicated in the physiological and behavioral responses to fear. The hippocampus and the amygdala are the two primary nuclei that make up the limbic system, which is recognized as the route that underlies emotions. The hippocampus, amygdala, and hypothalamus are anatomically connected.(Jbireal & Azab, 2019)

For the objective examination, the hypothalamic-pituitary-adrenocortical axis is activated in the neuroendocrine system, reacting to stress, which causes the glucocorticoid hormone cortisol to be released. Adrenaline and noradrenaline are released from the adrenal medulla throughout the bloodstream due to the sympathetic-adrenergic system being activated by the autonomic response. The primary glucocorticoid hormone in humans is cortisol, which is generated in the adrenal cortex. It is released through the hypothalamus-pituitary-adrenal axis in replied to many psychosocial events, including stress and anxiety. Endocrinological stress markers like cortisol are helpful for the objective assessment of psychosocial discomfort, including stress or anxiety. (Kim et al., 2021). Multiple neurotransmitter systems have currently been identified to be involved in any or all of the modulatory processes. The serotonergic and noradrenergic neurotransmitter systems are regarded as the most prevalent. It is widely accepted that both excessive and insufficient activation of the noradrenergic and serotonergic systems are involved. The monoamine neurotransmitter serotonin, also called 5-hydroxytryptamine (5-HT), is reabsorbed by presynaptic 5-HT transporters, preventing it from having postsynaptic activity. Each of these receptors has distinct subtypes, and there are in total seven groups formed from them (5-HT1 through 5-HT7). 5-HT1A, 5-HT2A, 5-HT1B, 5-HT2C, and 5-HT3 have all been linked to anxiety. Numerous studies have examined the significance and degree to which anxiety is influenced by imbalanced serotonergic neurotransmission. However, it is thought that norepinephrine-mediated neurotransmission abnormalities are a contributing factor to anxiety symptoms.(Ren et al., 2024)

The abnormal functioning of physiological response and the psychological assessment of this arousal are both the outcome of these systems being modulated and regulated by other neurological networks and routes in various sections of the brain. Many individuals believe that the development of this condition is brought on by a rise in the activity of the noradrenergic system and a decrease in the activity of the serotonin system. The function of corticosteroid regulation and the fact that cholecystokinin is a neurotransmitter that controls emotional moods and its connection to anxiety and stressor symptoms have garnered some focus. The activity of particular neural networks might be modulated by corticosteroids, which may possess a profound impact on the way the brain deals with fear-inducing experiences as well as behavior when it is stimulated by stress. Serotonin and GABA are inhibitory chemicals in the brain that attenuate the stress response, including extensive feedback mechanisms (Jbireal & Azab, 2019)

According to the American Psychiatric Association, having anxiety disorders could negatively impact a person's way of life, from thinking patterns to behavioral changes. If left untreated, anxiety

symptoms will persist and occur repeatedly over a long period, which can cause difficulties in socializing and disruption in daily life. Anxiety Perhaps addressed by cognitive–behavioral therapy (CBT) and with or without combination pharmacological medication such as synthetic antidepressants involving monoamine oxidase inhibitors, tricyclic antidepressants (TCAs), and selective serotonin reuptake inhibitors (SSRIs), which may induce excessive weight gain, exhaustion, sex difficulties, headache, drowsiness, constipation, and tachycardia. Improvement often requires 4 to 6 weeks. (Lizarraga-Valderrama, 2021). The adverse reactions of SSRIs include buzzing at the initiation of therapy, diminished emotional responses in certain individuals, gastrointestinal issues, lack of sleep, and sex difficulties, with warnings regarding an increase in these effects. Moreover, SSRIs, SNRIs, TCAs, and benzodiazepines have been correlated to a temporally constrained withdrawal syndrome. (Sartori & Singewald, 2019).

