

REVIEW ARTICLE

Essential oils for pain management in palliative care: Molecular mechanisms, clinical evidence, and therapeutic potential

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Abstract

Pain is one of the most distressing symptoms experienced by patients in palliative care, often requiring integrative approaches to ensure effective and compassionate management. Essential oils, used in aromatherapy and topical applications, have emerged as complementary options for alleviating pain and enhancing quality of life. This narrative review explores the potential of essential oils in pain management from an aromatherapy perspective, focusing on their mechanisms of action, clinical effectiveness, and application in real-world palliative care settings. A comprehensive literature search was conducted using PubMed, Web of Science, Scopus, and b-on, without date or language restrictions. Included studies ranged from randomized controlled trials and observational studies to case reports and systematic reviews. Essential oils such as lavender, peppermint, eucalyptus, chamomile, and clove demonstrate analgesic, anti-inflammatory, and anxiolytic properties, with evidence supporting their use in managing cancer pain, neuropathic pain, postoperative discomfort, and musculoskeletal conditions. Real-world insights from hospice and palliative care environments highlight their benefits for physical symptom relief, relaxation, emotional well-being, and improved sleep. While existing data are promising, further high-quality research is needed to standardize protocols and confirm long-term safety and efficacy. Essential oils represent a gentle yet effective adjunct in holistic palliative pain care.

Keywords: Pain management; Aromatherapy; Essential oils; Palliative care; Complementary therapy

1. Introduction

Pain is one of the most prevalent and distressing symptoms experienced by individuals receiving palliative care. It affects physical functioning and significantly impacts emotional well-being and overall quality of life.^{1,2} Despite advancements in pharmacological pain management, many palliative care patients continue to experience unrelieved or partially controlled pain, often accompanied by adverse effects from medications. As a result, there is growing interest in integrative approaches that complement conventional therapies while addressing the multifaceted nature of suffering in palliative care.

Aromatherapy, the therapeutic use of essential oils derived from plants, has emerged as a gentle, non-invasive option that may enhance pain relief and promote relaxation, particularly in vulnerable and medically complex populations.³ Essential oils such as lavender, peppermint, eucalyptus, chamomile, and clove are known for their analgesic, anti-inflammatory, and anxiolytic properties. Their use through topical application, inhalation, or massage can modulate pain perception, reduce anxiety, and improve emotional resilience.

This review explores the role of essential oils in pain management for palliative care patients, focusing on their mechanisms of action, clinical effectiveness, and practical applications. By synthesizing current evidence and real-world experiences, the aim is to assess the potential of aromatherapy as a supportive tool in holistic palliative care.

2. Methods

This study is a narrative (non-systematic) review that aims to provide an integrative overview of the evidence regarding the use of essential oils for pain management in palliative care from an aromatherapy perspective. Unlike systematic reviews that follow predefined protocols such as the Preferred Reporting Items for Systematic Reviews and Meta-Analyses, this review adopted a narrative and interpretative approach, integrating findings from experimental and clinical studies to provide a comprehensive synthesis of the available evidence.

A targeted literature search was conducted using the b-on, PubMed, Web of Science, and Scopus databases (accessed January 9, 2025). The search strategy combined the keywords “essential oils,” “aromatherapy,” “pain management,” “analgesic,” “palliative care,” and “complementary therapies” using Boolean operators (AND, OR). No restrictions on publication year were applied.

Studies were considered if they investigated the chemical composition, biological activities, or therapeutic

applications of essential oils or their bioactive constituents related to pain relief, including *in vitro*, animal, and clinical studies. Publications specifically addressing the use of essential oils in palliative care settings were also included. The identified records were screened for relevance based on their titles and abstracts; duplicate records were removed; and studies were selected based on their scientific relevance, methodological quality, and contribution to the objectives of this review.

As this is a narrative review, the literature search was designed to identify representative and relevant evidence rather than to achieve an exhaustive systematic retrieval. Consequently, a formal Preferred Reporting Items for Systematic Reviews and Meta-Analyses flow diagram and quantitative reporting of study selection were not considered applicable.

3. An overview of pain

Pain is a complex subjective experience and is one of the most prevalent and distressing symptoms in patients receiving palliative care. Its presence profoundly affects the quality of life, interfering with the patient’s physical well-being and emotional, psychological, social, and spiritual state. In palliative care, the approach to pain goes far beyond the simple administration of analgesics; it is a multidimensional intervention centered on the person and their needs.⁴

Pain in the palliative context can have a variety of origins and can be classified into different types: nociceptive pain results from tissue damage and is generally described as somatic or visceral pain; neuropathic pain results from damage to the central or peripheral nervous system; and total pain, which encompasses not only the physical aspects of pain but also the emotional, social, and spiritual components.⁵⁻⁷

Studies indicate that pain in palliative patients is often associated with comorbidities such as anxiety, depression, and deterioration in quality of life.⁶ Therefore, its assessment requires attentive listening, empathetic communication, and validated instruments to measure intensity, location, characteristics, and impact on daily life.

A rigorous pain assessment is essential to ensure effective symptom control. Instruments like the Visual Analog Scale are widely used to quantify pain intensity. However, it is essential to consider factors such as age, cognitive ability, and cultural aspects that can influence the perception and expression of pain.

Effective pain control requires an individualized therapeutic plan, which can include medication (such as opioids, analgesic adjuvants, and anti-inflammatories),

physical interventions (such as physiotherapy or massages), psychological support, and complementary therapies. It is important to stress that the aim is not just to eliminate the pain but to ensure that the patient can live with dignity, comfort, and as much autonomy as possible.^{8,9}

In addition, it is essential to involve family and caregivers in the pain control process, thereby promoting a strong, informed support network. Pain is not just a physical phenomenon; it is a subjective and complex experience that requires an attentive, compassionate, and competent approach from the palliative care team.

In summary, treating pain in palliative care is an ethical and professional imperative. It is a commitment to humanizing care, relieving suffering, and respecting each person's individuality throughout their life journey.

3.1. Definition and classification of pain

Pain is a complex sensory and emotional experience vital to human survival, as it alerts us to potential tissue damage. Understanding the mechanisms underlying pain is essential for developing effective therapeutic interventions, especially in the context of chronic pain, which affects millions of people worldwide.

In 2020, the International Association for the Study of Pain revised the definition of pain to "an unpleasant sensory and emotional experience associated with, or similar to that associated with, actual or potential tissue injury".¹⁰ This definition recognizes the subjective nature of pain and the influence of biological, psychological, and social factors on its perception.

Pain can be classified into different categories, including nociceptive, neuropathic, and nociplastic pain. Nociceptive pain results from the activation of nociceptors in response to potentially harmful stimuli, such as a burn or cut. Neuropathic pain is caused by injury or disease of the somatosensory nervous system, such as diabetic neuropathy. Nociceptive pain refers to conditions in which nociception is altered without evidence of tissue damage or damage to the nervous system, such as fibromyalgia.

3.2. Mechanisms of pain transduction and transmission

Pain perception begins with transduction, in which nociceptors convert noxious stimuli into electrical signals at their free nerve terminals in various tissues.¹¹ Mechanical, thermal, or chemical stimuli can activate these nociceptors. Once activated, the signals are transmitted via primary afferent fibers to the spinal cord. The fast-conducting A δ fibers are associated with acute, well-localized pain, while the slower-conducting C fibers are related to diffuse, persistent pain.¹²

In the spinal cord, nociceptive signals are modulated before being transmitted to the brain. Interneurons in the dorsal horn of the spinal cord can amplify or inhibit pain signals, influencing the final perception of pain.¹³

3.3. Pain modulation and the gate theory

Pain modulation involves mechanisms that can increase or decrease the transmission of nociceptive signals. The Gate Theory, proposed by Melzack and Wall,¹⁴ suggests that the activation of large-diameter nerve fibers can inhibit the transmission of pain signals in small-diameter fibers in the spinal cord, thus modulating pain perception. This mechanism, for example, explains pain relief through tactile stimulation or acupuncture.¹⁴

In addition, descending brain pathways can modulate pain by releasing neurotransmitters such as serotonin and norepinephrine, which can inhibit or facilitate nociceptive transmission in the spinal cord.

