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Essential oils for clinical aromatherapy: A comprehensive review

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ABSTRACT

Ethnopharmacological relevance: Aromatherapy, a holistic healing practice utilizing the aromatic essences of plant-derived essential oils, has gained significant attention for its therapeutic potential in promoting overall well-being. Use of phytoconstituent based essential oil has played a significant role in the evolving therapeutic avenue of aromatherapy as a complementary system of medicine.

Aim of the study: This comprehensive review article aims to explore the usage of essential oils for aromatherapy, shedding light on their diverse applications, scientific evidence, and safety considerations. Furthermore, the growing interest in using essential oils as complementary therapies in conjunction with conventional medicine is explored, underscoring the significance of collaborative healthcare approaches.

Materials and methods: Literature search was performed from databases like PubMed, ScienceDirect, Scopus, and Bentham using keywords like Aromatherapy, Aromatic Plants, Essential oils, Phytotherapy, and complementary medicine. The keywords were used to identify literature with therapeutic and mechanistic details of herbal agents with desired action.

Results: The integration of traditional knowledge with modern scientific research has led to a renewed interest in essential oils as valuable tools in contemporary healthcare. Various extraction methods used to obtain essential oils are presented, emphasizing their impact on the oil's chemical composition and therapeutic properties. Additionally, the article scrutinizes the factors influencing the quality and purity of essential oils, elucidating the significance of standardization and certification for safe usage. A comprehensive assessment of the therapeutic effects of essential oils is provided, encompassing their potential as antimicrobial, analgesic, anxiolytic, and anti-inflammatory agents, among others. Clinical trials and preclinical studies are discussed to consolidate the existing evidence on their efficacy in treating diverse health conditions, both physical and psychological. Safety considerations are of paramount importance when employing essential oils, and this review addresses potential adverse effects, contraindications, and best practices to ensure responsible usage.

Conclusions: This comprehensive review provides valuable insights into the exploration of essential oils for aromatherapy, emphasizing their potential as natural and potent remedies for a wide range of ailments. By amalgamating traditional wisdom and modern research, this article aims to encourage further investigation into the therapeutic benefits of essential oils while advocating for their responsible and evidence-based incorporation into healthcare practices.

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List of abbreviations

EOs	Essential oil
BBB	Blood brain barrier
CNS	Central nervous system
GIT	Gastrointestinal tract
SAR	Structure activity relationship
HSP	Heat shock protein
VAS	Visual analog scale
5-HT$_3$	5-hydroxytryptamine receptor 3
PMS	Premenstrual syndrome
CUMS	Chronic unpredictable mild stress
ELISA	Enzyme linked immunosorbent assay
GABA	Gamma-aminobutyric acid
BDNF	Brain derived neurotropic factor
ERK	Extracellular-signal-regulated kinase
MAPK	Mitogen-activated protein kinase
HAM-D24	Hamilton rating scale for depression
VFT	Verbal fluency assessment
fNIRS	Functional near-infrared spectroscopy
CgA	Chromogranin A
POMS	Profile of mood states
CRF	Corticotropin releasing factor
TH	Tyrosine hydroxylase
NGF	Nerve growth factor
HPA	Hypothalamus-pituitary-adrenal axis
TAS	Test anxiety schedule
STAS	State test anxiety scale
WHO	World health organization
CAM	Complementary and alternative medicine
GMP	Good manufacturing practices
FAO	Food and agriculture organization
FDA	Food and drug administration
CPSC	Consumer product safety commission
ARTG	Australian register of therapeutic goods
NNHPD	Natural and nonprescription health product directorate

1. Introduction

The awareness and usage of aromatherapy applications are increasing day by day in society. The term "aromatherapy" was coined in the early 20th century by French chemist René-Maurice Gattefossé, who discovered lavender oil's healing properties when treating a burn (Gattefossé et al., 1993). Marguerite Maury and Robert Tisserand made significant contributions, developing new application methods and blending techniques and promoting aromatherapy for relaxation and well-being (Bensouilah, 2005). The ancient Egyptians, Chinese, and Indians, along with contributions from Arab cultures and European herbalism, laid the groundwork for the contemporary understanding and application of aromatherapy. Aromatherapy utilizes essential oils for therapeutic purposes, promoting well-being and relaxation. Essential oils (EOs) are concentrated plant extracts obtained through processes such as steam distillation (Bhavaniramya et al., 2019). Aromatherapy has a long and rich history that spans from ancient civilizations to modern times. In ancient Egypt, essential oils such as frankincense (*Boswellia sacra* Fluck) and myrrh (*Commiphora myrrha* T.Nees) were used in religious rituals, embalming, and medicinal preparations (Association française de normalisation (AFNOR), 2000). Traditional Chinese medicine incorporates aromatic substances to balance energy and treat ailments. Ayurvedic medicine in India employs aromatic plants and oils for healing and spiritual purposes (Cimino et al., 2021; F. F. Li et al., 2019; McMullen and Dell'Acqua, 2023). During the Middle Ages, Arab cultures contributed significantly to aromatherapy, distilling aromatic substances and using them in remedies and perfumes (King, 2022). In Europe, herbal medicine and the use of aromatic plants continued to evolve, with scholars such as Hildegard von Bingen documenting their healing properties (Uehleke et al., 2012).

The term "essential oils" has been in use since the 16th century, derived from the drug Quinta Essentia and named by Paracelsus von Hohenheim of Switzerland (Guenther, 1988). They are referred to as essential oils or essences due to their volatility and fragrance. Various

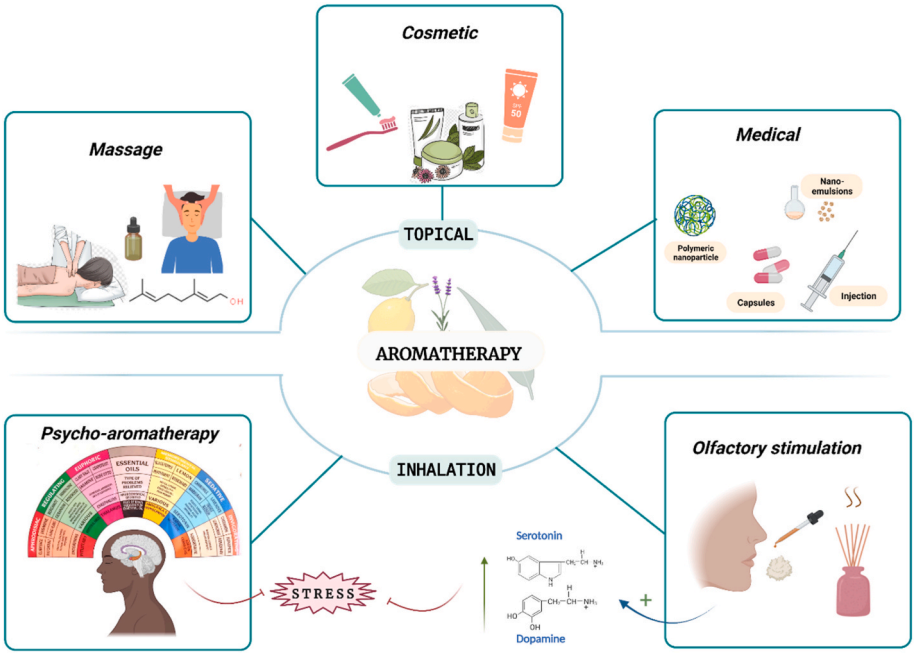


Fig. 1. Aromatherapy Classification. The basic classification is via the route of administration; oral or topical. It includes various techniques such as massage, psych-aromatherapy, cosmetic, medical, olfactory stimulation, etc. (Created with Biorender.com).

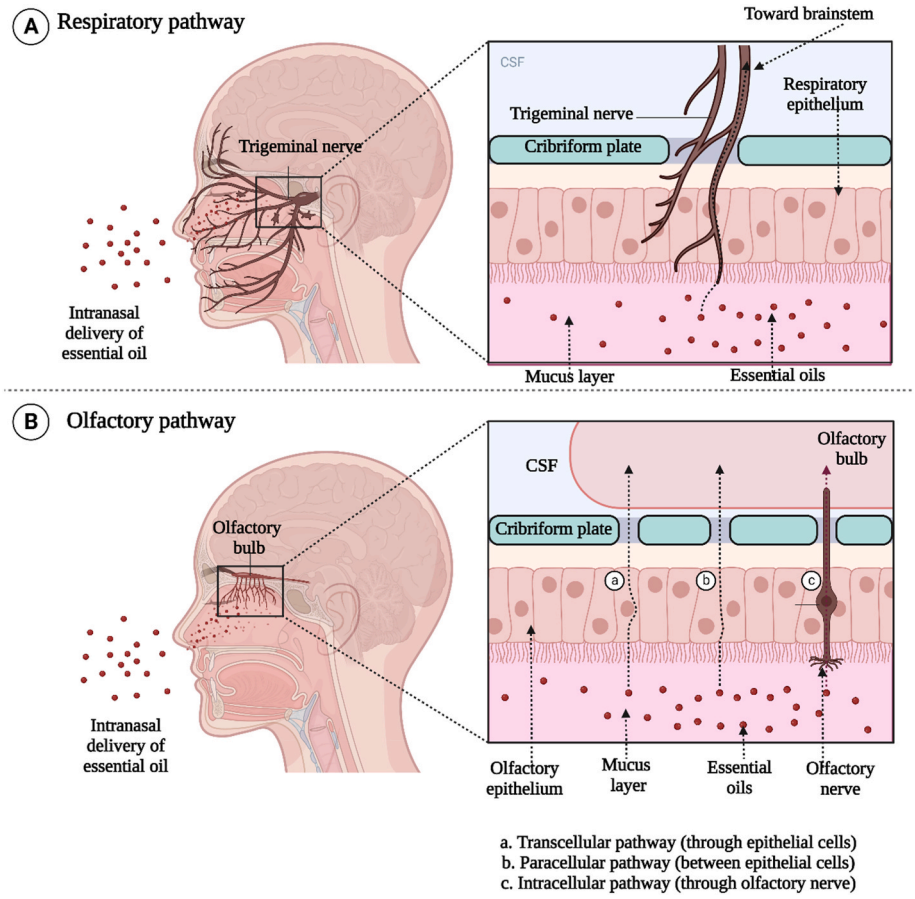


Fig. 2. The respiratory and olfactory pathways are involved in essential oil action in the human body system. The respiratory pathway contains entry of essential oil into the brain region through the respiratory cerebellum. The trigeminal nerve plays a vital role in this process. In the olfactory pathway, three modes of cell-to-cell diffusion exists for essential oil, including the transcellular, paracellular, and intracellular pathways, with the help of the olfactory nerve and olfactory bulb (Created with Biorender.com).

researchers have attempted to define essential oils. According to the French Agency for Normalisation (AFNOR), essential oils are products obtained from vegetable raw materials through steam distillation or mechanical processes from citrus epicarp, or "dry" distillation. They are later separated from the aqueous phase using physical methods (Association française de normalisation (AFNOR), 2000). This definition encompasses the raw materials and extraction methods used for essential oils, including the use of nonaqueous solvents or cold absorption.

Essential oils are highly soluble in volatile compounds such as alcohol, ether, and fixed oils but insoluble in water. Essential oils extracted from cinnamon (*Cinnamomum verum* J.Presl), sassafras (*Sassafras albidum* Nutt. Nees), vetiver (*Chrysopogon zizanioides* L. Roberty), and other natural sources are liquid and colorless at room temperature (Dhifi et al., 2016). As a result, they are extensively utilized in aromatherapy and the cosmetics industry. The volatile compounds present in essential oils, such as ketones, aldehydes, and aromatic compounds, play crucial roles in aromatherapy by reducing mental and physical stresses when inhaled. Essential oils find applications in various therapeutic purposes, including massage aromatherapy, psychoaromatherapy, and olfactory aromatherapy.

Additionally, essential oils function as chemical signals and aid plants in controlling and regulating their environments, protecting themselves from pests, and attracting beneficial insects such as pollinators. In ancient times, essential oils were produced through conventional hydro distillation, while earlier methods involved the primitive form of distillation employed by Romans and Greeks to produce turpentine and camphor (Lee et al., 2015). The method was refined by Arabic scientists, leading to its adoption for therapeutic use in Europe during the Middle Ages, as documented in the 13th-century work of Villanova (Hartley et al., 2013). In the late 20th century, essential oil-based aromatherapy gained popularity and widespread use due to its significance. Essential oils are major ingredients in aromatherapy and can be administered in trace amounts through inhalation, massage, or application on the skin surface. Inhalation and external application of essential oils are employed for a wide range of therapeutic purposes, promoting mental and physical balance, relieving stress, rejuvenating the individual, and even addressing microbial infections, Alzheimer's disease, cardiovascular issues, cancer, and labor pain during pregnancy (Ali et al., 2015; Jimbo et al., 2009; Shiina et al., 2008). Aromatherapy is also increasingly utilized for cancer and sleep disorders. Other organic compounds like alcohols, aldehydes, ketones, oxides, esters, and phenols (besides terpenes) present in essential oils contribute to a sense of well-being (Bowles, 2003).

Aromatherapy can be divided into two major classes based on application site which includes topical and inhalation aromatherapy. Topical aromatherapy includes massage therapy, medical application, and cosmetic purposes. Inhalation aromatherapy includes psychoaromatherapy and olfactory stimulation (Ali et al., 2015). This is depicted in detail in Fig. 1.

One of the major misconceptions present around aromatherapy is that it is linked to mere inhalation. The application of aromatherapy massage is one of the major techniques used in the broader domain of aromatherapy. Massage aromatherapy is a useful tool for relaxation during pregnancy (Mueller and Grunwald, 2021). Essential oils have been used in a variety of ways, including oral and rectal administration (Doukas et al., 2010; Horrigan et al., 2012). The vaginal route of

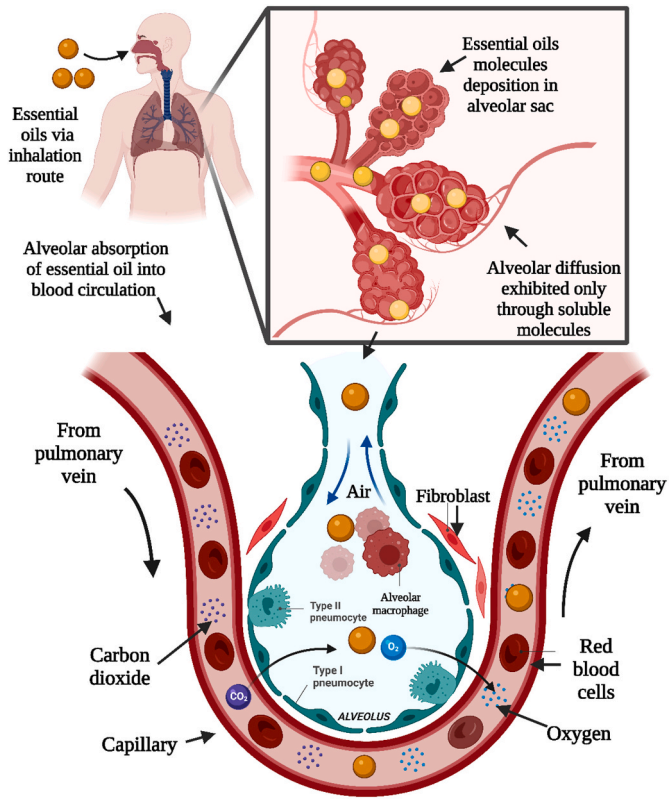


Fig. 3. The alveolar absorption of essential oil into blood circulation: The inhalation of essential oil allows these molecules to have access into the alveolar sac of the respiratory system. However, only soluble molecules showed alveolar diffusion to get mixed into the blood stream for further circulation into the body (Created with Biorender.com).

administration for essential oils has also been used many times by researchers across the globe. To use the highest possible application of essential oils, some sort of best-practice training will be required regarding more exploration of the physicochemical aspects and potential applications of the same for human benefits (Buckle, 2014; Hoover, 2010). In this manuscript, we will try to focus on the role of essential oils in aromatherapy providing in-depth detail on the role and mechanism of active constituent's pharmacological actions and recent advances made in the drug delivery systems for essential oil use as therapeutic agents. The review also provides insights into the regulatory aspects of essential oil applications and their clinical advances. The names of the plants from which essential oils are obtained have been verified from medicinal plant names services available on Kew science website (http://mpns.kew.org/) or world flora online (https://www.worldfloraonline.org/) unless otherwise specified.

2. Mechanism of action of essential oil in aromatherapy

Increased neurogenesis, regulation of hormonal levels, selective stimulation of certain brain regions, and alteration in blood biochemistry affecting both mood and emotions are the few outcomes that could be triggered by the potential use of essential oils (Timothy K.H. Fung et al., 2021). Such favorable outcomes result from inhaling the volatile elements constituted within such oils. When inhaled, the mechanisms through which they act typically consist of two pathways-the olfactory stimulation and the respiratory stimulation. Inhalation aromatherapy via olfactory stimulation principally works through the activation of the olfactory nerve extending from the nose toward the brain. The therapeutic stimulation that these oils offer is vastly due to their close structural resemblance with the physiological neurotransmitters and hormones. Such close structural chemistry enables the stimulation of olfactory chemoreceptors lining the nasal passage and thus activates the olfactory signaling as depicted in Fig. 2b. This signaling terminates in the higher cerebral cortex following which the olfactory sensory neurons convey electrical impulses to the limbic and hypothalamic regions of the brain through the olfactory bulb and upper olfactory cortex (Sattayakhom et al., 2023). Some highly volatile molecules can directly enter the brain and regulate the neuronal pathways upon inhalation and can bypass the entire olfactory signaling. Either way, the end physiological result is a surge of neurotransmitters and neuromodulators, causing an overwhelming sense of calmness in the mind and body, thus alleviating symptoms of anxiety and depression (J Cui et al., 2022).

Apart from olfactory stimulation, a prominent pathway taken by the EOs to alter brain functioning is through their alveolar absorption as seen in Fig. 3. This enables the EO molecules to enter the blood circulation, cross the blood–brain barrier (BBB), and thereby potentially interact with specific brain regions. Gaseous exchange occurs through the respiratory system, and the distribution of essential oils into the respiratory system occurs through the diffusion process. Alveolar diffusion remains a potential pathway for the molecular delivery of these volatile molecules into the systemic circulation entering the brain. EO molecules that are lipophilic in nature can be transported across the BBB and can activate specific regions of affinity within the CNS. Such an activation would induce positive psychological and physiological effects that aid in the symptomatic relief of mood disorders (Fung et al., 2021).