These factors have led to an upward trend in interest in and demand for alternative medications that ease anxiety and have minimal or no adverse effects. A successful approach for dealing with stress, anxiety, and depression involves alternative treatments such as massage and the practice of aromatherapy, which have recently garnered interest from researchers. (Aisyah et al., 2019). Lavender essential oil counts among the most potent and healthy choices for treating anxiety. There are two possible explanations for the modulation of anxiety: either an increase in electrical transmission via glutamate or an interference in inhibitory neurotransmission through gamma-aminobutyric acid (GABA). All of these pathways are important targets for the treatment of anxiety disorders because they play a large part in the control of anxiety. Both an imbalance in monoamine neurotransmitters (serotonin, dopamine, and noradrenaline) and an abnormality of the receptors for neurotransmitter molecules have been hypothesized to be associated with anxiety. (Yoo & Park, 2023)

Lavender Essential Oil

Aromatic plants produce diverse secondary metabolites that comprise essential oils (EOs). The most common chemical types included in essential oils (EOs) are monoterpenoids, sesquiterpenoids, benzenoids, and phenylpropanoids, with terpenes being the most prominent group. The three most prevalent substances in EOs are pinene, linalool, and limonene. The state of the plant's aromatic area, its geographical position, the method of extraction, and the time frame of extraction are some of the variables that can greatly affect the chemical makeup of EO. Additionally, there may be variations in the chemotypes of a given botanical and the drying process. Various extraction techniques are employed to create essential oils, including the process of steam distillation, evaporative distillation, hydro-distillation, and high-pressure distillation. Steam distillation is the most popular and extensively utilized process for the industrial synthesis of EOs. (Lizarraga-Valderrama, 2021). EOs can have a range of pharmacological actions that are specifically targeted to the central nervous system, including sedative, analgesic, antidepressant, anticonvulsant, neuroprotective, and anxiolytic properties. EOs have the potential to be utilized as a form of adjuvant therapy to prevent and alleviate symptoms tied to central neurological system-based disorders, including Alzheimer's disease (AD), anxiety, depression, dementia, and sleeplessness. (Soares et al., 2022) It was successfully demonstrated that

essential oils interfere with the simultaneously anti-inflammatory and pro-inflammatory chemical reactions of the central nervous system (CNS) brought on by stress. Essential oils of lavender can reduce anxiety by stimulating the GABAergic system. (Lizarraga-Valderrama, 2021). The most popular essential oil in the world is made from *Lavandula angustifolia* or lavender.

Lavandula angustifolia is a natural an odoriferous herb used in medicine in regions of France, Spain, and Italy. The flowers are violet to violet-blue in pigment and resemble the *Lamiaceae family* form. Numerous species with varying chemical properties exist, including Lavandula angustifolia (also known as *L. vera* or *L. officinalis*). Linalool and linalyl acetate are the principal components of L. angustifolia, the most broadly used lavender. Although linalool has a more significant proportion, it is the main active ingredient. Linalyl acetate (LA), detected in lavender oil, reveals anti-inflammatory properties by blocking NF-ϰB activation. Regarding the pharmacological effects of lavender, such as its supposedly sedative and soothing properties (Donelli et al., 2019). Referring to the European Medicines Agency's publication on lavender, lavender is a natural substance used for the following purposes: to help with sleep and soothe symptoms of psychological strain and exhaustion. Lavender oil is an essential oil that is steam-distilled from the lavender plant's flowers and stalks. The liquid is colorless or pale yellow and smells of herbs.