3.4. Peripheral and central sensitization

After tissue injury, inflammatory mediators such as prostaglandins and bradykinin are released, leading to peripheral sensitization.¹⁰ This process lowers the nociceptors' activation threshold, leading to hyperalgesia (increased pain sensitivity).

Persistent stimulation of nociceptors can induce changes in the excitability of dorsal horn neurons, a phenomenon known as central sensitization, which contributes to the maintenance of chronic pain.¹⁵ Studies indicate that the persistent activation of N-methyl-D-aspartate receptors and the continuous release of excitatory neurotransmitters, such as glutamate, in the dorsal horn of the spinal cord amplify pain signals, resulting in hyperalgesia and allodynia (painful perception of normally non-painful stimuli).^{15,16}

3.5. Neurobiological mechanisms of chronic pain

Chronic pain involves complex alterations in the nervous system, including synaptic plasticity and dysfunction of descending inhibitory pathways. Studies indicate that persistent activation of N-methyl-D-aspartate receptors and the continuous release of excitatory neurotransmitters, such as glutamate, in the dorsal horn of the spinal cord amplify pain signals, leading to hyperalgesia and allodynia. In addition, dysfunctions in specific brain networks, such as the default mode and salient networks, can increase pain perception and hinder its inhibitory control.¹⁷

3.6. Psychological and social factors in the perception of pain

Pain is a subjective experience influenced by psychological and social factors. Anxiety, depression, and stress can

amplify the perception of pain, while social support and effective coping strategies can mitigate it. Recent studies highlight the interrelationship between chronic pain and psychiatric disorders, suggesting that therapeutic approaches that take these factors into account may be more effective in managing chronic pain.^{18,19}

3.7. Recent advances in understanding pain

In recent years, research into chronic pain has advanced significantly, with particular attention to epigenetic mechanisms, demonstrating that chemical modifications in DNA, without altering its sequence, can influence individual sensitivity to pain and the effectiveness of therapeutic interventions.²⁰ At the same time, functional neuroimaging studies have identified changes in connectivity between brain regions involved in the perception and modulation of pain, contributing to a deeper understanding of the neurobiological basis of persistent pain.^{21,22}

4. Essential oils for pain management

4.1. Mechanisms of action: How essential oils may influence pain pathways

Essential oils exert their analgesic effects through several interconnected mechanisms. When inhaled or applied topically, the volatile compounds in essential oils interact with the olfactory and somatosensory systems. Upon inhalation, aromatic molecules stimulate olfactory receptors, sending signals to the limbic system, particularly the amygdala and hypothalamus, which regulate pain perception and emotional responses. This can modulate

the release of neurochemicals such as endorphins and serotonin, which are known to alleviate pain.²³⁻²⁵

Topically applied essential oils penetrate the skin and interact with underlying tissues. Bioactive compounds such as linalool, menthol, and eugenol can influence peripheral and central pain pathways by inhibiting pro-inflammatory mediators, such as prostaglandins and cytokines, modulating ion channels, and reducing oxidative stress.²⁶⁻²⁸ These actions may reduce pain sensitivity and inflammation. Moreover, essential oils are thought to interact with the transient receptor potential (TRP) channels, which play a key role in the perception of pain and temperature.^{29,30}

4.2. Commonly used essential oils and their analgesic properties

Several essential oils have been studied for their analgesic properties, making them valuable in palliative care.

4.2.1. Lavender

Lavender essential oil (*Lavandula angustifolia*) is one of the most extensively studied essential oils in pain management. Its primary bioactive compounds, linalool and linalyl acetate (Figure 1), have demonstrated significant anti-inflammatory, analgesic, and anxiolytic properties.³¹ These compounds are believed to modulate the nervous system by interacting with γ -aminobutyric acidergic pathways, reducing excitatory neurotransmission, and enhancing relaxation. Additionally, lavender essential oil inhibits pro-inflammatory mediators, such as prostaglandins and cytokines, thereby further contributing to its pain-relieving effects.³²

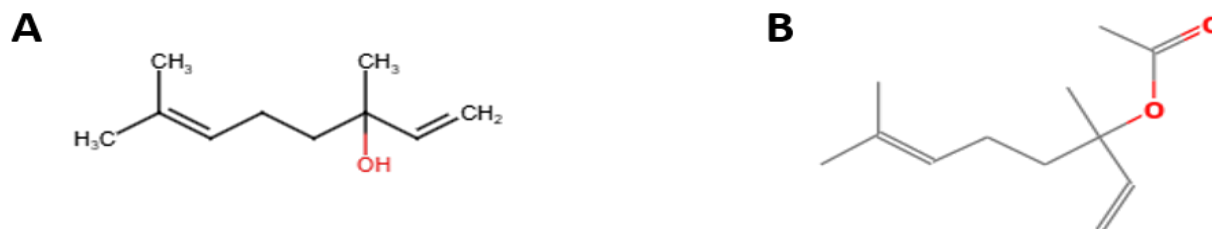


Figure 1. Bioactive compounds of lavender essential oil. (A) Linalool and (B) linalyl acetate are two major constituents of lavender essential oil. All chemical structures were drawn using RCSB PDB: Chemical Sketch Tool.³³

Topical applications of lavender essential oil may also enhance peripheral blood flow and reduce muscle tension. In contrast, inhalation of lavender essential oil stimulates the limbic system, which regulates emotional responses to pain.^{34,35}

A randomized controlled trial (RCT) investigating the

effects of lavender essential oil inhalation in postoperative cesarean patients found a significant reduction in pain intensity compared with a placebo group. The study highlighted that patients receiving lavender essential oil required fewer analgesics, demonstrating its potential as a complementary therapy.³⁶ In a clinical trial involving

patients with advanced cancer, lavender essential oil massage therapy reduced pain scores and improved emotional well-being. The study attributed lavender's dual action on physical and psychological symptoms, offering holistic relief in palliative care.³⁷

An RCT in patients with diabetic neuropathy showed that foot massages with lavender essential oil significantly reduced burning sensations and improved sleep quality. These results suggest that lavender oil can be an effective adjunct for managing chronic neuropathic pain conditions.³⁸

Systematic reviews on the use of essential oils in palliative care reported that lavender essential oil consistently reduced pain and anxiety levels in various patient populations, including those with cancer, postoperative conditions, and chronic pain syndromes. The reviews emphasize the importance of lavender essential oil's anxiolytic effects, which enhance its overall analgesic efficacy by reducing the emotional components of pain.^{39,40}

4.2.2. Peppermint

Peppermint essential oil (*Mentha piperita*) is widely recognized for its potent analgesic, anti-inflammatory, and antispasmodic properties. The primary bioactive compound in peppermint oil, menthol, is known for its cooling and soothing effects.⁴¹ Menthol (Figure 2) interacts with the TRP channel, which detects cold and mediates the sensation of cooling. Activating TRPM8 channels with menthol creates a cooling effect that helps reduce pain perception by desensitizing sensory nerve endings.⁴² Additionally, peppermint essential oil exhibits antispasmodic effects by relaxing smooth muscle tissues, which is beneficial for conditions involving muscle tension or cramping.⁴³

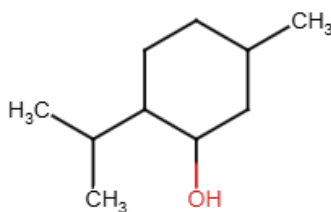


Figure 2. Menthol, the primary bioactive component of peppermint essential oil. All chemical structures were drawn using RCSB PDB: Chemical Sketch Tool.³³

Peppermint essential oil also possesses anti-inflammatory properties that reduce the release of pro-inflammatory mediators, such as cytokines and

prostaglandins, further alleviating pain.⁴⁴ These combined mechanisms make peppermint oil a versatile option for treating acute and chronic pain.