The integumentary system is also activated by essential oils. The analgesic effect obtained when using EOs topically, along with the feeling of well-being, results from the quick release of endorphins and certain pain modulators. Studies show that when applied on the forehead, lavender oil produces a sense of relief due to a complex pharmacopsychological cascade. Therapeutic advantages offered by the ayurvedic oil dripping treatment of Lavender oil were found to be induced by the somatoautonomic reflex through thermosensors or pressure sensors via the trigeminal cranial nerve. An elusive and complicated pharmacophysio- psychological interplay was found to be involved in producing the physiological effects (Dobetsberger and Buchbauer, 2011). The trigeminal innervations also provide a strong link between the nose and the brain drug-delivery system (Johnson et al., 2010). Well-established studies exist proving the efficiency of trigeminal nerve participation in nose-to-brain delivery of therapeutic agents and similarly for essential oil such pathway is predicted but the mechanistic involvement remains sparse due to the complexity of essential oil compositions (Y. Y. Li et al., 2019; Sanna et al., 2019) Fig. 2.

The topical application of essential oils mainly works through skin penetration by dissolving with the skin's cell membrane lipid constituent. The chemical composition of essential oil will determine the depth of penetrability of oils into the skin e.g., jojoba, avocado, soybean, almond, etc. are limited to the upper epidermis while oxygenated terpenes can penetrate deeper layers and through the skin (de Andrade et al., 2021). Some oils are also used as penetration enhancers both internally and topically depending on different mechanisms like enhancing drug partitioning, disintegrating highly ordered intercellular (between corneocytes in stratum corneum) lipid structure, and inducing conformational modification by interacting with intercellular protein domain (Herman and Herman, 2015).

Essential oils ideally contain a plethora of volatile compounds whose therapeutic importance is of great value. The molecular sizes of the essential oil molecules will determine their delivery to the brain through different routes. The inhalation rate and success of delivery increases as the size of the formulation decreases. The disadvantage of inhalational therapy is the improper penetration of these molecules into the brain due to their non-uniform varying sizes. But through the use of nanotechnology, the employment of encapsulated nanoparticles has yielded better absorption results of these essential oils making it a promising therapeutic future venture (Fung et al., 2021).

The emotional response change occurred through the essential oil

Table 1
Structures of active chemical constituents present in individual essential oils.

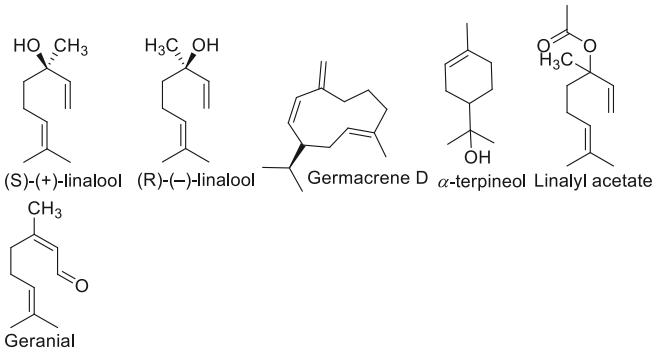
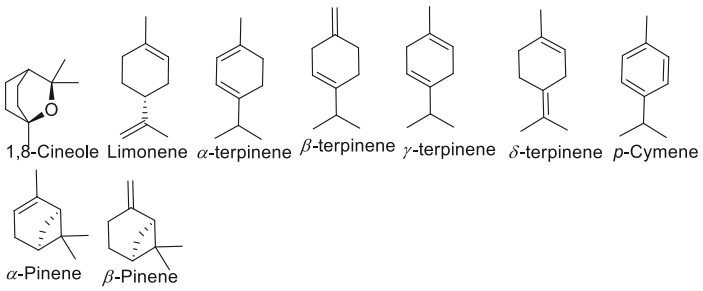
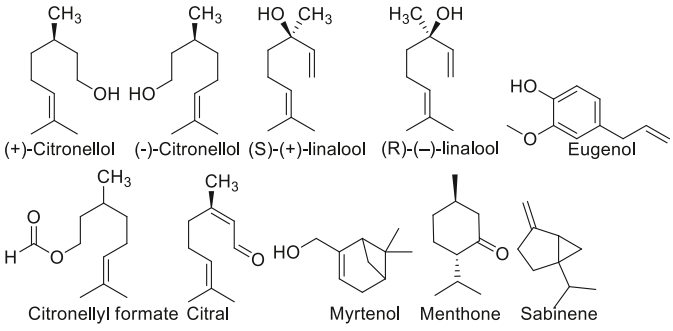
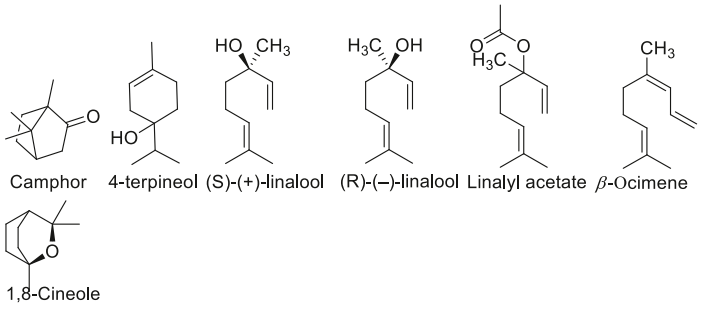
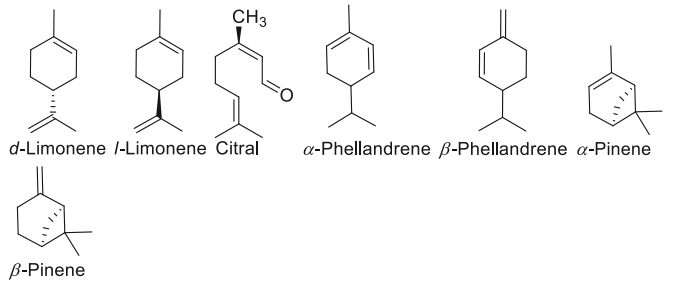
Name of essential oil	Chemical Constituent
Clary sage (*Salvia sclarea* L.)	
Eucalyptus (*Eucalyptus globulus* Labill.)	
Geranium (*Pelargonium graveolens* L'Her)	
Lavender (*Lavandula angustifolia* Mill.)	
Lemon (*Citrus limon* L. Osbeck)	

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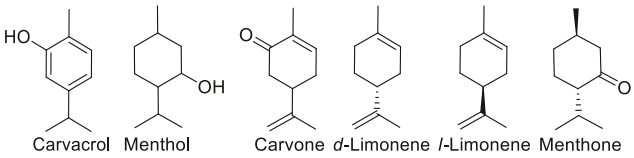
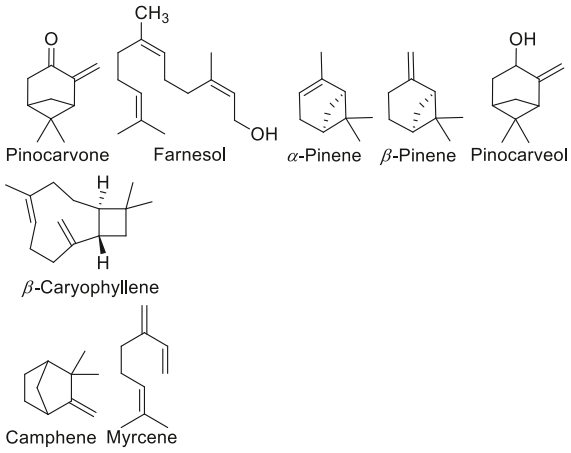
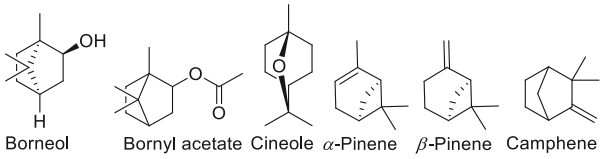
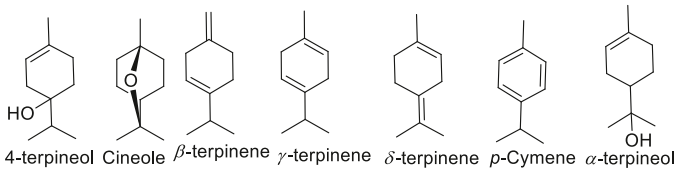
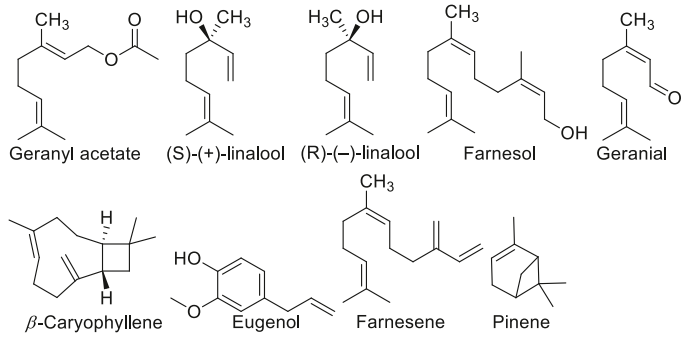
Table 1 (*continued*)

Name of essential oil	Chemical Constituent
Peppermint (*Mentha piperita* L.)	
Roman chamomile (*Chamaemelum nobile* L.)	
Rosemary (*Salvia Rosmarinus* Spenn.)	
Tea tree (*Melaleuca alternifolia* Maiden & Betche Cheel.)	
Ylang Ylang (*Cananga odorata* Lam.)	

due to its impact on the central nervous system. Some of the molecules can pass through the sensory neuron cells or the olfactory mucosa. Gaseous exchange occurs through the respiratory system, and the distribution of essential oils into the respiratory system occurs through the diffusion process (T K H Fung et al., 2021). This medium is used for the therapeutic interventions of the respiratory disease, where essential oils application in upper- and lower-respiratory tract infection and mood disorders (through olfactory interventions) has been well explored (Györgyi Horváth, 2015). There are three major mechanisms involved in the action of the essential oil on the brain. Many volatile components are present in the essential oil, and nanotechnology, such as nanoparticles, is used for better absorption of the essential oil with the help of the encapsulation technique (T K H Fung et al., 2021). The uptake of the nanoformulation of the essential oil is good. The molecular sizes of the essential oil molecules will determine their delivery to the brain through different routes. The inhalation route involves the olfactory and respiratory systems, while the first route is related to that of odorant signal transmission with the help of the olfactory bulb. The emotional response change occurred through the essential oil due to its impact on the central nervous system. Some of the molecules can pass through the sensory neuron cells or the olfactory mucosa. Gaseous exchange occurs through the respiratory system, and the distribution of the essential oil into the respiratory system occurs through the diffusion process, as presented in Fig. 3. There are three major mechanisms involved in the action of the essential oil on the brain. The first mechanism involves the activation of nasal olfactory chemoreceptors and the impact of olfactory signals on

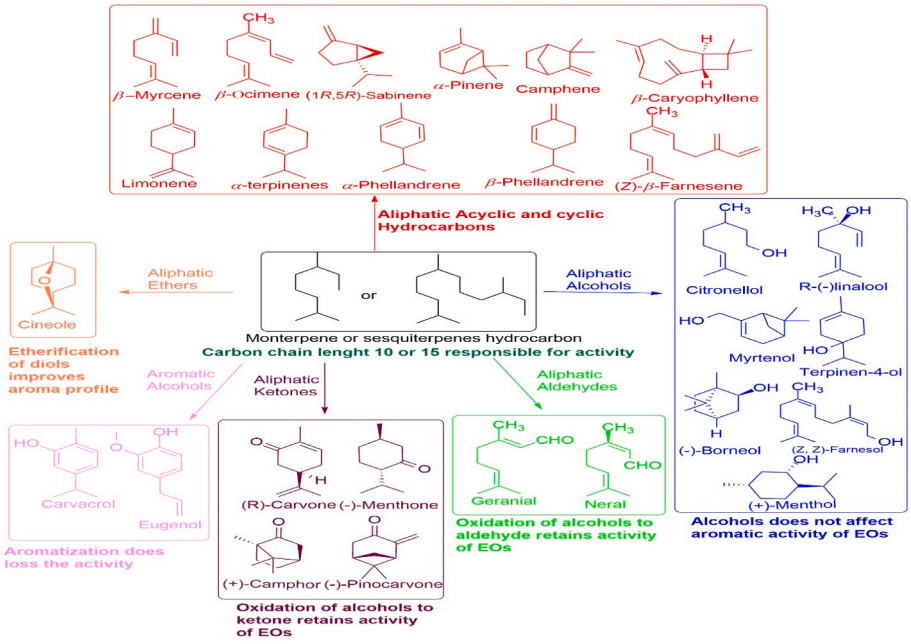


Fig. 4. Structure-activity relationship of major chemical constituents of essential oils used in aromatherapy.

the brain. The olfactory system is involved in the sensory system, which has a direct link to the limbic regions of the brain. There is a strong impact of olfactory stimuli on mood. The second mechanism involves the generation of several cellular and molecular events due to penetration of the essential oil through the olfactory nerve, which is connected to brain areas. The third mechanism involves the alveolar type of absorption of the essential oil through the blood circulation, which crosses the blood brain barrier to interact with that of the brain regions (Kotlik et al., 1986; Zimmerman et al., 1970).

3. Chemistry of essential oils

Essential oils (ethereal or volatile oils) are naturally occurring volatile organic compounds produced in significant quantities from raw plant materials or their organs, such as flowers, seeds, buds, leaves, fruits, wood, roots, bark, and twigs. These oils may comprise a mixture of more than 300 compounds. Usually, their molecular weight is below 300 Da. Chemically, those compounds belong to multiple chemical classes, such as amines, alcohols, phenols, ethers, and carbonyl compounds such as aldehydes, ketones, amides, and esters. The chemical constituents of essential oils include terpenes and phenylpropanoids.

3.1. Structural activity relationship (SAR) of the chemical constituents of EOs utilized in aromatherapy

Terpenes are the significant constituents found in essential oils responsible for aromatherapy. Terpenes are further classified into hemiterpenes (containing 1 isoprene unit), monoterpenes (containing 2 isoprene units), sesquiterpenes (containing 3 isoprene units), diterpenes (containing 4 isoprene units), sesterterpenes (containing 5 isoprene units), triterpenes (containing 6 isoprene units) and polyterpenes (containing many isoprene units) based on the number of isoprene units condensed into final molecules.

Acyclic hydrocarbon monoterpenes with 10 carbon chain lengths, such as myrcene and β-ocimene (Table 1, entries 1 and 2), are responsible for the fragrance and are ultimately used as sedative, antioxidant, anti-inflammatory, and anticancer agents (on lung cancer) (Bai and Tang, 2020; do Vale et al., 2002; Ojeda-Sana et al., 2013; Rufino et al., 2015). Myrcene is believed to assist cannabinoids in penetrating the BBB and enhancing psychoactive responses. Increment in the carbon chain length by 5 carbons, i.e., sesquiterpenes, farnesene, and polygodial act as anti-allergic and anti-inflammatory agents. Oxygenated acyclic alcoholic monoterpenoids such as linalool citronellol and their respective esters, such as geranyl acetate, linalyl acetate, and citronellyl formate, have anxiolytic and neuroprotective effects on the central nervous system (CNS) (Harada et al., 2018; Qneibi et al., 2019). Oxidized acyclic monoterpenoids having an aldehyde functional group, such as geranial and neral, act on the protein heat-shock protein (HSP) 90 (an ATP-dependent molecular chaperone), which is responsible for protein folding and stability in cancer disease. Therefore, it acts as an antitumor drug.

Cyclic hydrocarbon monoterpenes, such as limonene, pinenes, sabinene, and camphene, are also responsible for the flourishing profile of essential oils and play a crucial role in aromatherapy (Koyama and Heinbockel, 2020; Vieira et al., 2018; Weston-Green et al., 2021; Yang et al., 2016). Oxygenated cyclic monoterpenes with hydroxy functionalities, such as menthol, pinocarveol, myrtenol, terpinene-4-ol, and borneol, contribute to the aroma profile of essential oils. Oxidations of cyclic alcohols produce ketones, such as menthone, carvone, pinocarvone, and camphor, which are also used for aromatherapy. When inhaled through aromatherapy, those ketones have various benefits. It can help relieve respiratory congestion and improve breathing by opening the airways. It is also thought to have a calming effect on the mind, reducing stress and anxiety (J Cui et al., 2022). Apart from those chemical functionalities, aromatization of monoterpene hydrocarbons and alcohols, such as p-cymene, are equally responsible for the aroma of the essential oils and may be responsible for the bioactivity of aroma (Barboza et al., 2018). The SAR of the major chemical constituents of essential oils used in aromatherapy are illustrated in Fig. 4.

3.2. Aroma profiles of essential oils and their individual constituents

The flavor or fragrance of the essential oil mainly contributes to its biological activity, especially in aromatherapy. The aroma of the essential oil is either gratifying or revolting to humans. Thus, the pleasant effects of the essential oil may result in the desired therapeutic actions on the central nervous system, which further relieves stress or rejuvenates the individual. The active constituents of essential oils are naturally available in different chemical structures, few depicted in Table 1. Optical activity exists in compounds containing one or more

Table 2
Aroma profile of commonly used essential oils in aromatherapy.