The chemical components in lavender have a calming effect and can prevent acetylcholine from being released. The primary components of the 0.5%–3 % essential oil found in lavender blossoms *(Lavandula angustifolia)* are linalyl acetate (30–60%) and linalool (20–50%). Lavender's linalyl and linalyl acetate can impact emotional states by stimulating the parasympathetic nervous system, which makes you feel better and more rested, as well as more energetic and calm. (Algristian et al., 2022). Lavender oil comprises 60–65% monoterpene alcohols (e.g., linalool, linalyl acetate, Lavandula acetate, cis-ocimene, limonene, cineole, terpinene-4-ol, camphor, Lavandula, and α-terpineol, α-pinene, β-caryophyllene, geraniol), non-terpenoid aliphatic compounds (e.g., 3-octanone, 3-octanol, 1-octen-3-ol, 1-octen-3-yl acetate). Lavender oil revealed estrogenic, spasmolytic, antimicrobial agent, and cutaneous repair properties in vitro. In vivo studies in rats and mice have proven analgesic, anticonvulsant, sedative, and anti-inflammatory effects. Topically, β-caryophyllene, a sesquiterpene, was observed to enhance rejuvenation of dermatological wounds, while Linalool (3,7-dimethylocta-1,6-dien-3-ol), a monoterpene, has an anxiolytic effect. The chemical compounds in lavender oil, especially limonene and perillyl alcohol, are potent inhibitors of cancer-promoting growth. Moreover, their recognized antimicrobial qualities stem from the substantial amount of phenolic chemicals in their composition, including carvacrol, eugenol, and thymol, while certain terpenes are also beneficial in mitigating cardiovascular illnesses. This effect is mediated through the olfactory system for the best result and can also be used topically or orally. Massage treatment using lavender essential oil is a topical course and was the most commonly utilized strategy of superficial use owing to the flow within the cutaneous, which empowers higher retention of the biochemical elements of oil are concentrated within the bloodstream, advancing the help of muscle pressure and diminishing the physiological impacts.(Kenda et al., 2022). Due to its sedative, antidepressant, antibacterial, antifungal, comforting, and antiemetic actions, it can ease nausea and vomiting. It has been proven that the use of lavender essential oil as an adjuvant therapy prior to surgical procedures can contribute to lowering heart rate,

systolic and diastolic blood pressure, pain levels, and anxiety, while simultaneously increasing oxygen saturation values. In terms of the safety of utilizing lavender essential oil, a study found that a concentration of 0.1% of the essential oil was the most safely stored concentration for all of the formulations that were examined. (de Melo Alves Silva et al., 2023)

"Aromatherapy" is derived from the words "aroma" (which refers to a scent or fragrance) and "therapy" (which means treatment). It is a natural method of mending the mind, body, and spirit. Certain historical cultures, such as Egypt, India, and China, have taken up this as a conventional complementary and alternative therapy for a minimum of 6,000 years. According to the International Organization for Standardization, essential oils are theoretically highly concentrated chemicals that emerge from flowers, leaves, roots, fruits, and stalks, through distillation from materials, and are the principal medicinal substances that are utilized in aromatherapy. (Ali et al., 2015). Aromatherapy, with its oils, has shown incredible results, especially for treating anxiety and sleep disturbances. Aromatherapy, by inhaling the essential oil of lavender, and breathing techniques can be regarded as effective ways for managing anxiety in individuals who are depressed. (Bavarsad et al., 2023a). About the specifications established by the National Institute for Health and Care Excellence (NICE), alternatives to pharmaceutical treatment should be taken into consideration as adjuvant therapy for treating illness. Physical and mental illnesses can be modified by essential oils via three primary pathways: the olfactory mechanism, the integumentary nervous system, and the system of digestion. Essential oils can cause these effects. Following the addition of a few drops of essential oil to a carrier oil, such as olive oil, coconut oil, argan oil, or any other oil, the topical application requires rubbing the skin or the region of interest in order to facilitate the absorption of the essential oil by the pores and hair follicles. For patients to use inhalation treatment, a diffuser, humidifier, or soaking gauze containing essential oil is maintained close by for the patient to inhale. In addition to being specialized sensory nerves, the olfactory nerves that give us our sense of smell are stimulated when essential oils are inhaled. There is some evidence that aromatherapy through inhalation may be beneficial in the prevention or management or controlling of psychological conditions, including anxiety, depression, and sleep difficulties. However, the way that is both the quickest and the easiest to use is inhalation via the olfactory system or the nasal-brain pathways. (Soares et al., 2022)

Mechanism of Action

The essential oil can be used via topical, inhalation, and oral; it can affect the hypothalamus exactly amygdala as an emotion and memory through the olfactory system. Not only does the olfactory system contribute to this intervention, but the primary neural system of the human being is also directly impacted by odorant molecules. The olfactory system interacts with the limbic system, prefrontal brain, and hypothalamus to influence bodily reactions in both physiology and pathology. The hypothalamus–hypophysis–adrenal axis might experience a lower level of corticotropin-releasing hormone (CRH) as a result of essential oils and emotional cues from the hippocampus, amygdala, and prefrontal cortex. A diminished secretion of the stress hormone cortisol in the serum is attributable

to decreasing ACTH levels. Aromatherapy was effective in diverting participants' attention from pain, tension, and anxiety.(Sattayakhom et al., 2023)