Several clinical trials have demonstrated the efficacy of peppermint essential oil in relieving tension headaches. An RCT found that applying peppermint essential oil topically to the forehead and temples significantly reduced headache intensity within 15–30 minutes. The cooling and vasodilatory effects of menthol were identified as key contributors to these results, making peppermint oil a safe and effective alternative to over-the-counter analgesics.⁴⁵ Peppermint essential oil has shown promise in managing neuropathic pain conditions, including diabetic neuropathy and postherpetic neuralgia. Studies suggest that topical application of peppermint essential oil alleviated burning and tingling sensations in patients with neuropathy, likely due to its TRPM8-mediated cooling effect and anti-inflammatory properties.⁴⁶

Although primarily studied for gastrointestinal issues, peppermint essential oil has analgesic effects in patients with irritable bowel syndrome. Enteric-coated peppermint essential oil capsules have been shown to relax intestinal smooth muscle and reduce pain associated with abdominal cramping, highlighting their broader applicability in pain management.^{47,48} A 2021 systematic review on essential oils in pain management highlighted peppermint oil as one of the most effective oils for tension headaches and neuropathic pain. The review emphasized its rapid onset of action, safety profile, and minimal side effects when used correctly, making it particularly beneficial for palliative care patients with complex pain needs.⁴⁹

4.2.3. Eucalyptus

Eucalyptus essential oil, extracted from the leaves of *Eucalyptus globulus* and other species, is well-known for its potent analgesic, anti-inflammatory, and antispasmodic properties. The primary active component of eucalyptus oil is 1,8-cineole (also called eucalyptol), which is responsible for many of its therapeutic effects. Eucalyptol has been shown to reduce pain by interacting with the TRP channels, particularly TRP ankyrin 1 (TRPA1), which mediate pain and inflammation.^{50,51}

Eucalyptus essential oil also has muscle-relaxant effects, likely due to its ability to improve blood circulation in localized areas. Its anti-inflammatory activity is primarily due to its ability to inhibit pro-inflammatory cytokines such as tumor necrosis factor alpha (TNF- α) and interleukin (IL)-6, making it particularly effective for chronic inflammation and pain.^{52,53}

Additionally, eucalyptus essential oil has been noted for its respiratory benefits, which can indirectly improve pain

and quality of life for palliative care patients experiencing discomfort due to respiratory issues.⁵⁴

A clinical study investigating the effects of eucalyptus essential oil inhalation in rheumatoid arthritis patients found significant reductions in pain and improved joint function. The study attributed these results to eucalyptol's anti-inflammatory properties, which reduced swelling and stiffness.⁵⁵ Studies suggest that eucalyptus essential oil massage in patients with chronic musculoskeletal pain results in notable pain relief and enhanced mobility, further supporting its utility in pain management.^{56,57}

An RCT assessed the impact of eucalyptus essential oil inhalation on patients recovering from total knee replacement surgery. The results showed a significant reduction in pain scores and anxiety levels, suggesting that eucalyptus oil could act as a complementary therapy to standard analgesics in postoperative care.⁵⁶ Studies suggest that eucalyptus essential oil may help alleviate neuropathic pain. While direct clinical evidence is limited, its TRPA1-modulating effects and anti-inflammatory properties indicate potential benefits for diabetic neuropathy or chemotherapy-induced peripheral neuropathy.^{58,59}

Eucalyptus essential oil is widely used to alleviate respiratory discomfort associated with chronic obstructive pulmonary disease or pneumonia. Reducing airway inflammation and improving oxygenation indirectly reduces pain and discomfort in palliative patients with respiratory comorbidities.^{60,61}

In patients with advanced cancer, the use of eucalyptus essential oil for pain management has been explored with positive results. A study involving patients undergoing palliative care found that inhaling eucalyptus essential oil reduced pain intensity and improved mood. The soothing aroma of eucalyptus essential oil and its physical analgesic effects helped reduce the emotional burden of cancer pain. Patients reported feeling calmer and less anxious, which contributed to lower pain perception.⁶²⁻⁶⁴

A systematic review of essential oils in pain management identified eucalyptus essential oil as a promising option for musculoskeletal and cancer-related pain. The review emphasized that eucalyptus oil's ability to reduce inflammation, promote blood circulation, and relax muscles makes it a valuable addition to palliative care regimens. Additionally, eucalyptus essential oil was noted for its mild side-effect profile and ease of use, whether applied topically, inhaled, or diffused into the air.³⁹

4.2.4. Chamomile

Chamomile essential oil, extracted from *Matricaria chamomilla* (German chamomile) or *Chamaemelum nobile* (Roman chamomile), is highly regarded for its anti-inflammatory, antispasmodic, and analgesic properties. Its therapeutic effects are attributed mainly to bioactive compounds such as chamazulene, bisabolol, and flavonoids. Chamazulene, in particular, is known for its potent anti-inflammatory activity, while bisabolol helps reduce irritation and promotes tissue healing (Figure 3).⁶⁵

Chamomile essential oil's analgesic properties are mediated by its ability to modulate inflammatory pathways and relax smooth muscles, making it especially effective in addressing pain caused by inflammation, muscle spasms, and nervous system hyperactivity. Additionally, the essential oil's sedative and anxiolytic effects are calming and beneficial for patients experiencing pain-related stress or sleep disturbances.^{66,67}

Chamomile essential oil has been shown to alleviate pain in conditions such as arthritis and fibromyalgia. A study on patients with osteoarthritis found that chamomile oil, when used as a massage oil, significantly reduced joint pain and improved mobility. Its anti-inflammatory properties and ability to promote circulation were identified as key contributors to these effects.⁶⁸ Chamomile essential oil has shown promise in relieving neuropathic pain, particularly in conditions like diabetic neuropathy

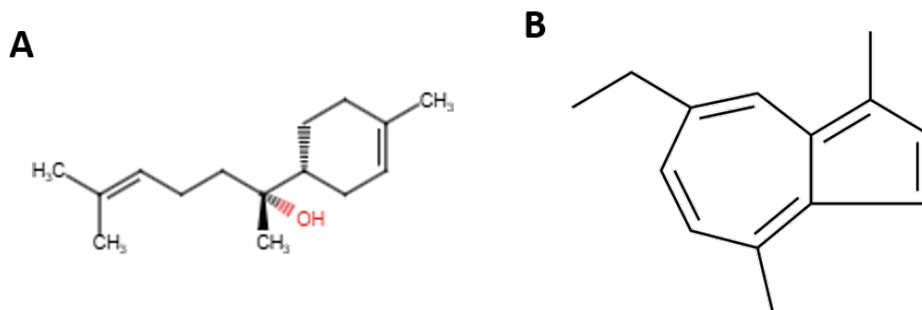


Figure 3. Bioactive components of chamomile essential oil. (A) Bisabolol and (B) chamazulene: two major constituents of chamomile essential oil. All chemical structures were drawn using RCSB PDB: Chemical Sketch Tool.³³

and postherpetic neuralgia. A clinical study reported that chamomile essential oil reduced nerve pain when applied topically, with patients experiencing less burning and tingling sensations. The essential oil's calming effects on the nervous system were highlighted as a complementary benefit.⁶⁹

In palliative care for cancer patients, chamomile essential oil has been used to alleviate pain associated with tumor progression and treatments like chemotherapy. A study involving aromatherapy massage with chamomile essential oil reported significant reductions in pain and anxiety among cancer patients. Its dual role in addressing physical pain and emotional distress makes it particularly valuable in this setting.⁷⁰

Chamomile essential oil has been studied for its ability to reduce postoperative pain and improve recovery. An RCT found that patients who received chamomile oil massages after surgery required fewer analgesics and reported greater comfort. Its anti-inflammatory and muscle-relaxant properties were noted as key factors.⁷¹

A review of essential oils in pain management identified chamomile essential oil as one of the most effective oils for inflammatory and neuropathic pain. The review highlighted its versatility, safety, and minimal side effects, making it a popular choice for palliative care patients with complex pain conditions.³