Common Name	Part of plant	Biological Name	Aroma Description	References
Clary sage	leaves	*Salvia sclarea* L.	Characteristic herbaceous odor	Perica Ž Pešić (2003)
Eucalyptus	leaves	*Eucalyptus globulus Labill.*	Fresh balsamic camphor-like	(de Groot and Schmidt, 2016; Sharmeen et al., 2021)
Geranium	Flowers and leaves	*Pelargonium Graveolens* L'*Her*	Sweet rose-like odor with a hint of mint or "greenness"	Pitman (2004)
Lavender	Flowers and leaves	*Lavandula angustifolia Mill.*	Sweet floral aroma	Sarkic et al. (2018)
Lemon	peels	*Citrus limon* L. *Osbeck*	Fresh lemon peel	(Aguilar-Hernendez et al., 2020; Burnett et al., 2019)
Peppermint	Flowers and leaves	*Mentha piperita* L.	Sweet minty, menthol-like	Zhang et al. (2022)
Roman chamomile	Lowers and Stalks	*Matricaria chamomilla* L.	Diffusive, fresh, sweet-warm fruity	Rhind (2012)
Rosemary	Whole plant	*Salvia Rosmarinus Schleid.*	Strong, warm, woody, balsamic aroma	Sarkic and Stappen (2018)
Tea tree	Branches	*Melaleuca alternifolia Maiden & Betche Cheel*	Intensive aromatic fresh camphoraceous odor	Sarkic and Stappen (2018)
Ylang Ylang	Flowers	*Cananga odorata Lam. Hoof & Thomson*	Characteristic, floral, recalling jasmine	Ng et al. (2022)

chiral carbon atoms. Because of their chirality, these compounds exist in different enantiomeric forms. These enantiomers and diastereomers have different applications in the food, pharmaceutical, fragrance, and flavor industries (Lahlou, 2004).

Moreover, those enantiomers have not only different applications but also different aroma profiles. For instance, the flavor of *R*- (−)-carvone is minty, while *S*-(+)-carvone is aromatic. Additionally, the aroma of the (+)-limonene enantiomer is significantly more activating than that of the (−)-limonene enantiomer (Heuberger et al., 2001). The variations in their aroma profile influence the therapeutic potential of individual enantiomers (Laska, 1999). Hence, this section describes the aroma profile of essential oils commonly employed in aromatherapy with their active constituents as listed in Table 2 while the aroma profile of the active constituent of the essential oil is enlisted in Table 3.

4. Applications of essential oils in aromatherapy

Aromatherapy is a complementary therapy that uses fragrant volatile compounds to promote physical, emotional, and spiritual well-being. This module of therapeutics intervention utilizes the essential oils obtained by distilling the extracts obtained from plants. The principal application includes stress management, analgesic activity, mood enhancement, and relaxation through administration routes such as inhalation, topical application, and rarely ingestion under medical supervision. Although the technique and practice of aromatherapy differ from those of herbal medicine, essential oils are commonly used in herbal medicine by researchers, especially botanists, who prefer to use whole plant applications for human benefits rather than plant constituents. The practitioner of aromatherapy is called an aromatherapist, which is quite different from that of a herbalist, while the latter is used to implement medicinal-grade essential oils for traditional and medical uses. The traditional way to use aromatherapy is for the care of the mind and body, along with holistic mental health (Auffarth, 2013; Croy et al., 2013; Hoskison, 2013). Aromatherapy has been shown to be efficacious in managing and treating certain illnesses, which sometimes fail to be managed by pharmacological interventions. Aromatherapy only existed after discovering the antiseptic and skin penetrating properties of essential oils. Essential oils are highly concentrated plant extracts obtained from oil glands or oil sacs of leaves, fruit peels, and flowers and are believed to have therapeutic properties when inhaled or applied to the skin. They can be broadly categorized based on their source aroma families, namely, citrus (lemon, bergamot, grapefruit, orange), herbaceous (chamomile, eucalyptus, fennel, rosemary, marjoram, rosemary, oregano, thyme), floral (lavender, neroli, rose, rosewood, jasmine, chamomile), minty (peppermint, spearmint), camphoraceous (camphor, eucalyptus), spicy (ginger, basil, aniseed, cinnamon, black pepper, clove, nutmeg, cardamom), musky (frankincense, myrrh, benzoin, Peru balsam) and woody (sandalwood, cedarwood, rosewood, valerian, patchouli).

Aromatherapy principally uses different modes of action, which remain poorly described in the available literature database. Alternative practice includes using synthetic oils obtained from petroleum products as a replica for some essential oils as malpractice with low to no therapeutic advantages. The complementary system of medicine works well when the different aspects of a healthy lifestyle and diet are followed. The ailments targeted using aromatherapy include anxiety, depression, insomnia, muscular soreness, respiratory issues, urinary incontinence, joint problems, or simply aesthetic purposes, as illustrated in Table 4. The application of essential oils ranges from cosmeceutical to therapeutic interventions, which are described further in the following sections (Ali et al., 2015; Jaruzel et al., 2019). Antibacterial and antiviral potential of essential oils have been widely focused upon by herbal medicine system. They possess cytotoxic property affecting the microbes due to the presence of several functional groups like phenolic group (thymol, carvacrol) ester group (geranyl acetate, bornyl acetate), terpene alcohols (geraniol), terpene aldehydes (citronellal), and sesquiterpenes (limonene) (Saad et al., 2013). The exact mechanism of antimicrobial and antiviral action of essential oil remains unknown but it is hypothesized to work through acting on bacterial membrane and inhibiting efflux (Yang et al., 2021).

4.1. Sleep promotion

Sleep promotion in patients and healthy adults has become a rising concern due to the changing lifestyle and overall screen time for healthy individuals. Sleep disorders have become more prevalent due to stress, substance abuse, aging, sleep-cycle nonuniformity, and lack of physical activity, leading to symptoms such as dizziness, fatigue, disorientation, and attention issue management (Demmer and Sauer, 2002).

Pharmacological interventions have led to side effects altering day-to-day activity, including confusion and lethargy during the daytime, in addition to an increased risk of habitual drug abuse. Hence, non-pharmacological interventions, especially aromatherapy, are adapted for sleep promotion based on their efficacy for the intended action. The active moiety of aromatic nature reaches the limbic system through the olfactory system, causing a relaxing effect and sedation affecting the heart rate, reproductive system, blood pressure, stress response, and memory. Agents such as lavender, bergamot, peppermint, chamomile, rosemary, clary sage, lemon grass, eucalyptus and rosewood are used for such actions. The single aroma inhalation method using lavender was reported to be more effective than mixed aroma inhalation in insomnia symptoms (Cheng et al., 2022; Cheong et al., 2021). The application

Table 3
Aroma profile of some active constituents of essential oils.

Name of active Constituent	Aroma Description	Reference
l-Borneol	Moldy, sharp camphor-like odor	Schreiner et al. (2018)
Bornyl acetate	Woody, camphor, mentholic, spicy	(El-Zaeddi, H. Martinez-Tome, J. Calin-Sanchez and Burlo, F. Carbonell-Barrachina, 2016)
α-(±)-Bisabolol	Sweet floral odor	Sarkic and Stappen (2018)
Camphene	Pungent odor	Thurman (2020)
Camphor	Odor like mothball	Evans and Evans (2009)
1,8-Cineole	Fresh camphor-like smell	Tripathi and Mishra (2016)
β-Caryophyllene	Woody and spicy	Skold et al. (2006)
Carvacrol	Phenolic, spicy odor	Clarke (2008)
R-(−)-carvone	Minty herbaceous	Zellner et al. (2006)
Citral	Lemony	Sarkic and Stappen (2018)
Citronellol	Intense floral, rose, sweet like	Ravi et al. (2007)
Citronellyl formate	Fruity, sweet, citrus-like, kumquat-like	Choi (2005)
p-Cymene	Wood-like and citrus-like	Schreiner et al. (2020)
Eugenol	Dry, herbaceous	Umano et al. (1994)
α-Farnesene	Sweet, fruity	Ravi et al. (2007)
(2*E*,6*E*)-Farnesol	Flowery, weak-citrus odor	Ravi et al. (2007)
Geraniol	Fresh, sweet, rose-like	Ravi et al. (2007)
Geranyl acetate	Pleasant, floral rose, herbal	
Germacrene D	Woody, spicy	El-Zaeddi et al. (2016)
Limonene	The strong odor of orange	Sarkic and Stappen (2018)
(*S*)-(+)- Linalool	Floral, grassy, pleasant, citrus	Ravi et al. (2007)
Linalyl acetate	Floral, sweet citrus	Zellner et al. (2006)
Menthol	Sweet minty, cooling and fresh scent	Sarkic and Stappen (2018)
Menthone	Aromatic and minty odor.	Brown et al. (1971)
Myrcene	Pleasant floral	Ravi et al. (2007)
Myrtenol	Woody, minty aroma	Bhatia et al. (2008)
cis and trans-(β)-ocimene	floral scents	Farre-Armengol et al. (2017)
Phellandrene	Mint, turpentine	(El-Zaeddi, H. Martinez-Tome, J. Calin-Sanchez and Burlo, F. Carbonell-Barrachina, 2016)
α-Pinene	Fresh, camphor, sweet, pine, earthy, woody	(El-Zaeddi, H. Martinez-Tome, J. Calin-Sanchez and Burlo, F. Carbonell-Barrachina, 2016)
β-Pinene	Woody, turpentine	Ravi et al. (2007)
Pinocarveol	Woody	Clarke (2008)
Terpinen-4-ol	Green, fruity, citrus-like	Choi (2005)
α-Terpineol	Resinous	Choi (2005)
γ-Terpineol	Green, woody	Choi (2005)
Sabinene	Woody, terpene, citrus, pine, spice	(El-Zaeddi, H. Martinez-Tome, J. Calin-Sanchez and Burlo, F. Carbonell-Barrachina, 2016)

methods include massage, direct inhalation, and indirect inhalation by spraying on a handkerchief or placing aroma in a necklace or pillow. Aromatherapy aids in improving the quality of sleep, sleep satisfaction, and overall sleep pattern in patients with sleep disorders (Hwang and Shin, 2015). Massage with chamomile and lavender oil 20 min before bedtime (3 sessions in a week) has been reported to improve the symptoms of anxiety and sleep deprivation in burn injury patients (Rafii et al., 2020). Silexan oral capsules consisting of lavender oil are prescribed for anxiety management in patients with disturbed sleep patterns, but a comparative analysis of oral versus inhalation therapy for lavender oil is not available (Greenberg and Slyer, 2018). Working professionals, especially women, are predisposed to an imbalance in the sleep-wake cycle and hence a disrupted overall quality of life. A clinical study reported the beneficial activity of blended essential oils obtained from lavender, *Salvia sclarea* (clary sage) and *Origanum majorana* for improving the quality of life and sleep pattern in working women (Kao et al., 2017). Deep sleep or the slow wave sleep percentage hike, decreased rapid-eye-movement sleep, and increased wake latency after sleep in women was observed to be higher than in men by lavender aromatherapy due to higher olfactory stimulus in the females (Goel et al., 2005). In addition to aromatherapy, exercise, cognitive stimulation, family participation and light/noise blockage aided in improving sleep and managing delirium incidences (Kang et al., 2022).

4.2. Improvement of preoperative anxiety

An unpleasant sense of fear and nervousness is termed anxiety. Patients undergoing surgery tend to experience preoperative anxiety, which may lead to altered physiological parameters such as elevated body temperature, hypertension, higher perspiration, tachycardia, nervousness, apprehension, aggression, and nausea. The psychological impact of preoperative anxiety causes over-sensitization of patients toward pain stimuli, leading to discomfort, which may hinder operative procedures such as cardiac or cancer surgery. Endocrinal and autonomic triggers because of preoperative anxiety also cause hemodynamic instability. This also affects the postoperative recovery phase, affecting pain, healing delay, vomiting, and a lengthened hospital stay. It is a contributor to increased surgical morbidity risk, and it has been reported that patients with higher anxiety in the preoperative phase also require a higher dose of an anesthetic agent and show poor recovery (Mulugeta et al., 2018). Pharmacological preanesthetic agents such as midazolam, ketamine, fentanyl, and diazepam are included in pharmacological interventions as anxiolytics, but adverse effects such as difficulty breathing, drowsiness, anesthetic-agent interactions, and prolonged recovery have limited their clinical use. Therefore, nonpharmacological interventions include counseling sessions by healthcare providers, music, family support, acupuncture, aromatherapy, massage, and hypnosis (Wang et al., 2022). A meta-analysis report suggests the effectiveness of lavender oil, citrus species oil, and rose oil in improving preoperative anxiety symptoms (Guo et al., 2020).

Aromatherapy with lavender oil reduced the anxiety score on the visual analog scale (VAS) in pre-versus post-aromatherapy sessions in patients preparing for major surgery (Koehler, 2021). A similar result was reported for using lavandin oil aromatherapy patches as preoperative care for anxiety in females preparing to undergo breast cancer surgery. In addition to the VAS for anxiety scoring, the study considered markers such as heart rate and mean arterial pressure. A significant decrease in VAS was reported, while heart rate and mean arterial pressure slightly decreased, although not statistically significant (Jaruzel et al., 2019). Another clinical study reported the efficacy of 5% Lavandula hybrida (*Lavandula latifolia* Medik) oil massage for 10 min before surgery on the morning of surgery, which offered a better improvisation of anxiety score over the group receiving no massage or oil massage on the evening before the colorectal surgery day (Ayik and Özden, 2018). The major limitation of currently reported clinical studies and meta-analysis results is that the study sample size remains very small, and therefore, study results, in a broader sense, remain inconclusive (Wang et al., 2022). The result also varies based on the study population heterogeneity; for example, lavender oil and *Citrus aurantium* L. were equivalently effective in the male population, while in female patients, *C. aurantium* was comparatively less effective in subsiding anxiety symptoms when compared to lavender oil (Ebrahimi et al., 2021). Indirect inhalation through the application of *Lavandula* oil on a handkerchief showed a decrease in anxiety levels in patients compared to the water-inhaled placebo group. Preoperative aromatherapy not only aids in relieving anxiety before surgery but also aids in the perioperative

Table 4
Aromatic agents active in various ailments and their mode of administration.

Herb Name	Route of Administration	Mechanism of Action	Outcome	References
Chamomile and lavender	Massage	Muscular relaxation	Improve sleep symptoms	Rafii et al. (2020)
Silexan (lavender)	Oral		Balanced sleep	Greenberg and Slyer (2018)
Lavender, Clary Sage, Origanum majorana	Inhalation	Olfactory stimulation	Improved quality of life in working women	Kao et al. (2017)
lavender	Inhalation	Olfactory stimulation	Improved deep sleep, decreased rapid-eye movement sleep and increased first wake latency after sleep	Goel et al. (2005)
Lavender, citrus, and rose	Inhalation or topical	Olfactory stimulation and Muscular relaxation	Decreases anxiety symptoms	Guo et al. (2020)
Lavender oil	Inhalation	Muscular relaxation	Improved VAS score for anxiety, normalized heart rate, blood pressure	Kang et al. (2022)
Citrus aurantium and lavender oil	Massage	Muscular relaxation	Citrus oil comparatively less effective in female to suppress anxiety symptoms	Ebrahimi et al. (2021)
Lavender oil	Indirect inhalation (handkerchief application)	Olfactory stimulation	Decrease anxiety symptoms and better perioperative condition management	Honig et al. (2023)
Blended oil of Ginger, spearmint, cardamom versus Peppermint only	Inhalation	Olfactory stimulation	Peppermint only group showed faster relief from nausea when compared with the blended oil group which showed better activity for perioperative procedure	Tate (2019)
QueaseEase™ (Lavender, ginger, mint, spearmint blend)	Aromatic inhaler	Olfactory stimulation	Nonsignificant improvement in postoperative nausea symptoms in children	Kiberd et al. (2016)
Peppermint and ginger	Inhalation	Olfactory stimulation	Relief of nausea symptoms and reduced dose and frequency of antiemetic requirement	Fearrington et al. (2019)
Cardamom	Inhalation	Olfactory stimulation	Decreased nausea in women undergoing cesarean section surgery	Khatiban et al. (2022)
Lemon, ginger, lavender, and peppermint	Inhalation	Olfactory stimulation	Reduced antiemetic requirement for postsurgery care	Marsh et al. (2022)
Rosa damascenes	Inhalation	Olfactory stimulation	Alleviates PMS symptoms including psychological, social and physical symptoms	Heydari et al. (2018)
Rose oil	Massage on abdomen	Muscular relaxation	Subsided endometriosis linked to dysmenorrhea pain	Shahr et al. (2015)
Lavender, sage, marjoram	Massage	Muscular relaxation	Reduce dysmenorrhea pain	Ou et al. (2012)
Cinnamon, clove, rose, lavender	Massage	Muscular relaxation	Decrease in pain intensity, menstrual bleeding, and duration of menses	Marzouk et al. (2013)
Lavender, ginger, clary sage, geranium	Effleurage massage	Muscular relaxation	Ameliorated menstrual pain and fatigue symptoms	Pujiati et al. (2019)
Lavender	Inhalation	Olfactory stimulation	Reduces labor pain	Es-Haghee et al. (2020)
Bergamot	Inhalation	Olfactory stimulation	Improved sleep quality and depressive symptoms in postpartum women	Watanabe et al. (2015)

process by keeping the patient in a calm state of mind and physiological condition (Honig et al., 2023).