Studies on both healthy individuals and those who suffer from anxiety have demonstrated the involvement of several molecules and neurotransmitters in anxiety. This condition is associated with neurotransmitters such as serotonin (5-HT), norepinephrine (NE), dopamine (DA), AchLEO, histamine (H), and GABA that are significantly displaced. 3-citalopram. Lavender essential oil has been studied for its capacity to engage with neuropharmacological substrates such as MAO-A, the serotonin transporter (SERT), and ionotropic receptors (GABAA and NMDA). It has also been shown to have protective properties against neurotoxic chemicals like amyloid peptide, hydrogen peroxide, and malonate. (López et al., 2017). Anxiolytic effects can also be induced by ion channel modulators. Anxiety is said to be reduced by blocking these channels with a variety of pharmaceutical substances, including ethosuximide, plant extracts of linalool or rosemary, with corticotropin-releasing factor. The substances for neuropeptide receptors, such as selective NK2 receptor antagonists and peptide CRF receptor antagonists, can generate anxiolytic-like effects. The lavender essence revealed an anxiolytic effect comparable to the effects of low-dose diazepam, and benzodiazepines may eventually be replaced by compounds that target particular neuropeptide receptors to treat anxiety disorders. Lavender might possess anxiolytic effects because its primary components can block tension-dependent calcium channels in mouse synaptosomes and antagonize the glutamatergic NMDA receptor. Lavender's anxiolytic, such as linalool interaction qualities, may stem from its primary constituents' ability by blocking tension-dependent calcium channels in a mouse synaptic membranes and primary hippocampus neurons. The inhibition of serotonin transporters (SERT) also influences constituents of GABA receptors, and both the sympathetic and parasympathetic systems reduce blood pressure. Affecting the 5HT-1A receptor in certain regions (the insula, temporal gyrus, fusiform gyrus, hippocampus, and anterior cingulate cortex) may mediate another potential action method by decreasing its expression and binding potential. This impact is similar to that of selective serotonin reuptake inhibitors (SSRIs), which are pharmaceutical treatments for depression and anxiety. (Donelli et al., 2019)

The GC-MS tests indicated that lavender essential oil predominantly comprised the following monoterpenes: linalyl acetate (52.1%), linalool (37.4%), geranyl acetate (5.4%), and β-caryophyllene (5.1%). The capacity of LEO to bind to the NMDA receptor, as determined by the CGP39653 binding experiment, was remarkable. The preferred chemical for NMDA receptor labeling is the competitive antagonist CGP39653. In drug research and development, NMDA receptors are regarded as pharmacological targets since they are neurochemically classified as ionotropic glutamate-receptor neurons (iGLURs), which have been associated with particular neurological and mental disorders. The binding of CGP39653 was displaced by LEO in a dependent on dosage approach, indicating that by altering NMDA receptors, this oil may possess nerve-calming properties. This affinity is being described for the first time and may help clarify the compound's anti-agitation characteristics. (López et al., 2017). It is possible that lavender essential oils possess an impact comparable to that of an antidepressant through this particular transporter since it binds to the SERT in an approach that is concentration-dependent. This effect was also observed for linalool, a principal constituent of

lavender essential oil. Linalool inhibits serotonergic targets, including the SERT, potentially revealing the antidepressant-like effects of lavender. (Yap et al., 2019) Lavender Essential Oils were also discovered to be active in the binding test for CGP39653—the NMDA receptor's affinity profile, along with the IC50 and Ki values. Lavender was found to be significantly active, exhibiting a distinct dose-response pattern. Linalool and linalyl acetate were additionally analyzed in this context, and NMDA receptor binding characteristics were demonstrated. (López et al., 2017). The purpose of taking advantage of lavender essential oils to treat anxiety targets the amygdala as a central emotional response, especially GABA, monoamine neurotransmitters (serotonin, dopamine, noradrenaline), and homeostasis with neurotransmitter receptors.