4.2.5. Clove

Clove essential oil, derived from the dried flower buds of *Syzygium aromaticum*, is widely recognized for its potent analgesic and anti-inflammatory properties. The essential oil's primary bioactive compound, eugenol, is a potent natural pain reliever with well-documented therapeutic effects.⁷² Eugenol (Figure 4) acts as a cyclooxygenase-2 (COX-2) inhibitor, reducing the production of inflammatory mediators such as prostaglandins, which play a significant role in pain pathways. Additionally, it exhibits antioxidant activity, which helps mitigate oxidative stress, a common feature of chronic pain and inflammation.⁴¹

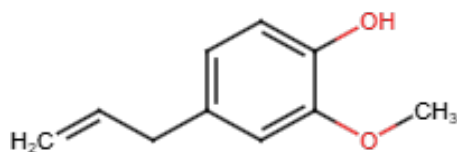


Figure 4. Eugenol: a major constituent of clove essential oil. All chemical structures were drawn using RCSB PDB: Chemical Sketch Tool.³³

Clove essential oil has shown promise in managing cancer-related pain, particularly in advanced stages

where tumor progression causes severe discomfort. A study investigating the use of clove essential oil in cancer patients found that its topical application reduced pain intensity and improved mobility in patients experiencing pain related to bone metastases. The anti-inflammatory and local anesthetic effects of eugenol were highlighted as key contributors to these outcomes.⁷³

In neuropathic pain conditions such as diabetic neuropathy and postherpetic neuralgia, an RCT demonstrated that a topical formulation containing clove oil reduced burning, tingling, and discomfort sensations. Patients also reported improvements in daily functioning and overall quality of life.^{74,75}

Although most widely known for its use in dental pain, clove essential oil's local anesthetic properties have broader applications in palliative care, particularly for patients with oral pain due to mucositis, infection, or cancer-related conditions. In such cases, its rapid numbing action provides immediate relief with minimal side effects.^{76,77}

Clove essential oil has also been applied in musculoskeletal conditions such as arthritis and muscle strain. One study found that a clove essential oil-based topical cream significantly decreased joint pain and improved physical function in patients with rheumatoid arthritis. These outcomes were attributed to its warming effect, enhanced microcirculation, and anti-inflammatory activity.^{78,79}

A review of essential oils for pain management identified clove oil as one of the most effective for localized inflammatory and neuropathic pain, emphasizing its rapid onset of action and potential to reduce reliance on opioids, a vital consideration in palliative care.³

The essential oils reviewed in this study demonstrate diverse mechanisms of action and applications relevant to pain management in palliative care. Table 1 summarizes the key bioactive compounds, proposed mechanisms, and specific pain conditions where each essential oil has shown therapeutic potential.

In addition to their pharmacological properties, the aromatic profiles of essential oils play a crucial role in their effectiveness within aromatherapy. The sensory experience of scent can influence emotional states, stress levels, and pain perception. Table 2 outlines the aroma characteristics of each essential oil, including plant origin and part used, to highlight their relevance in physiological and olfactory care dimensions.

4.3. Molecular mechanisms and emerging systems biology perspectives

Although genuine multi-omics investigations of essential

Table 1. Essential oils and their roles in pain management

Essential oil	Key bioactive compounds	Mechanism of action	Application in pain management
Lavender (<i>Lavandula angustifolia</i>)	• Linalool • Linalyl acetate	• Anti-inflammatory, sedative, and anxiolytic effects • Modulates serotonin and endorphin release	• Migraines • Arthritis • Muscle tension
Peppermint (<i>Mentha piperita</i>)	• Menthol	• Activates TRPM8 channels for cooling sensation • Reduces pain perception and muscle spasms	• Tension headaches • Myalgia • Neuropathic pain
Eucalyptus (<i>Eucalyptus globulus</i>)	• 1,8-cineole	• Inhibits inflammatory mediators like cytokines • Provides analgesic and anti-inflammatory effects	• Musculoskeletal pain • Joint inflammation
Chamomile (<i>Matricaria chamomilla</i>)	• Bisabolol • Flavonoids	• Anti-inflammatory, mild sedative • Relaxes smooth muscles and reduces spasms	• Abdominal cramping • Muscle spasms • General pain
Clove (<i>Syzygium aromaticum</i>)	• Eugenol	• Potent analgesic and anti-inflammatory • Reduces nerve-related pain	• Dental pain • Nerve pain

Table 2. Aroma profile of the studied essential oils

Common name / biological name	International Nomenclature of Cosmetic Ingredients	Part of the plant used	Aroma description	Reference
Lavender/ <i>Lavandula angustifolia</i>	<i>Lavandula angustifolia</i> oil	Flowers	Floral, herbaceous, soft, slightly sweet	⁸⁰
Peppermint/ <i>Mentha × piperita</i>	<i>Mentha piperita</i> oil	Leaves	Sharp, fresh, mentholated, cooling	⁸¹
Eucalyptus/ <i>Eucalyptus globulus</i>	<i>Eucalyptus globulus</i> leaf oil	Leaves	Fresh, camphoraceous, slightly woody	⁸²
Chamomile/ <i>Matricaria chamomilla</i> or <i>Chamaemelum nobile</i>	<i>Matricaria recutita</i> flower oil or <i>Anthemis nobilis</i> flower oil	Flowers	Sweet, apple-like, herbaceous	⁸³
Clove/ <i>Syzygium aromaticum</i>	<i>Eugenia caryophyllus</i> bud oil	Flower buds	Warm, spicy, slightly sweet, penetrating	⁸⁴

oils in pain remain limited, recent transcriptomic, metabolomic, and lipidomic studies, together with conventional molecular pharmacology, have begun to provide insights into the complex mechanisms underlying their analgesic activity. Most available evidence remains mechanistic rather than comprehensive omics profiling. Recent advances in omics technologies have substantially expanded our understanding of pain pathophysiology and the molecular mechanisms underlying the therapeutic effects of natural products. High-throughput approaches, including transcriptomics, metabolomics, lipidomics, proteomics, and epigenomics, have enabled researchers to investigate how bioactive compounds modulate complex biological networks involved in inflammation, nociception, neuroplasticity, and immune regulation. These approaches are particularly relevant in chronic and cancer-related pain, where alterations in multiple molecular pathways

contribute to persistent nociceptive signaling and central sensitization.⁸⁵

Essential oils are complex mixtures containing dozens of biologically active molecules that can interact with numerous cellular targets simultaneously. While traditional pharmacological studies have largely focused on receptor binding and enzyme inhibition, emerging omics-based investigations provide a broader systems-level perspective on how essential oil constituents influence gene expression, metabolic pathways, inflammatory mediators, and cellular signaling networks.⁸⁶ Such findings are increasingly important for identifying novel therapeutic targets and supporting the development of essential oil-derived compounds as innovative analgesic agents.

Several major constituents of the essential oils discussed in this review, including linalool, menthol, 1,8-cineole,

α -bisabolol, and eugenol, have been shown to modulate molecular pathways involved in pain processing. Omics studies have revealed effects on inflammatory cytokine production, oxidative stress responses, neurotransmitter signaling, and lipid mediator biosynthesis, all of which are critical contributors to nociceptive and neuropathic pain. Collectively, these findings suggest that essential oils exert their analgesic effects through multi-target mechanisms that extend beyond symptomatic relief and may influence the biological processes driving pain progression.^{87,88}

4.3.1. Transcriptome evidence

Transcriptomics has emerged as a valuable tool for elucidating the molecular mechanisms through which essential oil constituents influence pain-related pathways.⁸⁹ By analyzing global gene expression profiles, transcriptomic studies provide insights into how bioactive compounds regulate inflammatory responses, neuronal signaling, oxidative stress, and immune function. These mechanisms are particularly relevant in chronic pain conditions, where persistent activation of pro-inflammatory and neuroimmune pathways contributes to peripheral and central sensitization.