4.3. Postoperative management of nausea and vomiting

Surgical procedures are generally lengthy, requiring the patient to be in a state of unconsciousness for a while (minor surgery) or longer duration (major surgeries). This raises the demand for the administration of anesthetic agents for surgical procedures. Local anesthetics do not affect the nervous system and provide local action and are useful for minor processes such as dental tooth extraction or cavity filling. However, in regard to long procedures such as dental implants or cardiac surgery, local anesthetics are not useful due to deeper tissue damage and nervous system involvement. Hence, general anesthetic agents such as propofol are being used. As mentioned earlier, the major limitation of such general anesthetic agents is their side effects on the nervous system. The chemo-trigger zone in the brain, lying at the fourth ventricle, barely crossing the blood–brain barrier, is the main binding site for the anesthetic agents inducing undesired off-target effects. 5-Hydroxytryptamine receptor subtype 3 (5-HT_3) is selectively involved in the emetic response. In addition to the long duration of surgery, the selection of an anesthetic agent also influences postoperative emesis; for example, nitric oxide could stimulate the sympathetic nervous system due to catecholamine release, also affecting middle ear pressure and vestibular homeostasis, and it also causes increased distension of the abdomen due to mask ventilation. Other agents causing postoperative emesis due to their off-target action are ketamine, propofol, etomidate, and opioids. In addition to anesthetic agents, several other factors cause postoperative nausea and vomiting, including pain, ambulation, an opioid analgesic, and supplemental oxygen. Pharmacological agents such as ondansetron, scopolamine, and metoclopramide are used with major limitations of adverse effects such as dry mouth, visual disturbances, QT prolongation, sedation, and dyskinesia (Shaikh et al., 2016). To avoid such peripheral and central adverse effects, alternative modes of antiemetic action are currently being used, including acupuncture, music therapy, hypnosis, and aromatherapy (Kallush et al., 2018; Sandlin, 2006). Inhalation of peppermint oil acts rapidly to relieve nausea symptoms, while blended oils of agents such as ginger, spearmint, and cardamom can reduce nausea symptoms in perioperative care (Tate, 2019). QueaseEase™ consists of a blend of ginger, mint, spearmint, and lavender essential oils, and it was reported to have a nonsignificant improvement in postoperative nausea symptoms in children (Kiberd et al., 2016). Another study in adult patients reported that aromatherapy with either peppermint or ginger or in combination alleviated nausea symptoms in all forms for inhalation with a bare requirement of antiemetic agents (Fearrington et al., 2019). Females are more prone to nausea and vomiting during pregnancy and during cesarean section surgery for delivery. The use of cardamom inhalation therapy alleviated the mother's nausea and retching across the surgery duration (Khatiban et al., 2022). Another combination of essential oils from lemon, ginger, lavender, and peppermint aided in the reduction of antiemetic requirements post-surgery along with an overall dose reduction (Marsh et al., 2022). The complexity of postoperative nausea has made it difficult to manage such symptoms, and hence, there remains only one

pharmacological agent approved by the FDA, i.e., amisulpride, a dopamine D2 and D3 antagonist, as a rescue treatment after a failed prophylactic action (Habib et al., 2019). This might be one of the reasons why there exists variability in the reported results for aromatherapy. A better approach would be to use a mixture of essential oils acting through different pathways, which is challenging due to the multimodal action pathway for natural agents or extracts. This may be overcome by the coordinated use of pharmacological agents in combination with an alternative mode of emesis management, as no such reports exist as per our current literature knowledge.

4.4. Alleviating gynecological diseases

Women's reproductive system is under the complex and tight regulation of hormones and the menstrual cycle. The female body differs even in the immune response from the male body due to variability in the body's attack depending on the menstrual cycle. As such, females are said to have stronger immunity than males, but during ovulation, the female body makes itself ready for the reception of foreign fertilizing moiety against which the immune system should not react. Estrogen, at a peak level during ovulation, plays an important role as a proinflammatory agent and regulates the immune response (Klein and Flanagan, 2016; Oertelt-Prigione, 2012). On top of such routine predisposition, during pregnancy again, the reproductive tract undergoes many physiological and hormonal changes, which are tightly regulated by the endocrine system. Gynecological diseases include microbial and fungal infections in the reproductive tract at variable degrees. Reports suggest that essential oils have antimicrobial and antifungal actions, so they can be used in complementary mode with pharmacological agents in severe cases of infection and may be used independently in mild cases of infection (Arnal-Schnebelen et al., 2004). Gynecological cancers are another group of diseases that are difficult to manage symptomatically by drugs. A study reported the advantages of using aromatherapy for patients with gynecological cancer as a stimulant, mood stabilizer, and relief of symptom burdens such as nausea, pain, and routine skin care for the affected area (Czakert et al., 2023). The most prevalent gynecological problems among adolescent, young, and adult females are dysmenorrhea and premenstrual syndrome (PMS). *Rosa damascena* Herrm. essential oil has been reported to alleviate PMS symptoms affecting psychological, physical, and social symptoms by providing an inhalation session of 5 min daily during the 5 days in the luteal period of the menstrual cycle (Heydari et al., 2018). Massage of rose oil on the abdomen for primary dysmenorrhea pain in menstruating girls was reported to subside the pain compared to almond oil or massage group (without any oil) (Shahr et al., 2015). A mixture of lavender, sage, and marjoram was reported to reduce endometriosis-linked dysmenorrhea pain during menstruation if applied to the abdomen during the luteal stage (Ou et al., 2012). Similarly, massage with an essential oil mixture obtained from cinnamon, clove, rose, and lavender reduced pain, duration, and menstrual bleeding during menstruation (Marzouk et al., 2013). Effleurage massage with an essential oil mixture of lavender, ginger, clary sage, and geranium in equal ratio using almond oil base at a final concentration of 4% was found to be effective in ameliorating menstrual pain more effectively when compared with the 1% lavender oil only massage (Pujiati et al., 2019). A systematic analysis of the published literature also describes a positive effect of aromatherapy on PMS psychological symptoms such as anxiety, depression, and confusion while alleviating physical PMS symptoms, including pain and fatigue (Es-Haghee et al., 2020). Not only is aromatherapy useful for managing gynecological problems, but it also has wide application in obstetrics. Lavender aromatherapy during the active phase of delivery/labor has been reported to be active in reducing labor pain. Postmenopausal women face the problems of anxiety, impaired sexual function, and depression, which can be managed well using aromatherapy. A study reported using lavender oil combined with bergamot as an inhalation therapy for ameliorating depression and anxiety symptoms (Mojtehedi et al., 2022). The use of bergamot essential oil alone has also shown its effectiveness in improving sleep quality and depressive symptoms in postpartum women (Watanabe et al., 2015).

4.5. Hospice care

Therapeutic approaches, whether pharmacological or non-pharmacological, are useful for curing patients with different degrees of illness. Certain conditions arise where the patients become irresponsive to therapeutic intervention or do not wish to undergo certain treatment regimens at a terminal stage of illness. In such conditions, they are prescribed hospice care where the patient does not undergo any therapeutic intervention, but complementary care is provided to the patient for the remaining part of his life (generally 6 months or less) to manage their mental well-being, decreasing the pain, suffering, and anxiety as much as feasible with a positive effect on their vital signs. As no therapeutic pharmacological agents can be prescribed to such patients, an alternative approach such as aromatherapy, behavioral therapy, or spiritual therapy is the only way to manage such patients. Aromatherapy, a widely preferred method for hospice care, has positively affected patients' overall well-being during the hospice care period. A study tried to determine the parameters reported to be affected by aromatherapy. The report mentions alterations in vital signs such as blood pressure, pulse rate, and respiration rate improvised using massage therapy with essential oils (lavender or neroli). These also reduced the pain medication requirement in addition to positively affecting psychological conditions such as anxiety, depression, and overall well-being (Louis and Kowalski, 2002). A systematic review analyzed the efficacy of complementary medicine in palliative and hospice care but found only a short-term benefit for symptomatic relief (including anxiety, nausea, cough, pain, fatigue, and insomnia) from the disease condition, with no significant differences between the compared groups (Zeng et al., 2018). The variability in observation would probably be based on the level of distress a patient might undergo during therapeutic treatment, as higher distress levels are better managed using complementary aromatherapy compared to the low distress cases (Soden et al., 2004).

4.6. Essential oils and mood disorders

"Mood disorders, also often referred to as affective disorders, are a group of psychiatric illnesses that severely impact mood and its related functions." Mood disorders include anxiety, depression, sleep disorders, etc. Essential oils are used in aromatherapy, a supplementary and alternative practice, to treat and manage various health issues. The side effects caused by aromatherapy are negligible or much less severe compared to the psychotropic drugs used in the treatment of mood disorders. Essential oils can be administered through inhalation, topically or orally. The added advantage of the inhalation route is that these oils, through the nasal-brain route, can bypass the blood–brain barrier and thus act on various parts of the brain, such as the limbic system, thalamus, and cerebral cortex, to treat mood disorders (J Cui et al., 2022). Numerous studies have provided evidence for the potential role of essential oils in treating and managing mood disorders.

Chen et al. conducted an in vivo study to investigate the antidepressant activity of saffron (*Crocus sativus* L.) essential oil, which has been traditionally used in Islamic and Chinese medicine for the same purpose (Chen et al., 2023). The chemical composition of saffron essential oil was analyzed using the GC–MS technique. The major constituents of the oil were alcohols (63.23%), of which phenylethyl alcohol (57.96%) was the most abundant. A chronic unpredictable mild stress (CUMS)-induced depressed mouse model was used. Diluted saffron essential oil (2%, 4% and 6%, through inhalation) and fluoxetine were administered regularly to the mice. The antidepressant activity of the oil was evaluated by behavior tests, and ELISA was used to estimate the

serum levels of 5-HT, dopamine, GABA and BNDF. Using western blotting, the proportional levels of Raf1, MEK1, P-ERK1/2/ERK1/2, BDNF, P-CREB1/CREB1, and P-Trk B/Trk B in the hippocampus were identified. The results showed that saffron essential oil exhibited antidepressant activity in depressed mice. Significant elevations in serum concentrations of 5-HT, dopamine, GABA, and BNDF were observed. Neuronal damage in the hippocampus was reduced. Western blot analysis revealed that the fluoxetine and saffron essential oil groups had substantially higher expression levels of Raf1, MEK1, P-ERK1/2/ERK1/2, BDNF, P-CREB1/CREB1, and P-Trk B/Trk B than the CUMS group. The MAPK-CREB1-BDNF signaling pathway was identified as the primary pathway for the antidepressant activity of the oil. The most efficacious dilution of the oil was 4%. Thus, saffron essential oil was found to alleviate depression (Chen et al., 2023).

A human study was conducted by Wei et al. to assess the antidepressant potential of Cang-Ai volatile oil (oil blend obtained from 7 different herbs used in traditional Chinese medicine). Forty-six healthy individuals were administered the oil (10% Cang-Ai Volatile Oil and almond oil as a base) through the inhalation route for 1 min, five times per day for one month. The Hamilton Rating Scale for Depression (24 items) (HAM-D24) was used to assess depression, and functional near-infrared spectroscopy (fNIRS) was used to measure cortical activity. Two different verbal fluency assessments (VFTs) were used for the fNIRS test. The results indicated that the Cang-Ai volatile oil substantially reduced the HAM-D24 score and significantly elevated the mean concentration of oxygenated hemoglobin in the right frontal pole. Thus, Cang-ai was found to ameliorate depressed mood and enhance cortical excitability in the right frontal pole, which is linked with executive and emotional functions (Wei et al., 2023).

A 10-min inhalation of the scent of *Citrus junos* Siebold ex Yu. Tanaka (Yuzu) essential oil decreased the levels of salivary chromogranin A (CgA). Additionally, the psychological index termed the Profile of Mood States (POMS) showed a drastic decrease in total mood disturbance. Subscores of emotional symptoms such as tension-anxiety, depression-dejection, anger-hostility, and confusion were also significantly decreased upon a 30-min olfactory stimulation with the Yuzu scent (Matsumoto et al., 2014). Lavender essential oil was found to ameliorate depression-like symptoms by enhancing neurogenesis and dendritic complexity in SD rats. It also significantly elevated the levels of BDNF (Sanchez-Vidana et al., 2019). Of the essential oils of lavender, rose, and lemon, the latter citrus oil showed a significant reduction in stress-like symptoms and elevated the overall mood state. The findings suggest that the antidepressant-like effect of lemon oil acts via the 5-HT (1A) receptor. It accelerates the metabolic turnover of dopamine in the hippocampus and serotonin (5-HT) in the prefrontal cortex and striatum (Komiya et al., 2006). The essential oil of *Perilla frutescens* reverted the decreased levels of 5-hydroxytryptamine (5-HT) and its metabolite, 5-hydroxyindoleacetic acid (5-HIAA), to normal in a chronic, unpredictable, mild stress (CUMS)-induced depression mouse model (Ji et al., 2014). The inhalation of coriander volatile oil obtained from *Coriandrum sativum* L. fruits increased anxiolytic-antidepressant-like behaviors and decreased oxidative stress in a beta-amyloid (1–42)-treated rat model of Alzheimer's disease (Cioanca et al., 2014). The essential oil of *Asarum heterotropoides* F.Schmidt roots effectively inhibits depression-like behavioral responses, increases brain corticotropin releasing factor (CRF) and tyrosine hydroxylase (TH) expression, and decreases brain 5-hydroxy tryptamine (5-HT) expression in mice challenged with stress (Park et al., 2015). α-Pinene-rich *Rosmarinus officinalis* L. (checked from worldfloraonline.org) essential oil was found to elevate mood and decrease stress by inducing the stress response system by modulating the NGF pathway and the hypothalamus-pituitary-adrenal (HPA) axis, promoting dopamine production and secretion (Villareal et al., 2017). Essential oil isolated from the flowers of *Tagetes minuta* (10 and 50 mg/kg) reversed the depressive-like behavior induced by stress or inflammatory challenge in mice (Birmann et al., 2022). Essential oils of spearmint (*Mentha spicata* L.) and caraway (*Carum carvi* L.) are typically rich in the monoterpene carvone. A 21-day treatment with (R)-(−)-carvone (100 mg/kg) and (S)-(+)-carvone (100 mg/kg) prevented methylphenidate-induced hyperactivity, proving its potential as an antimanic agent (Nogoceke et al., 2016). With increasing awareness of mental illness and mental health wellbeing, essential oils could be one of the best and economic alternatives for potential employment in their treatment.

Numerous other essential oils and extracts have been reported to ameliorate various mood disorders, such as those obtained from lavender oil, Roman chamomile, Bergamot, *Melissa officinalis* L., Saint John's Wort (*Hypericum perforatum* L.), *Rhodiola Rosea* L., and so forth (J Cui et al., 2022).

4.7. For anxiolytic action

As described in the previous subsection, essential oils can be used in the treatment of mood disorders, including anxiety (J Cui et al., 2022). Many studies have been conducted to assess this property of essential oils. Silveira et al. investigated the anxiolytic activity of tangerine (*Citrus aurantium* L.) and Roman chamomile (*Chamaemelum nobile* L.) essential oils. The chemical composition of both oils was analyzed by GC−MS. The anxiolytic activity was examined in adult zebrafish (*Danio rerio*) by light-dark test. Roman chamomile oil was found to be rich in esters (pentadecyl-3-methyl-2-butenoate & hexadecyl-3-methyl-2-butenoate), alcohol (1-piperidinol) and alkanes (trans-1--ethyl-3-methyl-cyclopentane). Tangerine oil was found to be rich in limonene and γ-terpinene. The results indicated that Roman chamomile essential oil exhibited anxiolytic activity in adult fishes, while tangerine essential oil tended to lower anxiety (however, no definitive significant result was obtained) (Silveira et al., 2022).

Ozer et al. examined the anxiolytic potential of lemon essential oil in lowering exam anxiety in first-year nursing students (Özer et al., 2022). Forty-six students were randomized into 2 groups: control (24) and test (22) groups. Before the exam, as a pretest, all the students from both groups were administered the Test Anxiety Schedule (TAS) and State Test Anxiety Scale (STAS). The test group's students were then administered lemon essential oil for 15 min through the inhalation route. TAS and STAS were taken again for all the students in both groups as post-tests. For the test group, a substantial decrease in the mean posttest result for TAS and STAS (after smelling the essential oil) was found compared to the mean pretest result. The mean posttest results for the TAS and STAS (of both cognitive and physiological subdimensions) of the test group were also found to be much lower than those of the control group. A 43.3% reduction in exam anxiety was observed after inhalation of lemon essential oil. In conclusion, lemon essential oil was reported to exhibit anxiolytic action; however, repetition of this study is required with a large group of students to further assess the results (Özer et al., 2022). Another study by Calisir et al. revealed that lavender aromatherapy reduced intraoperative anxiety in women under spinal anesthesia for C-section. Hence, lavender essential oil can be administered along with a reduced dose of intraoperative anxiolytics (Çalışır et al., 2023). While essential oils are not a replacement for medication and therapy for anxiety disorders, they can be a useful adjunctive therapy to improve quality of life and reduce medication dosage.

5. Other applications of essential oils

Apart from previous applications, essential oils have a multitude of applications due to their antioxidative properties, spasmolytic activities, anticancer activities, antidiabetic properties, effects on GIT, effect on mood disorders, anxiolytic action, and insect-repellent properties. The details of these applications have been described in the subsequent subsections.

Essential oil extracts from citrus plants (generally rich in terpenes such as (+)-limonene, α-pinene, and camphene), such as *Citrus aurantium* L. and *Citrus bergamia* Risso (checked from worldfloraonline.org),

Table 5
Therapeutic use of aromatherapy: Description of the essential oils, their source, route of administration, experimental model employed and the respective results obtained. (NA- Not Applicable).