The limbic system functions as a center for the processing of discomfort, satisfaction, anger, worry, anxiety, depression, and a range of other emotions. The limbic system acquires information from the auditory, visual, and olfactory systems. The amygdala, a limbic system component, plays an important role in emotional responses to aromas. At the same time, the hippocampus plays an essential role in how memory works. and odor recognition. Lavender can affect the quantity of neurological chemicals such as GABA (γ-aminobutyric acid) and neuromonoamines. GABA is a neurotransmitter that has a calming effect on the brain. (Kianpour et al., 2018). The response that occurs is to stimulate neurochemical cells in the brain to increase GABA, which will inhibit monoamine neurons in the form of dopaminergic, noradrenergic, and serotoninergic so that it causes projections to the cerebral cortex, which will provide a stimulating effect and stimulate the autonomic nervous system which will reduce anxiety by providing a sedative and relaxing effect. (Yowana et al., 2021).

Numerous physiological scales were examined. Electroencephalography assesses the arousal and sedative qualities in humans and animals at the earliest stage of alertness. There was a sedative effect from lavender oil. It was common practice to test the autonomic nervous system following the level of alertness. Heart rate variability (HRV), respiratory rate (RR), blood pressure (BP), and heart rate (HR) were all assessed. By inhaling it, lavender demonstrated a change in autonomic nervous system (ANS) activity. Following a massage with lavender oils, the ANS was also impacted by lowering blood pressure and heart rate. Contrary to alertness, lavender enhances the objective quality of sleep. Lavender impacted salivary chromogranin A and cortisol hormone levels as a stress hormone in response to olfactory stimuli. It also influenced subjective emotional assessments. Most applications of essential oils have been demonstrated to alleviate stress and bad emotions by decreasing stress hormones and enhancing parasympathetic activation, exhibiting anxiolytic effects. Ultimately, lavender modified behaviors and cognitive functions at the most advanced levels. Linalool, which is found in lavender, has a calming effect just like that of diazepam, which reduces stress-related behaviors in girls. Lavender may alter cardiovascular parameters and cortisol secretion by modifying autonomic nervous system function. (Sattayakhom et al., 2023)

Lavender oil has several purposes in pain management. Linalool is thought to either suppress substance P's release or work antagonistically upon its interface, neurokinin-1 (NK-1). Furthermore, through the inhibition of the active field potentials that are produced as a result of the antidromic stimulation of the hilus, linalool tends to turn on the voltage-gated Na+ channels that are located in

the granular neurons of the dentate gyrus of the hippocampus. Additionally, it can reduce peripheral and central nerve excitability, which modulates neurogenic and inflammatory pain. Furthermore, in neuropathic pain models, lavender oil significantly reduced antinociception by inhibiting the breakdown of FAAH (fatty acid amide hydrolase) and MAGL (monoacylglycerol lipase). This was achieved by raising endocannabinoid levels. It increases AEA (anandamide), which has been linked to the modulation of emotions. (Soares et al., 2022).

The drugs or chemicals are capable of being carried intracellularly within the nerve axon through the intake of the substance. The drug will be absorbed by the nasal mucosa. In order to circumvent the blood-brain barrier, it must first be absorbed by the nasal mucosa, after which it will enter the systemic circulation. The formulation's qualities, such as increasing permeability and decreasing mucociliary clearance, can also be used to control this route. Dosage forms, molecular weight, pH, the degree of ionization of medications, osmolarity, viscosity, formulation penetration, mucociliary clearance, enzymatic degradation, and efflux transporters are some examples of the several significant parameters that are involved in the preparation of pharmaceuticals. These factors were significant for both local and systemic distribution, as well as for single or repeated dosages. Because the pH in the nasal cavity ranges from 5.5 to 6.5, molecules with a molecular weight that is less than 300 Da will be absorbed within a short amount of time, and nasal permeation will occur rapidly. Generally speaking, it remains unaffected by any other properties. To optimize drug use, researchers have concentrated on using nanocarrier technology that allows for the administration of medications to the brain through the nasal passages, taking into account dosages and Ranges of functioning during inhalation delivery. Although nose-to-brain drug delivery has several benefits, nose-to-brain medication delivery can reduce bioavailability due to sensitive drugs being broken down by enzymes on the mucosal surface, high clearance, and limitations caused by the nasal cavity's anatomy can all limit effectiveness. (de Barros et al., 2022)