Among the compounds commonly found in analgesic essential oils, linalool, a major constituent of lavender essential oil, has received considerable attention. Experimental studies suggest that linalool suppresses the expression of several pro-inflammatory factors, including TNF- α , IL-1 β , IL-6, and COX-2/prostaglandin-endoperoxide synthase 2.⁹⁰ These changes are frequently associated with inhibition of the nuclear factor kappa B (NF- κ B) signaling pathway, a central regulator of inflammatory pain. In parallel, linalool has been reported to enhance antioxidant defense systems by activating the nuclear factor erythroid 2-related factor 2 pathway, thereby reducing oxidative stress-mediated neuronal damage.^{91,92}

Similarly, α -bisabolol and chamazulene, two important constituents of chamomile essential oil, have demonstrated the capacity to modulate genes involved in innate immune responses. Evidence suggests that these compounds interfere with Toll-like receptor 4-dependent signaling, leading to reduced NF- κ B activation and downregulation of inflammatory cytokine transcriptio.⁹³ Such effects may contribute to the attenuation of neuroinflammation and nociceptor sensitization observed in inflammatory and neuropathic pain models.

Eucalyptol (1,8-cineole), the principal constituent of eucalyptus essential oil, has also been associated with significant transcriptomic changes.⁹⁴ Studies using macrophage and epithelial cell models have shown that 1,8-cineole suppresses the expression of genes involved in

inflammatory cascades, including TNF- α , IL-6, inducible nitric oxide synthase, and components of the mitogen-activated protein kinase (MAPK) pathway. The inhibition of these pathways is particularly relevant in chronic inflammatory states, where sustained cytokine production contributes to persistent pain signaling.

Eugenol, the major bioactive compound in clove essential oil, exhibits effects similar to those of the oil itself. Experimental evidence indicates that eugenol reduces the expression of pro-inflammatory mediators while modulating genes involved in oxidative stress regulation and neuronal excitability.⁹⁵ Furthermore, eugenol has been shown to influence signaling pathways linked to TRP channels and voltage-gated sodium channels, both of which play essential roles in nociceptive transmission.⁹⁶

Collectively, transcriptomic studies suggest that essential oil constituents regulate multiple genes and signaling networks involved in pain generation and maintenance. Rather than acting through a single molecular target, these compounds appear to exert pleiotropic effects that simultaneously modulate inflammatory, neuroimmune, and oxidative stress pathways. This systems-level activity may partly explain the broad therapeutic potential of essential oils in managing complex pain conditions commonly encountered in palliative care.

4.3.2. Metabolomic and lipidomic evidence

Metabolomics and lipidomics have emerged as powerful analytical approaches for investigating the biochemical mechanisms underlying pain and inflammation. Unlike traditional pharmacological studies that focus on individual molecular targets, these omics technologies enable the comprehensive characterization of endogenous metabolites and lipid mediators involved in physiological and pathological processes. In pain research, metabolomic and lipidomic profiling have identified significant alterations in inflammatory metabolites, oxidative stress markers, neurotransmitter precursors, and bioactive lipid species that contribute to nociceptive signaling, peripheral sensitization, and central sensitization.⁹⁷

Chronic pain conditions are frequently associated with dysregulation of lipid-derived inflammatory mediators, particularly metabolites originating from arachidonic acid metabolism. Prostaglandins, leukotrienes, thromboxanes, and other eicosanoids play critical roles in amplifying inflammatory responses and enhancing nociceptor excitability. Consequently, modulation of these metabolic pathways has become an important therapeutic strategy for pain management. Several bioactive constituents of essential oils have been shown to influence these pathways, supporting their potential as complementary analgesic agents.

Eugenol, the principal constituent of clove essential oil, has been extensively investigated for its effects on inflammatory metabolism. Experimental studies indicate that eugenol suppresses COX activity and reduces prostaglandin E2 production, a key mediator of inflammatory pain.⁹⁸ Metabolomic analyses have further demonstrated reductions in oxidative stress-related metabolites and lipid peroxidation products following eugenol administration, suggesting a broader impact on cellular redox homeostasis.⁹⁹ These biochemical changes may contribute to the attenuation of inflammatory signaling and the reduction of nociceptor sensitization.

Similarly, 1,8-cineole (eucalyptol), the major constituent of eucalyptus essential oil, has been shown to modulate inflammatory lipid mediators. Lipidomic investigations have reported decreases in pro-inflammatory eicosanoids and cytokine-driven lipid signaling pathways following exposure to 1,8-cineole.⁹⁸ These effects are accompanied by suppression of NF- κ B and MAPK signaling, resulting in reduced synthesis of inflammatory mediators involved in pain transmission. Such findings support the role of eucalyptus essential oil as a potential modulator of inflammatory metabolic networks.

Menthol, a major constituent of peppermint essential oil, also influences metabolic pathways relevant to pain regulation. Beyond its well-established activation of TRP melastatin 8 channels, menthol has been shown to alter cellular energy metabolism and oxidative stress responses.¹⁰⁰ Experimental metabolomic studies suggest that menthol may help restore metabolic homeostasis under inflammatory conditions, thereby reducing tissue damage and inflammatory signaling.¹⁰¹ These effects may complement its direct actions on sensory neurons and contribute to its analgesic properties.

Emerging evidence also indicates that essential oil constituents may influence endocannabinoid metabolism, a lipid signaling system increasingly recognized for its role in pain modulation. Endocannabinoids and related lipid mediators regulate inflammatory responses, neuronal excitability, and stress-related pathways, contributing to both the physical and emotional aspects of pain. Although direct evidence remains limited, preliminary studies suggest that certain terpenes and phenolic compounds present in essential oils may interact with components of the endocannabinoid system, potentially enhancing analgesic and anxiolytic effects.¹⁰²

Collectively, metabolomic and lipidomic investigations provide important insights into the multifaceted mechanisms through which essential oils influence pain-related biochemical pathways. By modulating inflammatory lipid mediators, oxidative stress metabolites, and

endogenous signaling molecules, essential oil constituents appear capable of targeting several interconnected processes involved in pain generation and maintenance. Future integration of metabolomic, lipidomic, and clinical data may facilitate the identification of novel biomarkers of response and support the development of more personalized approaches to aromatherapy-based pain management in palliative care.

4.3.3. Epigenetic and neuroimmune regulation

Growing evidence suggests that the analgesic effects of essential oil constituents may extend beyond direct receptor interactions and inflammatory pathway modulation, involving epigenetic and neuroimmune mechanisms that contribute to the development and persistence of chronic pain. Epigenetic processes, including DNA methylation, histone modifications, and microRNA regulation, play fundamental roles in controlling gene expression without altering the underlying DNA sequence. These mechanisms have emerged as important contributors to pain sensitization, neuroinflammation, and neuronal plasticity, particularly in chronic and cancer-related pain conditions.

Persistent nociceptive stimulation is associated with epigenetic alterations that promote the sustained expression of pro-inflammatory cytokines, chemokines, and pain-related receptors within both peripheral and central nervous system tissues.^{103,104} Such changes can facilitate central sensitization and enhance communication between immune cells and neurons, contributing to the transition from acute to chronic pain. Consequently, therapeutic agents that modulate epigenetic pathways have attracted increasing interest as potential targets for pain management.

Several bioactive compounds present in essential oils have demonstrated the ability to influence neuroimmune signaling pathways closely linked to epigenetic regulation. Linalool, one of the principal constituents of lavender essential oil, has been shown to attenuate neuroinflammatory responses by suppressing NF- κ B activation and reducing pro-inflammatory mediators such as TNF- α , IL-1 β , and IL-6.¹⁰⁵ These effects may indirectly influence epigenetic regulators involved in inflammatory gene expression, thereby contributing to long-term modulation of pain-related pathways.

Similarly, eugenol, the major phenylpropanoid component of clove essential oil, exhibits potent anti-inflammatory and antioxidant properties that may affect epigenetic mechanisms associated with oxidative stress and neuronal excitability. Experimental studies have demonstrated that eugenol suppresses inflammatory signaling pathways and reduces reactive oxygen species

production, both of which are recognized drivers of epigenetic alterations during chronic inflammation.¹⁰⁶ By limiting neuroinflammatory activation, eugenol may help prevent maladaptive molecular changes that perpetuate pain signaling.