Action displayed	Source	Active phyto-constituents	Route of administration	Experimental model	Experimental outcome	Reference
Anxiolytic effect	*Lavandula angustifolia* Mill.	Linalool, linalyl acetate, 1,8-cineole, β-ocimene, terpinen-4-ol, and camphor	Inhalation	Clinical study	Decreased Chromogranin A	Toda and Morimoto (2008)
			Inhalation	Clinical study	Decreased anxiety and stress of patients with cardiovascular diseases	Amin et al. (2022)
			Inhalation	Clinical study	Decreased ECT-related anxiety in depressed patients	Moghadam et al. (2022)
	Mentha piperita L.	Menthol, Menthone, Menthyl Acetate, Neomenthol, 1,8-Cineole, Menthofuran	Inhalation	Clinical study	Decreased anxiety of patients with acute coronary syndrome in emergency department	Soleimani et al. (2022)
	Citrus bergamia Risso	Limonene, α-pinene, camphene	Inhalation	Clinical study	Negative emotions and fatigue score improved	Watanabe et al. (2015)
	Citrus aurantium L.		Inhalation	Clinical study	Decreases anxiety in postmenopausal women	Farshbaf-Khalili et al. (2018)
			Inhalation	Clinical study	Improved chronic hemodialysis patients' quality of life, reduced their anxiety	Mohammadpourhodki et al. (2021)
	Citrus sinensis L. Osbeck		Inhalation	Clinical study	Reduced anxiety and improved mood in dental patients	Lehrner et al. (2005)
	Rosa damascena Herrm.	Geraniol, citronellol	Inhalation	Clinical study	Relieves pain and anxiety in burn patients	Bikmoradi et al. (2016)
			Inhalation	Clinical study	Relaxed and relieved state anxiety and improved sleep quality of operating personnel in COVID wards	Mahdood et al. (2022)
			Inhalation	Clinical study	Increased "comfortable," "relaxed," and "natural" feelings	Mohebitabar et al. (2017)
	Cananga odorata Lam. (ylang ylang)	trans-caryophyllene, ocimene E, E-α-farnesene, phenylmethyl ester, farnesyl acetone, τ-muurolol, farnesol, β-elemene, α-cadinol, α-copaene, benzyl benzoate	Oral	Zebra fish	Modulates the HPA axis and interferes with the MAPK/ERK/CREB pathway and relieves anxiety	Zhang et al. (2018)
	Origanum vulgare L.	carvacrol, β-fenchyl alcohol, thymol, and γ-terpinene				
	Thymus vulgaris L.	p-cymene, γ-terpinene, thymol				
	Rosmarinus officinalis L.	1,8-cineol, camphor, α-pinene, limonene, camphene, linalool				
Mood disorders	*Citrus junos* Yu. Tanaka	α-Pinene, β-pinene, myrcene, γ-terpinene, terpinolene and *p*-cymene	Inhalation	Clinical study	Profile of Mood States (POMS) showed a drastic decrease in the total mood disturbance Decreased salivary Chromogranin A	Matsumoto et al. (2014)
	Lavandula angustifolia Mill.	Linalool, linalyl acetate, 1,8-cineole, β-ocimene, terpinen-4-ol, and camphor	Oral Intraperitoneal	SD rats Mice	Increased neurogenesis and dendritic complexity Increased BDNF levels	(Ji et al., 2014; Sanchez-Vidana et al., 2019)
	Perilla frutescens L. Britton	Perillaldehyde, limonene, geraniol, perillene, benzaldehyde, perilla ketone, isoegomaketone, anisole, apiol, egomaketone, myristicin, elemicin			Increased 5-hydroxytryptamine (5-HT) and its metabolite, 5-hydroxyindoleacetic acid (5-HIAA)	
	Coriandrum sativum L.	Linalool, geranyl acetate	Inhalation	beta-amyloid (1–42) treated rat model of Alzheimer's disease	Decreased the oxidative stress	Cioanca et al. (2014)
	Asarum heterotropoides F. Schmidt	Methyl eugenol, sesamin, safrole, N-isobutyl-(2E,4Z,8Z,10E)-dodecatetraenamide, pentadecane	Inhalation	Mice	Increased brain corticotropin releasing factor (CRF) and tyrosine hydroxylase (TH) expression	Park et al. (2015)
	Rosmarinus officinalis L.	1,8-cineol, camphor, α-pinene, limonene, camphene, linalool	Inhalation	ICR mice	Modulates the NGF pathway and the hypothalamus-pituitary-adrenal (HPA) axis Promotes dopamine production	Villareal et al. (2017)
	Tagetes minuta L.	dihydrotagetone, E-β-ocimene, tagetone, cis-β-ocimene, Z-β-ocimene, limonene, epoxyocimene	Intragastric	Mice	Restores BDNF-Akt/ERK2 signaling and inhibits inflammation	Birmann et al. (2022)

were found to relieve anxiety after oral or inhalation administration by regulating vital parameters such as blood pressure (BP), heart rate (HR), and heart rate variability (HRV) in two separate clinical trials (Farshbaf-Khalili et al., 2018; Watanabe et al., 2015). A simple study conducted by Ozer et al. proved lemon essential oil to be effective in reducing neuronal test anxiety in nursing students (Özer et al., 2022). Aromatherapy massage with *Citrus aurantium* and lavender essential oils improved anxiety in patients undergoing chronic hemodialysis (Mohammadpourhodki et al., 2021). Inhaling the ambient odors of orange oil and lavender oil reduced the anxiety level and improved mood in dental patients (Lehrner et al., 2005).

Fairly recent individual inhalational aromatherapy clinical trials with *Rosa damascena* revealed the regulation of the anxiety state and sleep quality in OR personnel during the COVID pandemic as well as in hospitalized burn victims (Bikmoradi et al., 2016; Mahdood et al., 2022). Olfactory stimulation with rose and orange oil induced physiological and psychological relaxation by precipitating an increase in "comfortable," "relaxed," and "natural" feelings (Mohebitabar et al., 2017). Essential oils extracted from the genus *Salvia* are another widely explored anxiolytic. Clinical trials on *Salvia lavandulaefolia* Gams and *Salvia officinalis* L. proving its profound efficacy in healthy as well as post-cesarean women were also recently conducted (Phootha et al., 2022).

Apart from the collective clinical trial data mentioned above, there are numerous preclinical data on different animal models exploring the anxiolytic effect of essential oils. Anthemis nobilis L. (roman chamomile) and Citrus reticulata Blanco (tangerine) essential oils act as anxiolytics in adult zebra fish, as revealed by the light-dark anxiety test model (Silveira et al., 2022). The inhalation of linalool (41.8%), 3, 5-dimethoxytoluene (10.9%), and β-pinene (9.2%) containing *Piper guineense* Schumach. &Thonn. essential oil was found to reduce anxiety behaviors in mice during the light-dark transition test. Rose oil (containing the active constituents citronellol and 2-phenethyl alcohol), extracted from *Rosa centifolia* L., *Rosa damascena* Herrm., and *Rosa alba* L. upon inhalation or intraperitonial injection, presented anxiolytic effects in rodents (Silveira et al., 2022). Acute or chronic oral administration of lemongrass (*Cymbopogon citratus* DC. Stapf) oil and mountain pepper (*Litsea cubeba* Lour. Pers.) oil having citral as their major constituent showed marked anxiolytic activity in mice (Silveira et al., 2022). The stimulation of the MAPK-CREB-BDNF signaling pathway by saffron essential oil was found to ameliorate auxiliary anxiety and CUMS-induced depression-like behavior in mice (Chen et al., 2023). EPM, staircase and OF tests in mice and rats revealed the anxiolytic effects of terpene-rich conifer species such as *Chamaecyparis obtuse* Siebold & Zucc. Endl., *Thujopsis dolabrata* L.f. Siebold & Zucc., and *Abies sachalinensis* F.Schmidt Mast. Oral or intraperitoneal administration of the essential oils of *Achillea umbellate* Sm. and *Achillea wilhelmsii* K.Koch (verified from worldfloraonline.org) displayed anxiolytic effects in approach–avoidance tests (Silveira et al., 2022).

Major conclusions that can be drawn from the existing clinical and preclinical data are that the anxiolytic effects of essential oils are mediated by modulating six major neurotransmitter pathways, comprising the gamma-aminobutyric acid pathway, acetylcholine pathway, glutamate pathway, monoamine pathways (consisting of serotonin, dopamine, and norepinephrine), adenosine pathway, and melatonergic pathway (Phootha et al., 2022). Active constituents such as linalool, alpha-asarone, other oils derived from *Cananga odorata* Lam. (ylang ylang), *Origanum vulgare* L., *Thymus vulgaris* L., and *Rosmarinus officinalis* L. show anxiolytic effects by modulating the HPA axis and interfering with the MAPK/ERK/CREB pathway (Silveira et al., 2022). A summative view of every application is represented in Table 5.

6. Regulation guidelines of essential oils

Essential oils are present in diluted form in aromatic herbs. Essential oils become 100 times more concentrated on distillation from plant materials, making them highly potent substances. Essential oils, regulated as cosmetics by the U.S. Food and Drug Administration (FDA), do not undergo the stringent testing required for pharmaceuticals, highlighting the need for careful consumer use and education. Although derived from natural sources, these oils can provoke adverse reactions like allergic and primary contact dermatitis, phototoxic reactions, oral toxicity, and eye irritation. Topical application predisposes the risk of allergic reaction, local irritation, and photosensitization, while if accidently if it comes in contact with eyes and nose, then redness and lacrimation/respiratory irritation or distress may occur. Direct skin contact, especially with undiluted oils, may lead to itchy, worsening rashes, necessitating patch testing and dilution to mitigate risks. Citrus oils, in particular, can cause phototoxicity, resulting in potentially permanent skin damage when exposed to sunlight, underscoring the need for caution during use. Oral ingestion of essential oils without professional advice can lead to severe health issues, including gastrointestinal upset, CNS depression (Tisserand and Young, 2014). Furthermore, accidental contact with the eyes can cause significant irritation and chemical burns, requiring immediate and thorough flushing to prevent damage. Other important point to consider while working on essential oil safety is that they are susceptible to oxidative degradation like any other oils which may generate toxic byproducts or end products (Vostinaru et al., 2020). These considerations emphasize the importance of proper dilution, application, and a comprehensive understanding of each oil's safety profile to ensure their beneficial use while minimizing potential harm (Farrar and Farrar, 2020).

Hence, the regulation of essential oils and the aromatherapy sector is crucial (Başer and Demirci, 2011), even though essential oil legislative regulations have not frequently followed an organized approach, both international and national authorities have established some fundamental guidelines for their use. Different agencies regulate the use of essential oils in different countries or regions (Osaili et al., 1809). The World Health Organization (WHO) is the primary worldwide regulatory authority for the safe use of essential oils. It collaborates with various national governments to create and put into effect rules and plans that guarantee the safe usage of essential oils on a worldwide scale. In this regard, a threefold approach has been undertaken by the WHO to help member nations promote the safe use of products derived from plants as well as complementary and alternative medicine (CAM). First, the WHO manages an online portal (WHO Essential Medicines and Health Products Information Portal) that discusses the safety of plant products, including essential oils. The platform, which is updated monthly, has 5480 medications and health items. Second, the Good Manufacturing Practices (GMP) for herbal medicines were issued by the WHO. Third, the WHO published four volumes named "The WHO Monographs on Selected Medicinal Plants" to offer scientific data on the quality, reliability and effectiveness of essential oils (Hashemi et al., 2017; Osaili et al., 1809).

Other regulatory bodies at the international level are the Food and Agriculture Organization (FAO) of the United Nations, the FAO/WHO Codex Alimentarius Commission (CAC), and the International Organization for Standardization (ISO) (Hashemi et al., 2017; Osaili et al., 1809). Food and Agricultural Legislation (FAOLEX), a publication from the FAO, contains details on treaties, rules, and regulations pertaining to food, agriculture, and plant sources from all around the world (Organization, n.d.). The Joint FAO/WHO Expert Committee on Food Additives (JECFA) was established by the WHO and FAO with a mission to assess the safety of food additives, including essential oils. The committee's website provides access to this information for the general public ("Joint FAO/WHO Expert Committee on Food Additives (JECFA)," n.d.). The CAC, another joint venture of the WHO and FAO, is in charge of establishing global standards, directives, codes and regulations for food additives and is responsible for overseeing the execution of the joint FAO/WHO food standards program (Fao-who, n.d.). The ISO appoints representatives from its member nations to serve on technical committees that establish globally recognized standards. The ISO

technical committee 54 deals with the normative requirements for essential oils, particularly those pertaining to their characterization, packaging, labeling, and storage. It has standardized several methods of analysis and specifications for essential oils. Many nations have also adopted measures to control the use of essential oils in addition to the recommendations of these international regulatory bodies (Osaili et al., 1809).

In the United States of America, essential oils are regulated by the Food and Drug Administration (FDA) based on their intended use, i.e., cosmetic, drug, household item, or something else. The FDA decides on the intended use of a product based on variables such as the promises made in the labeling, on websites, and in advertisements, as well as what consumers anticipate it to do. A product is cosmetic if its sole purpose is to enhance a person's appearance or cleanse their body, e.g., cologne, shower gel, perfume, etc. FDA approval is not required by law for the selling of cosmetics. Nonetheless, if the FDA has evidence that a cosmetic product is not safe when used as directed by the label, as is customary or expected, or if it is not labeled properly, the FDA may take enforcement action. A product is a drug if it is meant for therapeutic application, such as prophylactic and curative use. Drug claims, for instance, include that a product would treat anxiety or depression, reduce pain, relax muscles, or relieve colic. Similar claims are occasionally made for items such as soaps, massage oils, and lotions that contain essential oils and are advertised as "aromatherapy". No product or material is exempted from drug regulation just because it contains fragrance or other ingredients of plant origin. FDA approval for efficacy and safety is required by law for the selling of drugs in the market. Products that are both drugs and cosmetics must adhere to the respective requirements of both drugs and cosmetics. e.g., an essential oil that cleans the skin as well as heals rashes or a baby lotion which claims to moisturize the skin as well as ease colic.

The Consumer Product Safety Commission (CPSC) regulates fragrance products such as scented candles, household cleansers, air fresheners, and household cleaners. Plant-source essential oils or other ingredients are natural and organic, but this does not mean that they are necessarily safe. They may be irritant, allergenic, or even toxic upon topical application. FDA regulations for cosmetics do not define 'organic' or 'natural; ' however, regardless of the source, all cosmetics and their ingredients must conform to the same safety standards. The Federal Trade Commission controls advertising claims, while the FDA supervises labeling for drugs and cosmetics (Administration, n.d.). All the essential oils that are generally considered by the FDA to be safe for their intended usage are listed on a frequently updated web platform (Title 21, section 182.20). Adverse reactions or problems due to any cosmetic or drug containing essential oils can be reported under the Safety Information and Adverse Event Reporting Programme created by the FDA.

In Australia, the Therapeutic Goods Administration (TGA) regulates the use of essential oils and aromatherapy. The regulatory guidelines for essential oils and aromatherapy are stated in the Australian Regulatory Guidelines for Complementary Medicines, Part IV, Section 4 – Aromatherapy. TGA regulates essential oils by determining whether essential oil products are making therapeutic claims (Subsection 4.1) or essential oils are used as starting materials (Subsection 4.2). Subsection 4.1 states that "Products which contain essential oils must be Listed or Registered in the Australian Register of Therapeutic Goods (ARTG) if they are intended for therapeutic use (e.g., therapeutic claims are made about the product such as: 'relief of premenstrual symptoms' or 'relief of sleeplessness')." Subsection 4.2 states that "Essential oils that are supplied solely as starting materials to practitioners, are generally exempt from the requirement to be included in the ARTG before supply," i.e., for the oils that are supplied for the intention of being later dispensed or compounded for a specific individual (Subsubsection 4.2.1). It also states that conditions of GMP do not apply to the essential oils that are produced to be utilized as raw materials for the manufacture of therapeutic goods, but the manufacturers of the finished dosage form must follow the conditions of GMP (Subsubsection 4.2.2) (Support, 2011).

The regulatory agency for essential oils in Canada is the Food and Drugs Act and the Natural Health Product Regulations (the Regulations) by the Natural and Nonprescription Health Product Directorate (NNHPD). The European Medicine Agency under directives 2001/83/EC and 2004/24/EC provides regulatory guidelines for essential oils in the European Union. In India, the Drugs and Cosmetics Act (D and C) of 1940 and Rules of 1945, the department of AYUSH lays down the guidelines about essential oils (Osaili et al., 1809). In conclusion, the regulatory guidelines for essential oils ensure that consumers have access to safe and effective products.

7. Clinical trials and considerations

Clinical aromatherapy involves the application of essential oils, renowned for their anxiolytic, analgesic, antiseptic, and other beneficial properties, to alleviate patients' symptoms. This method is often utilized as an adjunct to pharmacological treatments and recommended by healthcare professionals trained in aromatherapy techniques (Farrar and Farrar, 2020).

Although the positive effects of aromatherapy can be acknowledged by both patients and healthcare providers, a singular anecdote does not suffice to establish credibility among peers, regulatory authorities, and the broader community. Adhering to the principles of evidence-based medicine (EBM) could significantly enhance the credibility and acceptance of aromatherapy (Brennan et al., 2022; Farrar and Farrar, 2020).

In recent years, there has been a noticeable increase in the number of healthcare practitioners incorporating clinical aromatherapy into their practice. This trend is evidenced by the growing number of grant applications submitted for incorporating such protocols in healthcare settings, indicating a growing interest in integrating aromatherapy within the realm of integrative medicine. Despite the observed benefits to patients, some policymakers remain hesitant to endorse this complementary therapy due to insufficient familiarity with it and a scarcity of robust clinical evidence (Brennan et al., 2022).

This hesitancy is largely attributed to the methodological shortcomings observed in existing clinical studies on aromatherapy. Systematic reviews, such as those conducted by well-regarded research networks, have often highlighted that the evidence produced by many aromatherapy studies is of poor quality or inconclusive, citing issues like flawed study design, presentation, and insufficient statistical power. For instance, a recent scoping review aimed at evaluating the evidence supporting the use of aromatherapy in nursing since 2005 managed to include only a limited number of studies (Maddocks, 2023). For clinical aromatherapy to gain wider acceptance and recognition as a viable complementary therapy, it is crucial for researchers and practitioners to acknowledge and address these limitations in their clinical research efforts.

Conducting high-quality clinical trials in aromatherapy is crucial for establishing the efficacy and safety of essential oils as complementary therapies. Gattefossé Foundation Scientific Board produced the white paper with key considerations and guidelines for researchers aiming to contribute valuable evidence to the field of clinical aromatherapy (Anton et al., 2005).

Considerations for the well-informed clinical trials in aromatherapy:

a. Detailed chemical composition Protocol: Providing a comprehensive description of the aromatherapy intervention is critical. This includes specifying the scientific name, geographical origin, extraction method, chemotype, producer and supplier, and the exact composition of the essential oils used. Detailed protocols ensure reproducibility and facilitate comparative studies and meta-analyses.
b. Choice of evaluation method: It's important to differentiate between clinical and preclinical studies. Clinical trials aim to evaluate therapeutic value and safety in humans, using methodologies that range from observational studies to randomized controlled trials (RCTs).

Table 6
Clinical trials on essential oil incorporated into percussive aromatherapy.