Lavender Efficacy in Anxiety Disorders

In 1973, the French chemist and perfumer Gattefosse was the first to introduce the term "aromatherapy" in his book titled Aromatherapy. The earliest studies on lavender essential oil were carried out in 1928 by French scientist and perfumer René-Maurice Gattefossé. Despite easing the burning pain, Gattefossé conducted an experimental investigation of lavender essential oil as an adjuvant therapy. According to research, lavender essential oil could speed up and lessen pain from skin burning. Researchers have discovered that essential oils have healing qualities that help improve skin health, sleep issues, and discomfort. (Yoo & Park, 2023). Since that study, further research has been conducted on the adverse effects of essential oils in various areas, including anxiety reduction and relaxation. A study conducted in vivo demonstrated that inhaling lavender essential oil reduced, both male and female gerbils, exhibiting varying degrees of stress. The animals were given the EO dairy to inhale for 30 minutes over two weeks, which significantly increased the number of submissions that are open in the EPM evaluation. These outcomes were comparable to the same study's DZP (1 mg/kg i.p.) effect. Lavender essential oil can also reduce worry, which is one symptom

of anxiety. A trial that was grouped and randomized, and controlled measured anxiety levels among 340 patients waiting for a planned dental appointment. The patients were split into two groups: those with no odor and those with a lavender EO scent. According to the Modified Dental Anxiety Scale (MDAS), all groups displayed similar levels of generalized anxiety; however, the intervention group's current anxiety, as measured by the STAI-6, was considerably lower.(Lizarraga-Valderrama, 2021).

In Germany, a standardized and approved product of essential oil extract of Lavandula angustifolia (SLO) for oral consumption has been produced and licensed for use in the treatment of subsyndromal anxiety. Both linalyl acetate and linalyl linalool, which are the two primary components of lavender oil, may be found in the SLO product (Silexan, manufactured by W. Spitzner Arzneimittelfabrik GmbH in Ettlingen, Germany) in concentrations of between 36.8% and 34.2%, respectively. Additionally, research utilizing lavender was carried out in Germany in the year 2016. For this study, participants had to be patients suffering from moderate to severe anxiety disorders. There were a total of ten participants. Subjects will be asked to consume oral lavender essential oil products that have been standardized and guaranteed safe by the German Food and Drug Administration, with a dose of 80 mg or around 0.1 ml, twice daily for 6 weeks. The anxiety measurement tool in this study used the Hamilton Anxiety Rating Scale (HRS-A). Through this study, a decrease in anxiety symptoms can be identified as measured using the HRS-A both before and after treatment. When measured using the HRS-A, it was seen that the subjects experienced a decrease in points from 22 points before treatment to 12 after treatment, demonstrating a decrease in anxiety symptoms experienced and an enhancement in overall quality of life. It can be concluded that lavender can reduce symptoms of anxiety and sleep disorders and provide anxiolytic effects, such as comfort without sedation and dependence. The effectiveness of lavender in reducing anxiety symptoms can be seen within 2 weeks. The siloxane treatment improved overall mental and physical health without causing any undesirable side effects, and it had a notable positive impact on the length and quality of sleep. (Malcolm & Tallian, 2017)

According to Kang's research, Aromatherapy using a single lavender essential oil had an anxiolytic effect on both self-reported anxiety and physiological indications of anxiety, which can include heart rate, blood pressure, cortisol, or CgA, which are considered to be significant indicators of anxiety. Not one of the adverse effects was reported in the reviewed articles. Thus, lavender aromatherapy was found to have a positive anxiolytic effect on both the mental and physical elements of anxiety, suggesting that it could be a generally safe anxiolytic intervention. (Kang et al., 2019). A study has been conducted. Lavender's effects on anxiety, depression, and physiological markers were investigated by a systematic review and meta-analysis that adhered to PRISMA principles with specific eligibility criteria. The total population for examination anxiety is 3906 participants (control 1951 and experimental lavender 1955) who were randomized in the anxiety meta-analysis, and 3825 persons (control 1908 and experimental lavender 1917) were examined. The study populations for anxiety consisted of pregnant or postpartum women, individuals who suffered from anxiety and/or depressive disorders, those who were seriously ill with heart conditions or in intensive care units, healthy students in stressful situations, and patients undergoing surgery or invasive procedures. The participants in the experimental group were given lavender using one of four different methods of administration: inhalation, massage, tea, or oral preparation (siloxane). The participants who were assigned to the