Neuroimmune interactions involving microglia and astrocytes have also emerged as important therapeutic targets in chronic pain. Activated glial cells release cytokines, chemokines, and other inflammatory mediators that amplify neuronal sensitization and contribute to persistent pain states. Several essential oil constituents, including linalool, 1,8-cineole, α -bisabolol, and eugenol, have demonstrated the capacity to suppress microglial activation and attenuate neuroinflammatory responses in experimental models.¹⁰⁶ These findings suggest that essential oils may exert analgesic effects not only through direct actions on nociceptive pathways but also by modulating the neuroimmune environment that sustains chronic pain.

In addition, emerging research indicates that certain essential oil constituents may influence the expression of regulatory microRNAs involved in inflammation, oxidative stress responses, and neuronal survival.¹⁰⁷ Although the available evidence remains limited and further omics-based investigations are required, these observations support the hypothesis that essential oils may contribute to pain relief by coordinating the regulation of epigenetic and neuroimmune pathways. Future studies integrating transcriptomic, epigenomic, and proteomic approaches may help clarify the precise molecular networks involved and facilitate the identification of novel essential oil-derived compounds for pain management in palliative care.

Much of the evidence describing the molecular mechanisms of essential oils originates from *in vitro* and animal studies. These investigations provide valuable insights into the biological pathways involved in analgesic and anti-inflammatory effects but primarily establish mechanistic plausibility rather than clinical efficacy. In contrast, the available clinical studies, particularly in palliative care populations, mainly evaluate symptom relief and patient-reported outcomes rather than molecular endpoints. Therefore, caution is warranted when extrapolating experimental findings to clinical practice, and additional well-designed clinical studies are needed to validate these mechanisms in patients receiving palliative care.

4.4. Essential oil constituents as analgesic lead compounds

Natural products have historically served as an important

source of therapeutic agents, with numerous modern medicines originating from plant-derived bioactive compounds. In recent decades, increasing attention has been directed toward essential oils as reservoirs of structurally diverse molecules capable of interacting with multiple biological targets involved in pain signaling. The growing understanding of pain pathophysiology, coupled with advances in molecular pharmacology and omics technologies, has renewed interest in identifying essential oil constituents as lead compounds for the development of novel analgesic drugs.

Among the most extensively studied constituents is linalool, a monoterpene alcohol found predominantly in lavender essential oil. Experimental studies have demonstrated that linalool exerts analgesic, anxiolytic, and anti-inflammatory effects through interactions with several molecular targets, including γ -aminobutyric acid receptors, glutamatergic signaling pathways, and voltage-gated calcium channels.¹⁰⁸ Linalool has also been shown to inhibit the production of pro-inflammatory cytokines and modulate oxidative stress responses.¹⁰⁹ Its multimodal mechanism of action is particularly attractive for the management of chronic and neuropathic pain, where both neuronal hyperexcitability and neuroinflammation contribute to disease progression.

Menthol, the primary constituent of peppermint essential oil, represents another promising analgesic lead compound. Its effects are largely mediated through activation of TRP melastatin 8 channels, which are responsible for the characteristic cooling sensation associated with peppermint oil.⁴² Activation of TRP melastatin 8 has been linked to reduced nociceptive signaling and analgesia in both inflammatory and neuropathic pain models. The clinical success of menthol-containing topical formulations further supports its translational potential and highlights the therapeutic value of targeting TRP channels in pain management.

Eucalyptol (1,8-cineole), the major component of eucalyptus essential oil, has demonstrated substantial anti-inflammatory and analgesic properties through modulation of multiple signaling pathways, including NF- κ B, MAPK, and cytokine-mediated inflammatory cascades.⁶¹ In addition to reducing the production of inflammatory mediators, 1,8-cineole may influence sensory neuron activation by interacting with TRP channels, particularly TRPA1.^{61,110} These mechanisms suggest potential applications in inflammatory pain conditions and support further investigation into eucalyptol-derived therapeutic agents.

Chamomile essential oil contains several bioactive compounds, including α -bisabolol and chamazulene,

which have attracted interest due to their anti-inflammatory and neuroprotective properties.^{25,111} α -Bisabolol has been shown to inhibit Toll-like receptor 4-mediated signaling pathways and to suppress NF- κ B activation, leading to reduced cytokine production and attenuation of neuroinflammatory responses.¹¹² Given the growing recognition of neuroimmune interactions in chronic pain disorders, compounds that modulate glial activation and inflammatory signaling may represent valuable candidates for future analgesic development.

Eugenol, the principal phenolic constituent of clove essential oil, is perhaps one of the most extensively investigated essential oil-derived analgesic compounds. Its analgesic effects have been attributed to multiple mechanisms, including inhibition of COX enzymes, modulation of TRP vanilloid 1 channels, blockade of voltage-gated sodium channels, and suppression of inflammatory cytokine production.⁹⁸ These diverse pharmacological actions contribute to both peripheral and central analgesic effects. Eugenol has long been used in dentistry as a local analgesic and anesthetic agent, demonstrating the successful translation of an essential oil constituent into routine clinical practice. Its established safety profile and broad pharmacological activity make it an attractive scaffold for the development of novel pain therapeutics.¹¹³

A notable advantage of essential oil constituents as lead compounds is their multi-target pharmacology. Unlike many conventional analgesics that act on a single receptor or signaling pathway, essential oil-derived molecules frequently modulate several interconnected mechanisms simultaneously, including inflammation, oxidative stress, neuronal excitability, and neuroimmune activation.⁸⁶ Such pleiotropic activity may be particularly advantageous in complex pain conditions, where multiple biological processes contribute to symptom development and persistence.

Despite these promising characteristics, several challenges remain before essential oil constituents can be fully integrated into modern drug development pipelines. Issues related to bioavailability, pharmacokinetics, standardization, toxicity evaluation, and formulation optimization require further investigation. Nevertheless, advances in medicinal chemistry, nanotechnology-based delivery systems, and omics-guided target identification offer new opportunities to enhance the therapeutic potential of these natural compounds. Future research integrating pharmacological, molecular, and clinical evidence may facilitate the transformation of essential oil constituents into innovative analgesic agents capable of addressing unmet needs in pain management, including those encountered in palliative care settings.

To facilitate comparison of the principal bioactive constituents discussed in this review, their primary molecular targets, and their potential therapeutic applications in pain management, Table 3 summarizes the current evidence supporting the use of essential oil-derived compounds as promising analgesic lead molecules. The diversity of mechanisms highlighted underscores the potential of these natural products to serve as templates for the development of innovative multi-target analgesic therapies.

4.5. Application methods

Essential oils can be administered through various methods, each offering distinct benefits depending on the type and location of pain, patient preferences, and clinical context. In palliative care, the most common application routes include topical use, inhalation, and aromatherapy massage, with oral use being rare and generally avoided due to safety concerns.

4.5.1. Topical application

Topical administration involves applying diluted essential

Table 3. Essential oil constituents as novel analgesic lead compounds

Compound	Essential oil source	Principal molecular targets	Potential clinical application
Linalool	Lavender	GABAA, NMDA, Ca ²⁺ channels	Neuropathic and cancer pain
Menthol	Peppermint	TRPM8	Topical analgesia, neuropathic pain
1,8-cineole	Eucalyptus	NF- κ B, MAPK, TRPA1	Inflammatory pain
α -Bisabolol	Chamomile	TLR4, NF- κ B	Neuroinflammatory pain
Eugenol	Clove	COX-2, TRPV1, Na ⁺ channels	Local anesthesia, inflammatory pain

Abbreviations: COX-2: Cyclooxygenase-2; GABAA: γ -aminobutyric acid type A receptor; MAPK: Mitogen-activated protein kinase; NF- κ B: Nuclear factor kappa B; NMDA: N-Methyl-D-aspartate receptor; TLR4: Toll-like receptor 4; TRPA1: Transient receptor potential ankyrin 1; TRPM8: Transient receptor potential melastatin 8; TRPV1: Transient receptor potential vanilloid 1.

oils directly to the skin, often through localized massage or compresses. This method allows the active compounds to penetrate the skin and reach underlying tissues, relieving musculoskeletal pain, joint inflammation, and neuropathic discomfort.⁵⁷ Carrier oils, such as sweet almond or jojoba oil, are used to dilute essential oils, enhance skin absorption, and minimize the risk of irritation. Essential oils such as lavender, peppermint, chamomile, and clove are commonly used in this context for their anti-inflammatory and analgesic effects.