Conditions	Intervention	Enrolled	Age	Remarks	NCT number
Anxiety State Breast Cancer	Lavender aromatherapy tablets	150	18–85 years	Tablets of aromatherapy and control are administered in patients of BC. Anxiety state was evaluated with the help of "Spielberger State Anxiety Scale"	NCT05276505
Pain Management	Lavender-sandalwood scented aromatherapy sticker	600	18 years and older	Aromatherapy sticks are placed in the patient's gown prior to surgery and even after 72 h of surgery to facilitate pain management.	NCT04840212
Patient Engagement	Thyme oil	140	18 years and older	Can be used as add-on therapy in maintaining vitals and hemodynamic parameters in the patient of COVID-19. Individual action is yet to be studied.	NCT05197569
Anxiety	*Lavandula angustifolia* oil *Michelia alba* leaf oil Almond oil	200	18–100 Years	Lavender inhibits the voltage-gated calcium channel	NCT03445130
Major Abdominal Surgery	Lavender oil inhalation	121	18–80 years	Significant action in a wide range of pain, including IUC, chronic pain, and controlling the pain of labor. Cold application of lavender.	NCT04798040
Pain Psychosocial Effects of Cancer and Its Treatment Unspecified Adult Solid Tumor, Protocol Specific	Aromatherapy and essential oils reflexology procedure	100	18–120 Years	Comparative study between reflexology and aromatherapy. Measured by "Visual Analog Scale (VAS)"	NCT01217424
Stress	Elequil aromatabs ®	319	18 years and older	Study on management of job stress-associated symptoms in the nurses	NCT04819594
Bariatric Surgery Candidate Nausea, Postoperative	Peppermint oil aromatherapy	204	18–70 years	VAS was employed in the detection of nausea sensation. Employed targeting the nausea and vomiting induced by chemotherapy.	NCT03130218
Anxiety	Olfactory aromatherapy	294	18–90 years	Recovery room of patient comprises of 2 drops of essential oil besides the head of patient until he/she discharges. Anxiety is evaluated by "Amsterdam Preoperative Anxiety Scale (APAS)"	NCT03583801
Intensive Care Unit Delirium	Other: Blending of essential oils Other: Apricot vegetable oil	260	18 years and older	Foot massage with essential oils is performed every 8 h using 3 drops per foot.	NCT04529395
Cancer Distress Cancer Coping Hematopoietic Stem Cell Transplant Aromatherapy	Aromatherapy inhaler	128	18 years and older	Aims to evaluate the effect of aromatherapy inhaler in HSCT patents within the initial days. Not yet recruiting for patients	NCT05302583
Brain Tumors Leukemia Sarcomas Neuroblastoma Lymphoma Hodgkins Disease	Aromatherapy scented wand	132	7–21 years	Management efficacy of aromatherapy for various adverse events related to chemotherapy such as nausea, and vomiting. No results posted	NCT00754286
Anxiety Pain	Aromatherapy; aromatherapy and music concert	120	18–75 years	Helps in the management of anxiety, pain, and fear of death among patients of coronary angiography.	NCT05622383
Nausea, Postoperative	QUEASEEase aromatherapy quick tab	180	18–99 years	Management of nausea in the patients VAS is used to detect the sensation of nausea.	NCT04882501
Behavioral and Psychiatric Symptoms of Dementia	Home-based aromatherapy program	176	60 years and older	No clear guidance was described in the study.	NCT05032664
Burns	Inhalation aromatherapy	108	2 months to 7 years	Burns are traumatic conditions, especially for children Nurses incorporated lavender oil at 1st and 30th minutes after dressing, which is compared with a placebo. Helps in decreasing pain sensation along with decreasing blood pressure, heart rate, and mean arterial pressure.	NCT04237285
Postoperative Nausea and Vomiting	Lavender aromatherapy, rose aromatherapy, ginger aromatherapy	184	18–65 years	Change in nausea and vomiting sensation were recorded after the operation for 24 h Verbal Description Scale (VBC) was used to detect the sensation.	NCT02732379
Dementia	Aromatherapy	112	60 years and older	BPSD symptoms management with the help of aromatherapy. Comparative study between aromatherapy touch and aromatherapy smell.	NCT03576170
Chronic Pain	Aromatherapy	100	80 years and older	Comparative study between aromatherapy touch and aromatherapy smell. Numerical Rating Scale (NRS) was utilized to check the change in pain.	NCT03561844
Cancer	Ginger aromatherapy, orange aromatherapy, lavender aromatherapy, jojoba aromatherapy	108	8 years and older	Ginger, lavender, orange, jojoba oil mixture is effective in reducing chemotherapy induced symptoms such as sleep difficulties, lack of appetite, anxiety, vomiting, fatigue, nausea and pain. Treatment was continued for 7 days.	NCT03449511
Premenstrual Syndrome Aromatherapy	Aromatherapy	120	18–30 years	Premenstrual complaints are satisfied both psychological and physically by various essential oil such as rose, sage, lavender, Sardinia.	NCT05599594
Pain Aromatherapy Subcutaneous Injections	Topically administered lavender aromatherapy topically administered water	180	18 years and older	Needle phobia is suppressed in the patient of diabetes mellites by the analgesic property of topical application of lavender oil.	NCT04767737

(*continued on next page*)

Table 6 (*continued*)

Conditions	Intervention	Enrolled	Age	Remarks	NCT number
Sleep Hospitalization	Lavender oil Grapeseed Oil	108	18 years and older	Four-day study evaluate the effect on sleep during hospitalization. Verran and Snyder-Halpern sleep scale was used to evaluate the sleep cycle of patient.	NCT04648215
Pain, Procedural Aromatherapy Anxiety	Lavender essential oil	120	18–60 years	Lavender essential oil helps to deduct the anxiety level in patients of shock wave lithotripsy. It was observed that patients with anxiety experienced more pain (that can also be suppress by lavender through inhalation route).	NCT04848350
Rheumatoid Arthritis	Aromatherapy	102	20 years and older	Patients of RA experience difficulty in sleep quality, psychological disturbance and alleviated pain. Study tries to check the influence of 10-min massage with essential oil for thrice a week continued for three weeks. Pain was tested by NRS, sleep quality was evaluated by Pittsburg Sleep Quality and psychological stress was detected with the help of Hospital Anxiety and Depression scale.	NCT04549857
Postoperative Nausea and Vomiting (PONV)	Lavender essential oil Ginger essential oil	200	18 years and older	No details are posted.	NCT04822844
Spine Injuries and Disorders Back pain	Activated lavender Elequil aromatabs® (#372) Unactivated lavender Elequil aromatabs® (#372)	100	18 Years–85 Years	Anxiety prior to surgery could hurdle the success of treatment, Lavender oil is used prior to spinal procedure.	NCT04156009
Nausea Vomiting	Peppermint essential oil, ginger essential oil, or pure vanilla extract	144	21–80 Years	Patients were instructed to take 3 sniffs of essential oil trice a day and the sensation of nausea and vomiting was observed for 24 h (acute) and 72 h (chronic). Memorial Symptom Assessment Scale was utilized to check the respective sensation.	NCT04478630
Pediatric Cancer Sleep	Aromatherapy, music concert	105	1 Month-18 years	Music and aromatherapy can help children to get better sleep and hence adequate time for today to recover and fight against cancer. Comparative study is performed between aromatherapy and music exposure in children	NCT05164354
Menopause Hot Flashes Hot Flushes	Olfactory aromatherapy Yoga therapy	108	45–60 Years	Aromatherapy targets hot slashes and have therapeutic efficacy with little side effect when exposed by inhalation.	NCT01816360
Surgical Abortion Patient Satisfaction Anesthesia Pain	Lavender oil	220	18–50 years	Abortion before 10 weeks influence the mental health of patient. Lavender oil helps in patient satisfaction and is measured by lowa Satisfaction and Anesthesia Scale.	NCT04969900
Cholecystectomy Aromatherapy	Lavender intervention group, Geranium intervention group	150	18 Years and older	Laparoscopic cholecystectomy effects adversely sleep quality and physiological parameter which can be decreased by administration of lavender and geranium oil. Richard-Cambell Sleep Scale was used to collect information from individual patient.	NCT05464602
Pain	Peripheral venous cannulation (PVC) aromatherapy with lavender essential oil	106	18–65 Years	Anxiolytic and analgesic effect of lavender oil during and after PVC.	NCT02592044
Colposcopy	Lavender essential oil Lavender scent	262	18 Years or older	Negative emotional experience and anxiety were observed in patient undergoing cervical cancer screening. Lavender oil improves the mental state postcolposcopy.	NCT01214304

RCTs, especially double-blind trials, are considered the gold standard, although they can be challenging to implement with aromatherapy due to the sensory nature of the interventions.

c. Adapting methodological designs: Non-Pharmaceutical Interventions like aromatherapy require methodological designs that are traditionally used for drug evaluation. This involves pragmatic approaches to trial design, considering whether to compare the intervention against a placebo or another therapy based on the specific research question.
d. Endpoints selection: The choice of endpoints, whether quantitative (measurable physical or biological markers) or qualitative (subjective patient experiences), is fundamental. Utilizing validated scales and questionnaires for symptoms such as pain, anxiety, and well-being enhances the quality of evidence. Many aromatherapy studies suffer from small sample sizes, reducing their statistical significance. Therefore, the collaboration among institutions to increase patient numbers and standardize protocols can enhance the reliability of results. Multi-center studies are particularly encouraged for conditions amenable to aromatherapy treatment.
e. Rigorous reporting and reproducibility: The scientific merit of a study hinges on the ability of other researchers to reproduce its results. This requires clear reporting of study conditions, including detailed descriptions of the essential oils and administration methods used. Studies must adhere to established reporting guidelines like Consolidated Standards of Reporting Trials (CONSORT) ("EQUATOR Network | Enhancing the QUAlity and Transparency Of Health Research," n.d.) for herbal interventions and the Transparent Reporting for Essential Oils & Aroma Therapeutic Studies (TREATS) tool for evaluating the quality of published studies (Reven et al., 2023).
f. Emphasis on qualitative studies: Given the subjective nature of many benefits associated with aromatherapy, qualitative research plays a crucial role. This approach, which focuses on patient experiences and outcomes, complements quantitative methodologies and can inform the design of more targeted quantitative studies.

To make progress in clinical aromatherapy research, it is important to pay close attention to how studies are conducted, to be thorough in research methods, and to work collaboratively with other researchers. Following these steps will help build strong evidence that aromatherapy can be a valid addition to regular healthcare. This way, it can be accepted and used as a genuine complementary therapy. Some examples of clinical trial studies can be found in Table 6.

8. Conclusion

This comprehensive review highlights the multifaceted world of aromatherapy and its utilization of essential oils to enhance overall well-being. By blending historical knowledge with contemporary research, this article underscores the resurgence of interest in essential oils as valuable therapeutic tools in modern healthcare. The exploration of various extraction methods and their impact on essential oil properties underscores the significance of quality and purity in achieving desired therapeutic effects. Standardization and certification emerge as essential factors in ensuring safe and effective usage. The comprehensive assessment of essential oil therapeutic effects reveals their potential in addressing a wide array of health conditions, offering promising benefits as antimicrobial, analgesic, anxiolytic, anti-inflammatory, and more. Clinical trials and preclinical studies provide substantial evidence to support their efficacy in both physical and psychological applications. The paramount importance of safety considerations when employing essential oils is emphasized, and this review addresses potential adverse effects and contraindications. By outlining best practices, it aims to promote responsible usage and prevent unwanted consequences.

The growing interest in integrating essential oils with conventional medicine highlights the value of collaborative healthcare approaches. As complementary therapies gain recognition, this review encourages further research and clinical investigations to harness the full potential of essential oils in conjunction with established medical practices.

This review serves as a valuable resource for practitioners, researchers, and enthusiasts seeking to delve into the world of aromatherapy and essential oils. By amalgamating traditional wisdom and modern scientific evidence, it advocates for the responsible and evidence-based incorporation of essential oils into healthcare practices, further reinforcing their status as natural and potent remedies for a wide range of ailments. As we continue to unveil the therapeutic benefits of essential oils, their integration into mainstream healthcare may herald a new era of holistic well-being and enhanced patient care.

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Lalitkumar K. Vora: Conceptualization, Data curation, Formal analysis, Funding acquisition, Investigation, Methodology, Project administration, Resources, Supervision, Visualization, Writing – original draft, Writing – review & editing. **Amol D. Gholap:** Data curation, Resources, Visualization, Writing – original draft. **Navnath T. Hatvate:** Data curation, Formal analysis, Visualization, Writing – original draft, Writing – review & editing. **Padmashri Naren:** Formal analysis, Writing – original draft. **Sabiya Khan:** Writing – original draft, Data curation, Formal analysis, Writing – review & editing. **Vivek P. Chavda:** Supervision, Writing – original draft. **Pankti C. Balar:** Data curation, Writing – original draft. **Jimil Gandhi:** Writing – original draft. **Dharmendra Kumar Khatri:** Supervision, Writing – original draft, Writing – review & editing, Data curation, Formal analysis, Methodology, Project administration.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Data availability

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References

Administration, F. and D., n.d. Aromatherapy.
Aguilar-Hernendez, M.G., Sanchez-Bravo, P., Hernendez, F., Carbonell-Barrachina, A.A., Pastor-Perez, J.J., Legua, P., 2020. Determination of the volatile profile of lemon peel oils as affected by Rootstock. Foods 9, 241. https://doi.org/10.3390/foods9020241.
Ali, B., Al-Wabel, N.A., Shams, S., Ahamad, A., Khan, S.A., Anwar, F., 2015. Essential oils used in aromatherapy: a systemic review. Asian Pac. J. Trop. Biomed. 5, 601–611. https://doi.org/10.1016/J.APJTB.2015.05.007.
Amin, A., Gavanrudi, M.R., Karami, K., Raziani, Y., Baharvand, P., 2022. The role of aromatherapy with lavender in reducing the anxiety of patients with cardiovascular diseases: a systematic review of clinical trials. J. HerbMed Pharmacol. 11, 182–187. https://doi.org/10.34172/jhp.2022.22.
Anton, R., Boutefnouchet, S., Colls, P., Couic-Marinier, F., Kopferschmitt, J., Morel, J.-M., 2005. Need to Improve the Quality of Clinical Studies in Aromatherapy 1–8.
Arnal-Schnebelen, B., Hadji-Minaglou, F., Peroteau, J.F., Ribeyre, F., De Billerbeck, V.G., 2004. Essential oils in infectious gynaecological disease: a statistical study of 658 cases. Int. J. Aromather. 14, 192–197. https://doi.org/10.1016/J.IJAT.2004.09.003.
Association française de normalisation (AFNOR), 2000. Huiles Essentielles: Monographies Relatives Aux Huiles Essentielles, ume 2.
Auffarth, B., 2013. Understanding smell-The olfactory stimulus problem. Neurosci Biobehav. Rev.Biobehav. Rev. 37, 1667–1679. https://doi.org/10.1016/j.neubiorev.2013.06.009.
Ayik, C., Özden, D., 2018. The effects of preoperative aromatherapy massage on anxiety and sleep quality of colorectal surgery patients: a randomized controlled study. Compl. Ther. Med. 36, 93–99. https://doi.org/10.1016/J.CTIM.2017.12.002.
Bai, X., Tang, J., 2020. Myrcene exhibits antitumor activity against lung cancer cells by inducing oxidative stress and Apoptosis mechanisms. Nat Prod 15, 19345.
Barboza, J.N., Filho, C., Silva, R.O., Medeiros, J.V.R., 2018. An overview on the anti-inflammatory potential and antioxidant profile of Eugenol. Oxid. Med. Cell. Longev. https://doi.org/10.1155/2018/3957262.
Başer, K.H.C., Demirci, F., 2011. Essential oils. Kirk-othmer Encycl. Chem. Technol. 1–37 https://doi.org/10.1002/0471238961.1509121913151511.A01.PUB2.
Bensouilah, J., 2005. The history and development of modern-British aromatherapy. Int. J. Aromather. 15, 134.
Bhatia, S.P., McGinty, D., Letizia, C.S., Api, A.M., 2008. Fragrance material review on myrtenol. Food Chem. Toxicol. 46.
Bhavaniramya, S., Vishnupriya, S., Al-Aboody, M.S., Vijayakumar, R., Baskaran, D., 2019. Role of essential oils in food safety: antimicrobial and antioxidant applications. Grain Oil Sci. Technol. 2, 49.
Bikmoradi, A., Harorani, M., Roshanaei, G., Moradkhani, S., Falahinia, G.H., 2016. The effect of inhalation aromatherapy with damask rose (Rosa damascena) essence on the pain intensity after dressing in patients with burns: a clinical randomized trial. Iran. J. Nurs. Midwifery Res. 21, 247–254. https://doi.org/10.4103/1735-9066.180380.
Birmann, P.T., Casaril, A.M., Zugno, G.P., Acosta, G.G., Severo Sabedra Sousa, F., Collares, T., Seixas, F.K., Jacob, R.G., Brüning, C.A., Savegnago, L., Hartwig, D., 2022. Flower essential oil of Tagetes minuta mitigates oxidative stress and restores BDNF-Akt/ERK2 signaling attenuating inflammation- and stress-induced depressive-like behavior in mice. Brain Res. 1784, 147845 https://doi.org/10.1016/j.brainres.2022.147845.
Bowles, E.J., 2003. Chemistry of Aromatherapeutic Oils, third ed. Routledge. https://doi.org/10.4324/9781003115151.
Brennan, S.E., McDonald, S., Murano, M., McKenzie, J.E., 2022. Effectiveness of aromatherapy for prevention or treatment of disease, medical or preclinical conditions, and injury: protocol for a systematic review and meta-analysis. Syst. Rev. 11 https://doi.org/10.1186/S13643-022-02015-1.
Brown, H.C., Garg, C.P., Liu, K.-T., 1971. Oxidation of secondary alcohols in diethyl ether with aqueous chromic acid. Conv. Proced. Prep. ketones high epimeric purity, J. Org 36, 387.
Buckle, J., 2014. Clinical Aromatherapy: Essential Oils in Practice. Elsevier Health Sciences.
Burnett, C.L., Fiume, M.M., Bergfeld, W.F., Belsito, D.V., Hill, R.A., Klaassen, C.D., Liebler, D.C., Marks, J.G., Shank, R.C., Slaga, T.J., Snyder, P.W., Gill, L.J.,