control group were given either regular or routine care, a placebo, or no therapy at all. Measures of anxiety were either standardized (using a visual analog scale) or validated (using the Hamilton Anxiety Scale, the Beck Anxiety Inventory, the Depression Anxiety Stress Scale, the Hospital Anxiety and Depression Scale, the Modified Dental Anxiety Scale, the State-Trait Anxiety Inventory, or the Zung Self-Rating Scale). Other than the effects of massage and siloxane, the total impact of inhalation was found to be the biggest, as determined by the subgroup analysis that was conducted based on the mode of administration. This research indicates that inhaling lavender oil can significantly reduce anxiety in situations that cause much worry. Lavender essential oil inhalation can be suggested as a successful strategy for reducing anxiety in those experiencing a variety of anxiety-related issues. (Kim et al., 2021)

The lavender essential oil exhibits a notable anti-inflammatory effect. In a study conducted on animal subjects, lavender oil demonstrated anti-inflammatory activity in comparison to dexamethasone. The involvement of G protein-coupled receptors is critical in this mechanism, as they interact with one of the intercellular second messenger systems. The antinociceptive properties and anti-inflammatory activity are intricately interconnected. When pain is present, inflammation is frequently present at the same time. Medications that are classified as non-steroidal anti-inflammatory medicines have been utilized widely in the practice of dentistry to manage nociception. Alternative methods of pain management are now being developed as a result of the adverse effects that are linked to the pharmaceuticals that are already being used. There is a need for research in order to expound further on this subject. There is evidence that lavender essential oil possesses antinociceptive qualities, and this evidence has been positively assessed. Based on research conducted at King's College London, the state-trait anxiety scores of patients undergoing dental procedures who were given aromatherapy with lavender essential oil were significantly lower than those who did not receive such therapy, indicating the promising therapeutic potential of lavender essential oil. In a separate study, emotions, alertness, tranquility, and anxiety parameters were assessed using a comparative analysis of lavender scent and music therapy, with aromatherapy with lavender fragrance producing greater results. The influence of lavender essential oil on serotonin neurotransmission through 5-HT receptors may be the underlying mechanism that is responsible for this effect. Furthermore, studies have identified a correlation between vital physiological signs and the application of aromatherapy incorporating lavender. Specifically, a notable reduction in postoperative blood pressure has been observed in patients receiving aromatherapy during dental procedures. Moreover, the intranasal application of lavender and fennel has demonstrated a reduction in salivary cortisol levels, which are known to elevate in response to anxiety. (Hugar et al., 2022)

Applied lavender cream topically in healthy pregnant or postpartum women significantly reduced stress, anxiety, and depression. All eleven trials in the study used anxiety level measurement tools, and ten of them found that inhaling lavender oil significantly reduced anxiety. Moreover, inhaling lavender essential oils helped reduce anxiety in the children's anxiety intervention group prior to tooth extraction, in postmenopausal women who were diagnosed with depression and received treatment for four weeks, in adult patients who went through general surgery, in elderly patients who were awaiting surgery for benign prostate hyperplasia, in women who were undergoing intrauterine

insemination, in adult patients who were receiving trigger indicate injections for myofascial pain syndrome, in adult patients who were getting electroconvulsive therapy, and in adult patients who were waiting for cataract surgery. These routes of drug administration through inhalation are defined by an extensive range of advantages, including greater patient compliance, high safety, amazing simplicity in administration, early commencement of action, reduced systemic exposure, and inexpensive and noninvasive. Based on the experiment and studies, this lavender oil formulation is safe for treating the symptoms of anxiety disorders. In summary, the lavender essential oil is a safe substitute for anxiolytics, sedatives, and relaxation. Its effects are linked to a GABAergic system and neurotransmitter interaction in the amygdala. An increase in neurotransmitters such as serotonin levels explains these effects, while linalool's action on gamma-aminobutyric acid receptors influences the GABAergic pathway to produce a sedative effect, and lower cortisol levels by the hypothalamic-pituitary-adrenal axis is the mechanism via which this is triggered. (Yoo & Park, 2023)