4.5.2. Inhalation

Inhalation of volatile compounds in essential oils can stimulate the olfactory system, which, in turn, influences the limbic system—the brain region involved in pain perception, emotions, and memory. This route is especially effective for managing psychological distress associated with pain, such as anxiety, insomnia, and agitation.¹¹⁴ Inhalation methods include using diffusers or inhalers, or placing a few drops on a tissue or a pillow. Lavender and eucalyptus oils are often chosen for this route due to their calming and respiratory-supporting properties.

4.5.3. Aromatherapy massage

Aromatherapy massage combines the therapeutic effects of essential oils. This integrative approach promotes relaxation, reduces muscle tension, improves circulation, and enhances the absorption of essential oils through the skin.¹¹⁵ Studies have shown that aromatherapy massage can significantly lower pain intensity, reduce anxiety, and improve overall well-being in palliative patients. It is beneficial for addressing generalized pain, muscle stiffness, and emotional discomfort.^{116,117}

4.5.4. Compresses

Compresses are a traditional yet effective method of applying essential oils for localized pain relief. They involve soaking a cloth in a mixture of warm or cold water and diluted essential oils and then applying it directly to the affected area. Warm compresses are typically used to relieve muscle tension, joint stiffness, or abdominal cramps, while cold compresses may be more appropriate for acute inflammation, swelling, or sharp nerve pain.¹¹⁸

Essential oils such as chamomile, peppermint, and clove are commonly used in compresses due to their combined analgesic, anti-inflammatory, and antispasmodic properties. This method is suitable for patients who may not tolerate massage or prolonged topical application. Compresses are easy to prepare, non-invasive, and offer focused relief, making them a practical and gentle option in palliative settings. As with all topical methods, skin sensitivity and the temperature of the compress should be carefully monitored.

4.5.5. Safety and individualization

Regardless of the method, the application should be tailored to the patient's condition, sensitivity, and preferences. Essential oils must be used at appropriate dilutions (typically 1–3% for adults in palliative care) and tested on a small area of skin before widespread use. Special caution is needed for patients with compromised skin integrity, allergies, or respiratory issues. Health professionals should always ensure that the essential oils are therapeutic and free from synthetic additives.²³

Various methods can be used to administer essential oils in palliative care, each offering specific advantages depending on the patient's condition, type of pain, and therapeutic goals. The application route influences the speed and nature of the therapeutic response, whether physical, emotional, or both. Table 4 provides an overview of the primary application methods used in clinical and caregiving contexts, highlighting their key characteristics, typical indications, and considerations for safe and effective use.

5. Discussion

This narrative review synthesizes current knowledge on the role of essential oils in pain management within palliative care settings. The findings highlight a growing body of evidence supporting the therapeutic potential of essential oils as complementary agents that can address both the physical and emotional dimensions of pain.⁶⁴ Essential oils such as lavender, peppermint, eucalyptus, chamomile, and clove were consistently associated with analgesic, anti-inflammatory, antispasmodic, and anxiolytic effects, making them valuable additions to holistic pain relief strategies.⁶⁵

Essential oils' key strengths in palliative care are their versatility in application and low invasiveness, which allow for personalized, patient-centered use. In particular, lavender and peppermint oils have demonstrated robust evidence of efficacy for conditions such as cancer, neuropathic, and postoperative discomfort. Moreover, their impact on mood and sleep quality positions essential oils as beneficial for symptom control and enhancing patients' overall well-being.

Real-world applications from hospice and palliative care settings further validate their utility, with anecdotal reports from patients and caregivers indicating improvements in comfort, relaxation, and emotional resilience.¹¹⁹ However, despite these promising findings, the integration of essential oils into standard palliative protocols remains limited, primarily due to gaps in clinical research, regulatory oversight, and practitioner education.

Table 4. Application methods of essential oils in palliative pain management

Method	Description	Commonly used essential oils	Indications	Notes/Considerations
Topical application	Direct application to the skin, usually diluted in a carrier oil	• Lavender • Peppermint • Chamomile • Clove	Localized musculoskeletal pain, joint inflammation, neuropathic pain	Requires dilution (1–3%); avoid broken skin or irritations
Inhalation	Breathing in vaporized essential oils via diffuser, steam, or inhaler	• Lavender • Eucalyptus • Peppermint	Emotional distress, anxiety, insomnia, mild respiratory discomfort	Rapid emotional/psychological effects; suitable for non-invasive use
Aromatherapy massage	Integration of essential oils into massage for a combined tactile and olfactory effect	• Lavender • Chamomile • Clove • Eucalyptus	Generalized pain, tension, stress, anxiety, sleep disturbances	Enhances absorption and relaxation; offers dual benefit (touch + aroma)
Compresses	Cloth soaked in essential oil solution applied to the painful area (hot or cold)	• Chamomile • Peppermint • Clove	Muscle cramps, localized swelling, joint or nerve pain	Suitable for focused relief; monitor skin sensitivity

Integrating essential oils into palliative care requires a coordinated, interdisciplinary approach.⁶⁴ Nurses, physicians, pharmacists, aromatherapists, and other allied health professionals must work collaboratively to ensure that essential oil interventions are safe, evidence-based, and tailored to each patient's needs. Nurses often play a frontline role in applying essential oils, whether through massage, compresses, or inhalation, while pharmacists can support appropriate selection, dilution, and compatibility with other medications. Trained aromatherapists bring essential expertise in oil quality, indications, and contraindications, particularly when customizing blends for complex symptom profiles. This team-based model ensures that the use of essential oils is not only therapeutically effective but also aligned with patient preferences and cultural values. As integrative care continues to gain recognition in palliative practice, fostering interdisciplinary education and communication will be key to maximizing the benefits of aromatherapy within holistic treatment plans.

An important consideration in palliative care is the potential interaction between essential oils and conventional pharmacological therapies, as patients frequently receive multiple medications to manage pain and other symptoms.^{120, 121} Although essential oils are generally considered safe when appropriately administered, certain constituents may influence drug metabolism by modulating cytochrome P450 enzymes or drug transporters, potentially altering the pharmacokinetics of concomitant medications. In addition, pharmacodynamic interactions

may occur.¹²² For example, lavender essential oil may enhance the sedative effects of opioids, benzodiazepines, or other central nervous system depressants.¹²³ In contrast, clove essential oil, due to its high eugenol content, may increase the risk of bleeding when used with anticoagulant or antiplatelet agents. Furthermore, topical application of essential oils may increase skin sensitivity or irritation in patients receiving chemotherapy or radiotherapy. Although clinically significant interactions remain poorly documented and are considered uncommon when essential oils are used appropriately, careful assessment of each patient's medication regimen, monitoring for adverse effects, and collaboration among physicians, pharmacists, nurses, and qualified aromatherapists are essential to ensure the safe integration of aromatherapy into palliative care.

In comparison to standard pharmacological therapies such as opioids, non-steroidal anti-inflammatory drugs, and adjuvants like anticonvulsants or antidepressants, essential oils offer a more integrative and less invasive approach. While conventional analgesics remain central to pain control in palliative care, they are frequently associated with adverse effects such as sedation, constipation, nausea, and cognitive impairment, which are particularly burdensome for patients nearing the end of life.^{124, 125} Essential oils, by contrast, are generally well-tolerated when used appropriately and have the added benefit of promoting relaxation, improving sleep, and reducing anxiety, all of which contribute to the multidimensional experience of pain relief.⁶³

Although not as potent as opioids in cases of severe pain, essential oils can be beneficial for managing mild to moderate discomfort or as adjuncts that enhance the effectiveness of pharmacological treatments. Their integration may also reduce the need for higher drug dosages, thereby minimizing side effects and supporting a more person-centered model of care. This complementary role aligns well with the goals of palliative care, which emphasize comfort, dignity, and quality of life.^{3,115}

While essential oils are not a replacement for pharmacological interventions, their growing evidence base and patient-centered nature highlight their potential as meaningful additions to the palliative care toolkit. Their ability to address both pain and psychological distress supports a more compassionate and holistic model of care.