Heldreth, B., 2019. Safety assessment of citrus-derived peel oils as used in cosmetics. Int. J. Toxicol. 38, 33.
Çalışır, F., Urfalıoğlu, A., Bilal, B., Tok, A., Bolcal, H.A., Öksüz, H., 2023. The effect of lavender aromatherapy on the level of intraoperative anxiety in caesarean case under spinal anesthesia: a randomized controlled trial. Explore 19, 356–361. https://doi.org/10.1016/J.EXPLORE.2022.11.008.
Chen, Z., Gu, J., Lin, S., Xu, Z., Xu, H., Zhao, J., Feng, P., Tao, Y., Chen, S., Wang, P., 2023. Saffron essential oil ameliorates CUMS-induced depression-like behavior in mice via the MAPK-CREB1-BDNF signaling pathway. J. Ethnopharmacol. 300, 115719 https://doi.org/10.1016/j.jep.2022.115719.
Cheng, H., Lin, L., Wang, S., Zhang, Y., Liu, T., Yuan, Y., Chen, Q., Tian, L., 2022. Aromatherapy with single essential oils can significantly improve the sleep quality of cancer patients: a meta-analysis. BMC Complement. Med. Ther. 22 https://doi.org/10.1186/S12906-022-03668-0.
Cheong, M.J., Kim, S., Kim, J.S., Lee, H., Lyu, Y.S., Lee, Y.R., Jeon, B., Kang, H.W., 2021. A systematic literature review and meta-analysis of the clinical effects of aroma inhalation therapy on sleep problems. Medicine (Baltim.) 100, e24652. https://doi.org/10.1097/MD.0000000000024652.
Choi, H.-S., 2005. Characteristic odor components of Kumquat (Fortunella japonica Swingle) peel oil. J. Agric. Food Chem. 53, 1642.
Cimino, C., Maurel, O.M., Musumeci, T., Bonaccorso, A., Drago, F., Souto, E.M.B., Pignatello, R., Carbone, C., 2021. Essential oils: pharmaceutical applications and encapsulation Strategies into lipid-based delivery systems. Pharm. Times 13 (2021), 327. https://doi.org/10.3390/PHARMACEUTICS13030327, 13, 327.
Cioanca, O., Hritcu, L., Mihasan, M., Trifan, A., Hancianu, M., 2014. Inhalation of coriander volatile oil increased anxiolytic-antidepressant-like behaviors and decreased oxidative status in beta-amyloid (1-42) rat model of Alzheimer's disease. Physiol. Behav. 131, 68–74. https://doi.org/10.1016/j.physbeh.2014.04.021.
Clarke, S., 2008. Families of compounds that occur in essential oils. Chem. Aromather, Elsevier. https://doi.org/10.1016/B978-0-443-10403-9.00003-0.
Croy, I., Bojanowski, V., Hummel, T., 2013. Men without a sense of smell exhibit a strongly reduced number of sexual relationships, women exhibit reduced partnership security–a reanalysis of previously published data. Biol. Psychol. 92, 292. https://doi.org/10.1016/j.biopsycho.2012.11.008.
Cui, J., Li, M., Wei, Y., Li, H., He, X., Yang, Q., Li, Z., Duan, J., Wu, Z., Chen, Q., Chen, B., Li, G., Ming, X., Xiong, L., Qin, D., 2022. Inhalation aromatherapy via brain-targeted nasal delivery: natural volatiles or essential oils on mood disorders. Front. Pharmacol. 13.
Czakert, J., Stritter, W., Blakeslee, S.B., Grabowski, J.P., Sehouli, J., Seifert, G., 2023. "Like one part of a puzzle" — individualized aromatherapy for women with gynecological cancers in aftercare: results from a qualitative-focused mixed-methods study. Support. Care Cancer 31, 1–14. https://doi.org/10.1007/S00520-022-07543-Z/TABLES/5.
de Andrade, S.F., Rijo, P., Rocha, C., Zhu, L., Rodrigues, L.M., 2021. Characterizing the mechanism of action of essential oils on skin homeostasis—data from Sonographic Imaging, epidermal water Dynamics, and skin Biomechanics. Inside Cosmet. 8 (2021), 36. https://doi.org/10.3390/COSMETICS8020036. Page 36 8.
de Groot, A.C., Schmidt, E., 2016. Essential oils, Part IV: contact Allergy. Dermatitis 27, 170.
Demmer, C., Sauer, J., 2002. Assessing complementary therapy services in a hospice program. Am. J. Hosp. Palliat. Care 19, 306–314. https://doi.org/10.1177/104990910201900506.
Dhifi, W., Bellili, S., Jazi, S., Bahloul, N., Mnif, W., 2016. Essential oils- chemical characterization and investigation of some biological activities: a critical review. Medicines 3, 25.
do Vale, T.G., Furtado, E.C., Santos, J.G., Viana, G.S.B., 2002. Central effects of citral, myrcene and limonene, constituents of essential oil chemotypes from Lippia alba (Mill.) N. E. Brown. Phytomedicine 9, 709.
Dobetsberger, C., Buchbauer, G., 2011. Actions of essential oils on the central nervous system: an updated review. Essential oil effects on the CNS. Flavour Fragr J 26, 300.
Doukas, D.J., McCullough, L.B., Wear, S., Flexner, R., 2010. Re-visioning Flexner: educating physicians to be clinical scientists and humanists. Am. J. Med. 123, 1155–1156. https://doi.org/10.1016/j.amjmed.2010.05.027.
Ebrahimi, A., Eslami, J., Darvishi, I., Momeni, K., Akbarzadeh, M., 2021. An overview of the comparison of inhalation aromatherapy on emotional distress of female and male patients in preoperative period. J. Complement. Integr. Méd. 19, 111–119. https://doi.org/10.1515/JCIM-2020-0464.
El-Zaeddi, H., Martinez-Tome, J., Calin-Sanchez, F., Burlo, F., Carbonell-Barrachina, A., 2016a. Volatile composition of essential oils from different aromatic herbs grown in mediterranean regions of Spain. Foods 5, 41.
El-Zaeddi, H., Martinez-Tome, J., Calin-Sanchez, A., Burlo, F., Carbonell-Barrachina, A. A., 2016b. Volatile composition of essential oils from different aromatic herbs grown in mediterranean regions of Spain. Foods 5, 41. https://doi.org/10.3390/foods5020041.
EQUATOR Network | Enhancing the QUAlity and Transparency Of Health Research [WWW Document], n.d. URL https://www.equator-network.org/(accessed 3.14.24).
Es-Haghee, S., Shabani, F., Hawkins, J., Zareian, M.A., Nejatbakhsh, F., Qaraaty, M., Tabarrai, M., 2020. The effects of aromatherapy on premenstrual syndrome symptoms: a systematic review and meta-analysis of randomized clinical trials. Evid. base Compl. Alternative Med. 2020. https://doi.org/10.1155/2020/6667078.
Evans, W.C., Evans, D., 2009. Volatile Oils and Resins, sixteenth ed. Trease and Evans' Pharmacognosy. https://doi.org/10.1016/B978-0-7020-2933-2.00022-8.
Fao-who, A.C., (n.d. No Title. n.d).
Farrar, A.J., Farrar, F.C., 2020. Clinical aromatherapy. Nurs. Clin. 55, 489–504. https://doi.org/10.1016/j.cnur.2020.06.015.
Farre-Armengol, G., Filella, I., Llusia, J., Penuelas, J., 2017. β-Ocimene, a key floral and foliar volatile involved in multiple interactions between plants and other organisms. Molecules 22, 1148. https://doi.org/10.3390/molecules22071148.
Farshbaf-Khalili, A., Kamalifard, M., Namadian, M., 2018. Comparison of the effect of lavender and bitter orange on anxiety in postmenopausal women: a triple-blind, randomized, controlled clinical trial, Complement. Ther. Clin. Pr. 31, 132.
Fearrington, M.A., Qualls, B.W., Carey, M.G., 2019. Essential oils to reduce postoperative nausea and vomiting. J. perianesthesia Nurs. Off. J. Am. Soc. PeriAnesthesia Nurses 34, 1047–1053. https://doi.org/10.1016/J.JOPAN.2019.01.010.
Fung, Timothy K.H., Lau, B.W.M., Ngai, S.P.C., Tsang, H.W.H., 2021. Therapeutic effect and mechanisms of essential oils in mood disorders: interaction between the nervous and respiratory systems. Int. J. Mol. Sci. 22, 4844. https://doi.org/10.3390/IJMS22094844.
Gattefossé, R.-M., Tisserand, R., Davies, L., 1993. Gattefossé's Aromatherapy 163.
Goel, N., Kim, H., Lao, R.P., 2005. An olfactory stimulus modifies nighttime sleep in young men and women. Chronobiol. Int. 22, 889–904. https://doi.org/10.1080/07420520500263276.
Greenberg, M.J., Slyer, J.T., 2018. Effectiveness of Silexan oral lavender essential oil compared to inhaled lavender essential oil aromatherapy for sleep in adults: a systematic review, JBI Database Syst. Rev Implement Rep 16, 2109.
Guenther, E., 1988. Essential oils. J. Vet. Dent. https://doi.org/10.1177/089875648800500404.
Guo, P., Li, P., Zhang, X., Liu, N., Wang, J., Yang, S., Yu, L., Zhang, W., 2020. The effectiveness of aromatherapy on preoperative anxiety in adults: a systematic review and meta-analysis of randomized controlled trials. Int. J. Nurs. Stud. 111 https://doi.org/10.1016/J.IJNURSTU.2020.103747.
Györgyi Horváth, K.Á., 2015. Essential oils in the treatment of respiratory tract diseases highlighting their role in bacterial infections and their anti-inflammatory action: a review: essential oils in the treatment of respiratory tract diseases, Flavour Fragr. Flavour Fragrance J. 30, 331.
Habib, A.S., Kranke, P., Bergese, S.D., Chung, F., Ayad, S., Siddiqui, N., Motsch, J., Leiman, D.G., Melson, T.I., Diemunsch, P., Fox, G.M., Candiotti, K.A., 2019. Amisulpride for the rescue treatment of postoperative nausea or vomiting in patients failing prophylaxis: a randomized, placebo-controlled phase III trial. Anesthesiology 130, 203–212. https://doi.org/10.1097/ALN.0000000000002509.
Harada, H., Kashiwadani, H., Kanmura, Y., Kuwaki, T., 2018. Linalool odor-induced anxiolytic effects in mice. Front. Behav. Neurosci. 12.
Hartley, L., Igbinedion, E., Holmes, J., Flowers, N., Thorogood, M., Clarke, A., Stranges, S., Hooper, L., Rees, K., 2013. Increased consumption of fruit and vegetables for the primary prevention of cardiovascular diseases. Cochrane Database Syst. Rev. 2021.
Hashemi, S.M.B., Khaneghah, A.M., de Souza Sant'Ana, A., 2017. Essential Oils in Food Processing: Chemistry, Safety and Applications. John Wiley & Sons, Ltd.
Herman, A., Herman, A.P., 2015. Essential oils and their constituents as skin penetration enhancer for transdermal drug delivery: a review. J. Pharm. Pharmacol. 67, 473–485. https://doi.org/10.1111/JPHP.12334.
Heuberger, E., Hongratanaworakit, T., Böhm, C., Weber, R., Buchbauer, G., 2001. Effects of chiral fragrances on human autonomic nervous system parameters and self-evaluation. Chem. Senses 26, 281–292. https://doi.org/10.1093/CHEMSE/26.3.281.
Heydari, N., Abootalebi, M., Jamalimoghadam, N., Kasraeian, M., Emamghoreishi, M., Akbarzaded, M., 2018. Evaluation of aromatherapy with essential oils of Rosa damascena for the management of premenstrual syndrome. Int. J. Gynecol. Obstet. 142, 156–161. https://doi.org/10.1002/IJGO.12534.
Honig, A.J., Galassi, M.G., Ogungbe, O.O., Uranga, T., Cuevas, D.K., 2023. Implementation of aromatherapy, a nonpharmacological intervention, to reduce anxiety during the preoperative period. J. perianesthesia Nurs. Off. J. Am. Soc. PeriAnesthesia Nurses. https://doi.org/10.1016/J.JOPAN.2022.06.011.
Hoover, K.C., 2010. Smell with inspiration: the evolutionary significance of olfaction. Am. J. Phys. Anthropol. 143, 63.
Horrigan, B., Lewis, S., Abrams, D.I., Pechura, C., 2012. Integrative medicine in America-how integrative medicine is being practiced in clinical centers across the United States. Glob. Adv. Health Med. 1, 18–94. https://doi.org/10.7453/gahmj.2012.1.3.006.
Hoskison, E.E., 2013. Olfaction, pheromones and life. J. Laryngol. Otol. 127, 1156.
Hwang, E., Shin, S., 2015. The effects of aromatherapy on sleep improvement: a systematic literature review and meta-analysis. J. Alternative Compl. Med. 21, 61–68. https://doi.org/10.1089/ACM.2014.0113.
Jaruzel, C.B., Gregoski, M., Mueller, M., Faircloth, A., Kelechi, T., 2019. Aromatherapy for preoperative anxiety: a pilot study. J. PeriAnesthesia Nurs. 34, 259–264. https://doi.org/10.1016/j.jopan.2018.05.007.
Ji, W.-W., Li, R.-P., Li, M., Wang, S.-Y., Zhang, X., Niu, X.-X., Li, W., Yan, L., Wang, Y., Fu, Q., Ma, S.-P., 2014. Antidepressant-like effect of essential oil of Perilla frutescens in a chronic, unpredictable, mild stress-induced depression model mice. Chin. J. Nat. Med. 12, 753–759. https://doi.org/10.1016/S1875-5364(14)60115-1.
Jimbo, D., Kimura, Y., Taniguchi, M., Inoue, M., Urakami, K., 2009. Effect of aromatherapy on patients with Alzheimer's disease. Psychogeriatrics 9, 173.
Johnson, N.J., Hanson, L.R., Frey, W.H., 2010. Trigeminal pathways deliver a low molecular weight drug from the nose to the brain and orofacial structures. Mol. Pharm. 7, 884.
Joint FAO/WHO Expert Committee on Food Additives (JECFA) [WWW Document], n.d. URL https://www.who.int/groups/joint-fao-who-expert-committee-on-food-additives-(jecfa)/about.
Kallush, A., Riley, C.A., Kacker, A., 2018. Role of complementary and alternative medicine in otolaryngologic perioperative care. Ochsner J. 18, 253–259. https://doi.org/10.31486/TOJ.18.0014.