Adverse Effect

Aromatherapy is one of the complementary therapies that draws interest from families, practitioners, and patients as it seems not likely to produce adverse effects. Essential oils are generally safe and have minimal side effects and withdrawal. Topical application of lavender essential oil on human skin can use a dose of 2-5%. However, if applied using a nasal spray on the skin and without proper dilution, lavender essential oil can trigger allergic reactions such as itching, redness of the skin, or swelling. According to studies, a 1% dilution is the right amount because a nasal spray can increase plasma concentration in the blood up to 2.6 times more than oral/topical drugs.(de Barros et al., 2022).

However, some side effects can arise due to the application of essential oils, such as skin irritation, which can occur as a direct effect of an allergic reaction, such as itching, red rashes, or dermatitis. Skin irritation also depends on the level of sensitivity of a person's skin. Toxic to the body, essential oil vapor can reduce stress, but can also be toxic if exposed for too long. Exposure to essential oils for more than 6 hours per day can be toxic to the Respiratory tract. (Api et al., 2022). The application of essential oils, especially in the form of diffusers, can cause symptoms of irritation in the respiratory tract. Symptoms can be mild to severe, such as coughing, sneezing, shortness of breath, and anaphylaxis. (Hawkins, 2019). Several categories of patients, including children with burns, patients above the age of 65 who have mild to moderate dementia, patients undergoing breast reconstruction, and patients receiving coronary bypass surgery, continued to experience adverse effects.(Sattayakhom et al., 2023)

Lavender contains chemicals that may induce anticoagulant/antiplatelet effects and so increase the chance of bleeding when using medicines with comparable effects all at once. (Yeung et al., 2018). The majority of the adverse events linked to the use of siloxane in the examined trials were gastrointestinal issues, including nausea, eructation or breath odor, diarrhea till palpitation, and headache. However, no serious adverse events were discovered. (Yap et al., 2019).

CONCLUSION

Anxiety, which is described as the psychological and behavioral components of worrying, is a sensation of excessive fear that affects a person and interferes with their everyday activities, caused by genetic background and developmental stress, trauma, or adversity. Anxiety can cause problems in life if it is not managed well. Pharmacological medications or treatments can be used to address anxiety. Essential oils are a complementary therapy that can potentially treat it. In aromatherapy, lavender *(Lavandula angustifolia)* is an essential oil used for various therapeutic illnesses, including anxiety. The two primary components of *L. angustifolia*, linalyl acetate and linalool, influence the neurological system, particularly the amygdala. They target GABA and neuro-monoamines. They activate the parasympathetic nervous system and produce a relaxing effect that calms the individual. The most promising method of administering lavender essential oil as an adjuvant therapy for people with anxiety is inhalation, which produces minimal adverse effects and withdrawal symptoms.

Nevertheless, future studies should focus on more comprehensive and prolonged clinical trials and in-depth studies about the safety, side effects, and ideal dosages of lavender essential oils and the most promising route, either orally, topically, or inhaled.

To contextualize the results and direct future research, it is necessary to note several limitations in conducting this systematic review. In the first place, the inclusion criteria, which were intended to guarantee rigor and relevance, might have unintentionally left out relevant studies, which could have introduced selection bias. Secondly, methodological heterogeneity makes it challenging to synthesize results and restricts the generalizability of the conclusions. The data is currently sparse and inconsistent due to variances in the composition of the substance and quality of essential oils, the lack of rigorous clinical studies, and the lack of standardized outcome measures. Finally, even though strict screening and data extraction procedures were used to reduce subjectivity, the interpretive aspect of qualitative synthesis could introduce a degree of researcher bias. These restrictions emphasize the necessity of carefully interpreting the results and pointing out opportunities.

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