Despite their therapeutic potential, several barriers hinder the integration of essential oils into conventional palliative care protocols. These include the limited number of high-quality RCTs, variability in essential oil composition due to botanical, geographical, and manufacturing factors, the lack of standardized formulations, dosages, and administration protocols, and concerns regarding product quality and regulatory oversight. In addition, healthcare professionals often receive limited training in aromatherapy, and uncertainty regarding potential contraindications and interactions with conventional medications may reduce clinicians' confidence in recommending these therapies. Addressing these challenges through standardized quality control, rigorous clinical research, clear clinical guidelines, and interdisciplinary education will be essential for the broader adoption of essential oils as evidence-based complementary interventions in palliative care.

5.1. Essential oils, the gut microbiota, and the gut-brain-pain axis

Recent advances in microbiome research have highlighted the critical role of the gut microbiota in regulating pain perception, immune responses, and psychological well-being.¹²⁶ The bidirectional communication network linking the gastrointestinal tract and the central nervous system, commonly referred to as the gut-brain axis, involves complex interactions among neural, endocrine, immune, and metabolic pathways. Growing evidence suggests that alterations in gut microbial composition, known as dysbiosis, may contribute to the development and persistence of chronic pain, anxiety, depression, and systemic inflammation, all of which are highly relevant in palliative care populations.¹²⁷

The gut microbiota influences pain modulation through several mechanisms, including the production of neurotransmitters, short-chain fatty acids, and other

bioactive metabolites that affect both peripheral and central nervous system function. Microbial metabolites can regulate immune cell activity, intestinal barrier integrity, and neuroinflammatory processes, thereby influencing nociceptive signaling and pain sensitivity. Disruptions in these microbial-host interactions have been associated with enhanced inflammatory responses and increased susceptibility to chronic pain conditions.¹²⁸

Essential oils may interact with the gut microbiota through their well-documented antimicrobial, anti-inflammatory, and antioxidant properties. Several essential oil constituents have demonstrated selective activity against pathogenic microorganisms while potentially supporting microbial balance and reducing intestinal inflammation.¹²⁹ These effects may contribute indirectly to pain relief by improving gut barrier function, decreasing systemic inflammatory burden, and modulating signaling pathways involved in the gut-brain axis.

Chamomile essential oil and its bioactive constituents, including α -bisabolol and chamazulene, have been associated with anti-inflammatory effects within the gastrointestinal tract.¹¹⁴ Experimental studies suggest that chamomile-derived compounds may help preserve intestinal mucosal integrity and attenuate inflammatory responses, thereby creating conditions that support a healthier microbial environment.¹³⁰ Such effects may be particularly relevant in patients experiencing gastrointestinal dysfunction, a common challenge in palliative care.

Similarly, eugenol, the principal constituent of clove essential oil, has demonstrated antimicrobial and anti-inflammatory activities that may influence microbial composition and metabolic activity. Experimental evidence suggests that eugenol can reduce intestinal inflammation and oxidative stress while modulating the growth of selected microbial populations.¹³¹ Through these mechanisms, eugenol may contribute to reduced systemic inflammation and subsequent attenuation of pain-related signaling pathways.

Lavender essential oil, widely recognized for its anxiolytic and analgesic properties, may also exert indirect effects through the gut-brain axis. Although direct evidence linking lavender to modulation of the microbiota remains limited, reductions in stress and anxiety may influence gut microbial stability through neuroendocrine pathways involving the hypothalamic-pituitary-adrenal axis.¹³² Given the close relationship between psychological distress and pain perception, these interactions may represent an additional mechanism underlying the therapeutic benefits of lavender aromatherapy.

Emerging evidence also suggests that certain terpenes found in essential oils may influence the production of short-chain fatty acids and other microbial metabolites involved in immune regulation and neuroprotection. These metabolites can affect microglial activation, cytokine production, and neuronal signaling, thereby influencing both pain perception and emotional well-being.¹⁰⁵ Such observations further support the concept that essential oils may exert multidimensional effects extending beyond direct pharmacological interactions with nociceptive pathways.

It is important to emphasize that the current evidence supporting interactions between essential oils, the gut microbiota, and pain modulation is derived predominantly from *in vitro* experiments and animal models. Although these studies provide important mechanistic insights into how essential oil constituents may influence microbial composition, intestinal inflammation, and gut-brain signaling, clinical evidence in humans remains limited. To date, only a small number of clinical studies have investigated the effects of essential oils on the human gut microbiota, and even fewer have examined the relationship between microbiota modulation and pain outcomes.¹³³ Moreover, no robust clinical studies have specifically evaluated these mechanisms in palliative care populations. Therefore, while the gut-brain-pain axis represents a promising area of investigation, the proposed microbiota-mediated analgesic effects of essential oils should currently be regarded as biologically plausible rather than clinically confirmed. Well-designed human studies integrating microbiome analysis with clinical outcomes are needed to establish the translational relevance of these findings.

5.2. Limitations

This review is subject to several limitations. First, as a narrative rather than a systematic review, it did not employ formal risk-of-bias assessments or meta-analytic techniques, which may affect the objectivity and reproducibility of findings. While care was taken to prioritize peer-reviewed, high-quality studies, including diverse study designs ranging from clinical trials to case reports, this introduces variability in the level of evidence presented.

Second, many of the included studies had small sample sizes, short follow-up periods, or lacked blinding, reducing the generalizability of their findings. Furthermore, essential oils are complex mixtures with variable chemical compositions depending on the botanical source, extraction method, and storage conditions. These factors were not always specified or standardized across studies, complicating comparisons and clinical translation.

Whenever possible, the interpretation of the evidence was based on studies reporting the botanical source and principal bioactive constituents of the essential oils. Nevertheless, inconsistencies in chemical characterization across the literature remain an important limitation that should be addressed in future studies through standardized reporting of essential oil composition.

Lastly, while anecdotal and real-world applications were included to reflect practical relevance, such evidence lacks the rigor of controlled trials and should be interpreted cautiously.

5.3. Future research

Future research must address several key gaps to fully harness the potential of essential oils in palliative pain management. High-quality RCTs are needed to evaluate their efficacy, optimal dosages, delivery methods, and long-term safety across diverse palliative populations. Standardization of essential oil composition and reporting protocols is necessary to ensure reproducibility and comparability across studies.

In addition to focusing solely on essential oils, future research should also explore a broader spectrum of natural plant-based therapies. This includes whole plant preparations, infusions, hydrolates, and topical herbal compresses, which may offer similar analgesic and anti-inflammatory benefits. These alternatives could provide more accessible or culturally relevant options, especially in low-resource or rural palliative care settings.

Furthermore, research should incorporate patient-reported outcomes, such as pain intensity, emotional well-being, and quality of life, and explore the perspectives of caregivers and healthcare providers. Interdisciplinary collaboration will be critical in designing integrative care models that safely incorporate these therapies within standard palliative protocols. As interest in natural and holistic approaches grows, exploring essential oils and other plant-based remedies could significantly expand the toolkit for person-centered palliative care.

6. Conclusion

Although essential oils show promise as complementary interventions for pain management, there is currently insufficient clinical evidence to conclude that they reduce analgesic medication requirements. Their potential analgesic-sparing effect remains to be confirmed through robust clinical trials. Oils such as lavender, peppermint, eucalyptus, chamomile, and clove demonstrate analgesic, anti-inflammatory, and calming effects that can enhance comfort and quality of life. While evidence is encouraging, further rigorous research and standardization are needed

to support broader clinical use. Essential oils can be valuable to holistic, person-centered care when applied safely and thoughtfully.

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