Kang, J., Cho, Y.S., Lee, M., Yun, S., Jeong, Y.J., Won, Y.H., Hong, J., Kim, S., 2022. Effects of nonpharmacological interventions on sleep improvement and delirium prevention in critically ill patients: a systematic review and meta-analysis. Aust. Crit. Care. https://doi.org/10.1016/J.AUCC.2022.04.006.
Kao, Y.H., Huang, Y.C., Chung, U.L., Hsu, W.N., Tang, Y.T., Liao, Y.H., 2017. Comparisons for effectiveness of aromatherapy and acupressure massage on quality of life in career women: a randomized controlled trial. J. Alternative Compl. Med. 23, 451–460. https://doi.org/10.1089/ACM.2016.0403.
Khatiban, M., Mirzaie, M., Fazeli, A., Tapak, L., Khalili, Z., 2022. Effect of cardamom inhalation therapy on intra-and postoperative nausea and vomiting of mothers undergoing spinal anesthesia for elective cesarean section. J. perianesthesia Nurs. Off. J. Am. Soc. PeriAnesthesia Nurses 37, 452–457. https://doi.org/10.1016/J.JOPAN.2021.09.008.
Kiberd, M.B., Clarke, S.K., Chorney, J., d'Eon, B., Wright, S., 2016. Aromatherapy for the treatment of PONV in children: a pilot RCT. BMC Compl. Alternative Med. 16 https://doi.org/10.1186/S12906-016-1441-1.
King, A., 2022. Medieval islamicate aromatherapy: medical perspectives on aromatics and perfumes. Senses Soc. 17, 37.
Klein, S.L., Flanagan, K.L., 2016. Sex differences in immune responses. Nat. Rev. Immunol. 16, 626–638. https://doi.org/10.1038/nri.2016.90.
Koehler, T., 2021. Lavender aromatherapy as a nurse-driven intervention for preoperative anxiety. Nurs. Womens. Health 25, 286–295. https://doi.org/10.1016/J.NWH.2021.05.005.
Kotlik, B.A., Petrova, L.M., Red'ko, A.I., Eiu, K., 1986. Sources of equipment measurement error in stimulation electromyography. Fiziol. Chel. 12, 691.
Koyama, S., Heinbockel, T., 2020. The effects of essential oils and terpenes in relation to their routes of intake and application. Int. J. Mol. Sci. 21, 1558.
Lahlou, M., 2004. Essential oils and fragrance compounds: bioactivity and mechanisms of action. Flavour Fragrance J. 19, 159–165. https://doi.org/10.1002/ffj.1288.
Laska, M., 1999. Olfactory discrimination ability of human subjects for ten pairs of enantiomers. Chem. Senses 24, 161.
Lee, S.-H., Do, H.-S., Min, K.-J., 2015. Effects of essential oil from hinoki cypress. Chamaecyparis obtusa. Physiol. Behav. Flies, PLOS ONE 10.
Lehrner, J., Marwinski, G., Lehr, S., Johren, P., Deecke, L., 2005. Ambient odors of orange and lavender reduce anxiety and improve mood in a dental office. Physiol. Behav. 86, 92–95. https://doi.org/10.1016/j.physbeh.2005.06.031.
Li, F., Xu, B., Wang, P., Liu, L., 2019. Traditional Chinese medicine non-pharmaceutical therapies for chronic adult insomnia. Méd. 98 (Baltimore).
Li, Y., Wang, C., Zong, S., Qi, J., Dong, X., Zhao, W., Wu, W., Fu, Q., Lu, Y., Chen, Z., 2019. The trigeminal pathway dominates the nose-to-brain transportation of intact polymeric nanoparticles: evidence from aggregation-caused quenching probes. J. Biomed. Nanotechnol. 15 https://doi.org/10.1166/jbn.2019.2724.
Louis, M., Kowalski, S.D., 2002. Use of aromatherapy with hospice patients to decrease pain, anxiety, and depression and to promote an increased sense of well-being. Am. J. Hosp. Palliat. Care 19, 381–386. https://doi.org/10.1177/104990910201900607.
Maddocks, W., 2023. Aromatherapy in nursing and midwifery practice: a scoping review of published studies since 2005. J. Holist. Nurs. 41, 62–89. https://doi.org/10.1177/08980101221078736.
Mahdood, B., Imani, B., Khazaei, S., 2022. Effects of inhalation aromatherapy with Rosa damascena (damask rose) on the state anxiety and sleep quality of operating room personnel during the COVID-19 pandemic: a randomized controlled trial. J. perianesthesia Nurs. Off. J. Am. Soc. PeriAnesthesia Nurses 37, 493–500. https://doi.org/10.1016/j.jopan.2021.09.011.
Marsh, E., Millette, D., Wolfe, A., 2022. Complementary intervention in postoperative care: aromatherapy's role in decreasing postoperative nausea and vomiting. J. Holist. Nurs. 40, 351–358. https://doi.org/10.1177/08980101211065555.
Marzouk, T.M.F., El-Nemer, A.M.R., Baraka, H.N., 2013. The effect of aromatherapy abdominal massage on alleviating menstrual pain in nursing students: a prospective randomized cross-over study. Evid. Based. Complement. Alternat. Med., 2013 https://doi.org/10.1155/2013/742421.
Matsumoto, T., Asakura, H., Hayashi, T., 2014. Effects of olfactory stimulation from the fragrance of the Japanese citrus fruit yuzu (Citrus junos Sieb. ex Tanaka) on mood states and salivary chromogranin A as an endocrinologic stress marker. J. Alternative Compl. Med. 20, 500–506. https://doi.org/10.1089/acm.2013.0425.
McMullen, R.L., Dell'Acqua, G., 2023. History of natural ingredients in cosmetics. Inside Cosmet. 10 (2023), 71. https://doi.org/10.3390/COSMETICS10030071. Page 71 10.
Moghadam, Z.E., Delmoradi, F., Aemmi, S.Z., Vaghee, S., Vashani, H.B., 2022. Effectiveness of aromatherapy with inhaled lavender essential oil and breathing exercises on ECT-related anxiety in depressed patients. Explore 18, 683–687. https://doi.org/10.1016/j.explore.2021.12.006.
Mohammadpourhodki, R., Sadeghnezhad, H., Ebrahimi, H., Basirinezhad, M.H., Maleki, M., Bossola, M., 2021. The effect of aromatherapy massage with lavender and citrus aurantium essential oil on quality of life of patients on chronic hemodialysis: a parallel randomized clinical trial study. J. Pain Symptom Manag. 61, 456–463. https://doi.org/10.1016/j.jpainsymman.2020.08.032 e1.
Mohebitabar, S., Shirazi, M., Bioos, S., Rahimi, R., Malekshahi, F., Nejatbakhsh, F., 2017. Therapeutic efficacy of rose oil: a comprehensive review of clinical evidence. Avicenna J. phytomedicine 7, 206–213.
Mojtehedi, M., Salehi-Pourmehr, H., Ostadrahimi, A., Asnaashari, S., Esmaeilpour, K., Farshbaf-Khalili, A., 2022. Effect of aromatherapy with essential oil of Lavandula angustifolia mill- citrus bergamia and mindfulness-based intervention on sexual function, anxiety, and depression in postmenopausal women: a randomized controlled trial with factorial design. Iran. J. Nurs. Midwifery Res. 27, 392–405. https://doi.org/10.4103/IJNMR.IJNMR_129_21.
Mueller, S.M., Grunwald, M., 2021. Effects, side effects and contraindications of relaxation massage during pregnancy: a systematic review of randomized controlled trials. J. Clin. Med. 10 (2021), 3485. https://doi.org/10.3390/JCM10163485. Page 3485 10.
Mulugeta, H., Ayana, M., Sintayehu, M., Dessie, G., Zewdu, T., 2018. Preoperative anxiety and associated factors among adult surgical patients in Debre Markos and Felege Hiwot referral hospitals, Northwest Ethiopia. BMC Anesthesiol. 18, 1–9. https://doi.org/10.1186/S12871-018-0619-0/TABLES/6.
Ng, F., Thong, A., Basri, N., Wu, W., Chew, W., Dharmawan, J., 2022. Profiling of aroma-active compounds in ylang-ylang essential oils by aroma extract dilution analysis (AEDA) and chemometric methods. J. Agric. Food Chem. 70, 260.
Oertelt-Prigione, S., 2012. Immunology and the menstrual cycle. Autoimmun. Rev. 11 https://doi.org/10.1016/J.AUTREV.2011.11.023.
Ojeda-Sana, A.M., van Baren, C.M., Elechosa, M.A., Juarez, M.A., Moreno, S., 2013. New insights into antibacterial and antioxidant activities of rosemary essential oils and their main components. Food Control 31, 189.
Organization, F. and A., n.d. FAOLEX database. Food and Agriculture Organization of the United Nations.
Osaili, T.M., Dhanasekaran, D.K., Zeb, F., Faris, M.E., Naja, F., Radwan, H., Ismail, L.C., Hasan, H., Hashim, M., Obaid, R.S., Status, A., 1809. Review on health-promoting properties and global regulation of essential oils. Molecules 28, 2023.
Ou, M.C., Hsu, T.F., Lai, A.C., Lin, Y.T., Lin, C.C., 2012. Pain relief assessment by aromatic essential oil massage on outpatients with primary dysmenorrhea: a randomized, double-blind clinical trial. J. Obstet. Gynaecol. Res. 38, 817–822. https://doi.org/10.1111/J.1447-0756.2011.01802.X.
Özer, Z., Teke, N., Turan, G.B., Bahçecik, A.N., 2022. Effectiveness of lemon essential oil in reducing test anxiety in nursing students. Explore 18, 526–532. https://doi.org/10.1016/j.explore.2022.02.003.
Park, H.-J., Lim, E.-J., Zhao, R.J., Oh, S.R., Jung, J.W., Ahn, E.-M., Lee, E.S., Koo, J.S., Kim, H.Y., Chang, S., Shim, H.S., Kim, K.J., Gwak, Y.S., Yang, C.H., 2015. Effect of the fragrance inhalation of essential oil from Asarum heterotropoides on depression-like behaviors in mice. BMC Compl. Alternative Med. 15, 43. https://doi.org/10.1186/s12906-015-0571-1.
Perica Ž Pešić, V.M.B., 2003. Investigation on the essential oil of cultivatedSalvia sclarea L. Flavour Fragrance J. 18, 228.
Phootha, N., Yongparnichkul, N., Fang, Z., Gan, R.-Y., Zhang, P., 2022. Plants and phytochemicals potentials in tackling anxiety: a systematic review. Phytomedicine 2, 100375. https://doi.org/10.1016/j.phyplu.2022.100375.
Pitman, V., 2004. Aromatherapy: a Practical Approach. Nelson Thornes Ltd, p. 2004.
Pujiati, W., Siagian, Y., Hardivianty, C., 2019. Application of essential oils: lavender, clary sage, ginger and Geranium as aromatherapy through effleurage massage for menstrual pain. Int. J. Sci. Res. 8, 1476.
Qneibi, M., Jaradat, N., Hawash, M., Zaid, A.N., Natsheh, A.-R., Yousef, R., AbuHasan, Q., 2019. The neuroprotective role of Origanum syriacum L. And Lavandula dentata L. Essent. Oils through their eff. AMPA recept. BioMed Res 1 (2019).
Rafii, F., Ameri, F., Haghani, H., Ghobadi, A., 2020. The effect of aromatherapy massage with lavender and chamomile oil on anxiety and sleep quality of patients with burns. Burns 46, 164–171. https://doi.org/10.1016/J.BURNS.2019.02.017.
Ravi, R., Prakash, M., Bhat, K.K., 2007. Aroma characterization of coriander (Coriandrum sativum L.) oil samples. Eur. Food Res 225, 367.
Reven, M.E., Bowles, E.J., Audia, D.D., Cohen, M.M., Joswiak, D.J., Kurkas Lee, B.A., May-Fitzgerald, A.C., Peppers-Citizen, M., Resnick, J.A., Tomaino, J.M., Unger, B.J., 2023. Quality appraisal of research reporting for aromatherapy and essential oil studies in humans: proposed checklist for "transparent reporting for essential oil and aroma therapeutic studies.". J. Integr. Complement. Med. https://doi.org/10.1089/JICM.2023.0006.
Rhind, J.P., 2012. Essential Oils: A Handbook for Aromatherapy Practice, second.
Rufino, A.T., Ribeiro, M., Sousa, C., Judas, F., Salgueiro, L., Cavaleiro, C., Mendes, A.F., 2015. Evaluation of the anti-inflammatory, anti-catabolic and pro-anabolic effects of E-caryophyllene, myrcene and limonene in a cell model of osteoarthritis. Eur. J. Pharmacol. 750, 141.
Saad, N.Y., Muller, C.D., Lobstein, A., 2013. Major bioactivities and mechanism of action of essential oils and their components. Flavour Fragrance J. 28, 269–279. https://doi.org/10.1002/FFJ.3165.
Sanchez-Vidana, D.I., Po, K.K.-T., Fung, T.K.-H., Chow, J.K.-W., Lau, W.K.-W., So, P.-K., Lau, B.W.-M., Tsang, H.W.-H., 2019. Lavender essential oil ameliorates depression-like behavior and increases neurogenesis and dendritic complexity in rats. Neurosci. Lett. 701, 180. https://doi.org/10.1016/j.neulet.2019.02.042.
Sandlin, D., 2006. Alternative treatment options for postoperative nausea and vomiting. J. PeriAnesthesia Nurs. 21, 436–438. https://doi.org/10.1016/j.jopan.2006.09.003.
Sanna, M.D., Les, F., Lopez, V., Galeotti, N., 2019. Lavender (Lavandula angustifolia mill.) essential oil alleviates neuropathic pain in mice with spared nerve injury. Front. Pharmacol. 10, 472.
Sarkic, A., Stappen, I., 2018. Essential oils and their compounds in cosmetics-A critical review. Cosmetics 5, 11. https://doi.org/10.3390/cosmetics5010011.
Sarkic, A., Stappen, I., Oils, E., Single, T., 2018. Compounds in cosmetics-A critical review. Cosmetics 5, 11.
Sattayakhom, A., Wichit, S., Koomhin, P., 2023. The effects of essential oils on the nervous system: a scoping review. Molecules 28. https://doi.org/10.3390/MOLECULES28093771.
Schreiner, L., Bauer, J., Ortner, E., Buettner, A., 2020. Structure-odor activity studies on derivatives of aromatic and oxygenated monoterpenoids synthesized by modifying p -cymene. J Nat. Prod 83, 834. https://doi.org/10.1021/acs.jnatprod.9b00339.
Schreiner, L., Bauer, P., Buettner, A., 2018. Resolving the smell of wood - identification of odour-active compounds in Scots pine (Pinus sylvestris L.). Sci. Rep. 8, 8294.

Shahr, H.S.A., Saadat, M., Kheirkhah, M., Saadat, E., 2015. The effect of self-aromatherapy massage of the abdomen on the primary dysmenorrhoea. J. Obstet. Gynaecol. (Bristol) 35, 382. https://doi.org/10.3109/01443615.2014.958449.

Shaikh, S., Nagarekha, D., Hegade, G., Marutheesh, M., 2016. Postoperative nausea and vomiting: a simple yet complex problem. Anesth. Essays Res. 10, 388. https://doi.org/10.4103/0259-1162.179310.

Sharmeen, J.B., Mahomoodally, F.M., Zengin, G., Maggi, F., 2021. Essential oils as natural sources of fragrance compounds for cosmetics and cosmeceuticals. Molecules 26, 666.

Shiina, Y., Funabashi, N., Lee, K., Toyoda, T., Sekine, T., Honjo, S., Hasegawa, R., Kawata, T., Wakatsuki, Y., Hayashi, S., Murakami, S., Koike, K., Daimon, M., Komuro, I., 2008. Relaxation effects of lavender aromatherapy improve coronary flow velocity reserve in healthy men evaluated by transthoracic Doppler echocardiography. Int. J. Cardiol. 129, 193.

Silveira, V., Santos Rubio, K.T., Poleti Martucci, M.E., 2022. Anxiolytic effect of Anthemis nobilis L. (roman chamomile) and Citrus reticulata Blanco (tangerine) essential oils using the light-dark test in zebrafish (Danio rerio). J. Ethnopharmacol. 298, 115580 https://doi.org/10.1016/j.jep.2022.115580.

Skold, M., Karlberg, A.-T., Matura, M., Borje, A., 2006. The fragrance chemical β-caryophyllene—air oxidation and skin sensitization. Food Chem. Toxicol. 44, 538–545. https://doi.org/10.1016/j.fct.2005.08.028.

Soden, K., Vincent, K., Craske, S., Lucas, C., Asley, S., 2004. A randomized controlled trial of aromatherapy massage in a hospice setting. Palliat. Med. 18, 87–92. https://doi.org/10.1191/0269216304PM874OA.

Soleimani, M., Kashfi, L.S., mirmohamadkhani, M., Ghods, A.A., 2022. The effect of aromatherapy with peppermint essential oil on anxiety of cardiac patients in emergency department: a placebo-controlled study. Compl. Ther. Clin. Pract. 46, 101533 https://doi.org/10.1016/j.ctcp.2022.101533.

Support, O. of P. and S, 2011. Australian Regulatory Guidelines for Complementary Medicines Part IV V4, vol. 2.

Tate, C., 2019. Using Aromatherapy to Alleviate Nausea Symptoms in Phase 2 Recovery Patients, vol. 110, pp. 17–18.

Thurman, E.M., 2020. Analysis of terpenes in hemp (Cannabis sativa) by gas chromatography/mass spectrometry: isomer identification analysis. Compr. Anal. Chem. 90, 197–233. https://doi.org/10.1016/bs.coac.2020.04.013.

Tisserand, R., Young, R., 2014. General safety guidelines. Essent. Oil Saf 649–654. https://doi.org/10.1016/B978-0-443-06241-4.00015-1.

Toda, M., Morimoto, K., 2008. Effect of lavender aroma on salivary endocrinological stress markers. Arch. Oral Biol. 53, 964–968. https://doi.org/10.1016/j.archoralbio.2008.04.002.

Tripathi, A.K., Mishra, S., 2016. Plant monoterpenoids (Prospective Pesticides). In: Ecofriendly Pest Manag. Food Secur. Elsevier, pp. 507–524.

Uehleke, B., Hopfenmueller, W., Stange, R., Saller, R., 2012. Are the Correct Herbal Claims by Hildegard von Bingen Only Lucky Strikes? A New Statistical Approach. In: Approach, A.N.S. (Ed.), Forsch. Forschende Komplementärmedizin und Klassische Naturheilkunde/Res. Complement. Med., vol. 19, pp. 187–190.

Umano, K., Hagi, Y., Tamura, T., Shoji, A., Shibamoto, T., 1994. Identification of volatile compounds isolated from Round Kumquat (Fortunella japonica Swingle). J. Agric. Food Chem. 42, 1888.

Vieira, A.J., Beserra, F.P., Souza, M.C., Totti, B.M., Rozza, A.L., Aroma, L., 2018. Limonene: aroma of innovation in health and disease. Chem. Biol. Interact. 283, 97. https://doi.org/10.1016/j.cbi.2018.02.007.

Villareal, M.O., Ikeya, A., Sasaki, K., Arfa, A. Ben, Neffati, M., Isoda, H., 2017. Anti-stress and neuronal cell differentiation induction effects of Rosmarinus officinalis L. essential oil. BMC Compl. Alternative Med. 17, 549. https://doi.org/10.1186/s12906-017-2060-1.

Vostinaru, O., Heghes, S.C., Filip, L., Vostinaru, O., Heghes, S.C., Filip, L., 2020. Safety profile of essential oils. Essent. Oils - Bioact. Compd. New Perspect. Appl. https://doi.org/10.5772/INTECHOPEN.91363.

Wang, R., Huang, X., Wang, Y., Akbari, M., 2022. Non-pharmacologic approaches in preoperative anxiety, a comprehensive review. Front. public Heal 10. https://doi.org/10.3389/FPUBH.2022.854673.

Watanabe, E., Kuchta, K., Kimura, M., Rauwald, H.W., Kamei, T., Imanishi, J., 2015. Effects of bergamot (citrus bergamia (Risso) Wright & Arn.) essential oil aromatherapy on mood states, parasympathetic nervous system activity, and salivary cortisol levels in 41 healthy females. Complement. Med. Res. 22, 43–49. https://doi.org/10.1159/000380989.

Wei, Y., Cui, J., Fu, C., Xu, B., Shi, M., Dai, Y., Huang, X., Hai, Q., Ni, A., Chen, B., Xiong, L., Qin, D., 2023. Effects of Cang-Ai volatile oil on depressed mood and cortical excitability in human, Pharmacol. Res. - Mod. Chin. Med. 6, 100215.

Weston-Green, K., Clunas, H., Naranjo, C.J., Review, A., 2021. Of the potential use of pinene and linalool as terpene-based medicines for brain health: discovering novel therapeutics in the flavours and fragrances of cannabis. Front. Psychiatr. 12.

Yang, H., Woo, J., Pae, A.N., Um, M.Y., Cho, N.-C., Park, K.D., Yoon, M., Kim, J., Lee, C. J., Cho, S., 2016. ? -pinene, a major constituent of pine tree oils, enhances non-rapid eye movement sleep in mice through GABA A -benzodiazepine receptors. Mol. Pharmacol. 90, 530.

Yang, S.K., Tan, N.P., Chong, C.W., Abushelaibi, A., Lim, S.H.E., Lai, K.S., 2021. The missing piece: recent approaches investigating the antimicrobial mode of action of essential oils. https://doi.org/10.1177/1176934320938391.

Zellner, B.D.A., Lo Presti, M., Soares Barata, L.E., Dugo, P., Dugo, G., Mondello, L., 2006. Evaluation of leaf-derived extracts as an environmentally sustainable source of essential oils by using gas chromatography-mass spectrometry and enantioselective gas chromatography-olfactometry. Anal. Chem. 78, 883–890. https://doi.org/10.1021/AC051337S/ASSET/IMAGES/LARGE/AC051337SF00003.JPEG.

Zeng, Y.S., Wang, C., Ward, K.E., Hume, A.L., 2018. Complementary and alternative medicine in hospice and palliative care: a systematic review. J. Pain Symptom Manag. 56, 781–794. https://doi.org/10.1016/J.JPAINSYMMAN.2018.07.016 e4.

Zhang, J., Li, M., Zhang, H., Pang, X., 2022. Comparative investigation on aroma profiles of five different mint (Mentha) species using a combined sensory. Spectrosc. Chemom. study. Food Chem. 371, 4.

Zhang, N., Zhang, L., Feng, L., Yao, L., 2018. Cananga odorata essential oil reverses the anxiety induced by 1-(3-chlorophenyl) piperazine through regulating the MAPK pathway and serotonin system in mice. J. Ethnopharmacol. 219, 23–30. https://doi.org/10.1016/J.JEP.2018.03.013.

Zimmerman, W.B., Mentation, S., Thresholds, A.A., 1970. Sleep mentation and auditory awakening thresholds. Psychophysiology 6, 540.