ISSN: 1693-8666

available at http://journal.uii.ac.id/index.php/JIF

# Potential advancement utilizing nanotechnology-based delivery system to enhance the therapeutic properties of lavender essential oil: a review article

A. M. Bagas Trianloka<sup>1</sup>, Lutfi Chabib<sup>2\*</sup>, Arba Pramundita Ramadani<sup>2</sup>

#### **Abstract**

**Background:** Essential oils (EO), such as lavender (Lavandula spp.), which are derived from its flower, have become a growing trend in recent years as an alternative medicine in therapy. However, the poor physicochemical properties of EOs have several disadvantages for their application. Integrating nanotechnology into the formulation of medicinal dosage forms may provide a viable way to mitigate these limitations and improve the effectiveness of EO utilization.

**Objective:** This literature review aims to gather information on the medicinal benefits of lavender EO and the prospective applications of nanotechnology-based delivery systems for EOs.

**Method:** Online databases such as PubMed, Science Direct, Research Gate, Google Scholar, and other reliable sources were used to find 65 publications between 1991 and 2021, which are assessed in this review.

**Results:** It is revealed that the main constituents of lavender EO are linalool, linally acetate, and lavandulyl acetate. Its effectiveness as an antibacterial, antioxidant, anticancer, anti-anxiety, and having effects on the central nervous system, along with other qualities including pain relief, has been demonstrated via numerous studies. Additionally, it was demonstrated to have dermatological properties that helped treat dermatitis and encouraged both hair growth and wound healing. Furthermore, it was also found that the application of nanotechnology in EOs has improved the concentration of active compounds in the blood and produced a stable dosage form while also increasing its efficacy.

**Conclusion:** It is feasible to create nanoparticle dosage forms from lavender EO that can improve the substance's solubility, stability, and pharmacological effects. More research is necessary to formulate lavender EO by applying nanotechnology.

Keywords: Lavender, essential oil, therapeutic activity, nanotechnology, nanoparticle

#### 1. Introduction

Essential oils (EO) have become increasingly valuable for their potential use in medicine, cosmetics, aromatherapy, fragrance, and spirituality. Depending on the section and kind of plant, different methods are used to extract EOs from the leaves, flowers, stems, fruit, seeds, bark, and roots of a variety of aromatic plants. The unique aromas of EO can be attributed to about 3000 phytochemicals, including saturated and unsaturated hydrocarbons, terpenes, sesquiterpenes, alcohols, phenols, aldehydes, ketones, esters, acids, phenolic ethers, oxides, lactones, and coumarins. These colorless liquid oils are extremely powerful and concentrated, reviving and stimulating pressure points in addition to supporting a range of medical functions (Ali *et al.*, 2015; Dunning, 2013).

Lavender (Lavandula spp.), a beloved garden herb that has long been used as medicine, is one of the most common uses of essential oils. Lavenders are native to the mountainous regions of the Mediterranean and belong to the Labiatae (Lamiacae) family. They are utilized for a number of therapeutic and cosmetic uses. More than 30 species of plants belong to the Lamiaceae family, and

<sup>&</sup>lt;sup>1</sup>Magister of Pharmacy, Universitas Islam Indonesia, Yogyakarta, Indonesia

<sup>&</sup>lt;sup>2</sup>Department of Pharmacy, Universitas Islam Indonesia, Yogyakarta, Indonesia

<sup>\*</sup>Corresponding author: <a href="lutfi.chabib@uii.ac.id">lutfi.chabib@uii.ac.id</a>

the most well-known are *Lavandula stoechas* (French lavender), *Lavandula latifolia* (wide leaves lavender), and *Lavandula angustifolia* Mill (narrow leaves lavender). Due to its unique medicinal properties, the narrow-leaved lavender (*Lavandula angustifolia*, originally *L. officinalis* Chaix or *L. vera*), also referred to as garden lavender, is the most valuable genus of lavender (Adaszyńska *et al.*, 2013). Lavender EO is obtained through steam distillation of both the flower heads and the leaves; however, due to their distinct chemical compositions, the flower yields a more fragrant and sweeter oil. It is a pale yellowish liquid with a smell that varies from fresh and flowery to aromatic and woodsy. In addition to its supposed benefits for burns and bug bites, the oil is also reported to possess antibacterial, antifungal, carminative (smooth muscle relaxing), sedative, and antidepressive qualities (Cavanagh & Wilkinson, 2002; Miastkowska *et al.*, 2021).

At present, EO's potential as a therapeutic agent has never completely utilized due to its lipophilic component and extreme volatile. Consequently, EOs may be impacted by conversion and degrading processes. EOs are prone to oxidation and polymerization, which can lead to degradation and changes in their pharmacological properties (Turek & Stintzing, 2013). The use of nanoparticle technology in the pharmaceutical industry can offer several benefits that can increase EO effectiveness to address these shortcomings. Currently, there have been multiple studies showcasing the applications of nanotechnology to formulate lavender EO dosage form. However, there aren't any articles that specifically review the actions and recent advancement of lavender EO. Thus, the purpose of this review is to compile extensive data regarding the activity of lavender EO as well as its possible advancement via the application of nanotechnology.

# 2. Method

This literature review is performed by examining article publication available online in PubMed, Science Direct, Research Gate, Google Scholar and other reliable sources via terms like "lavender essential oil", "chemical compounds", "therapeutic activity", "nanotechnology", and "nanoparticle" that were used for each of the searches. From the database, 65 articles were selected which are published national and international article between 1991 through 2021, in either English or Indonesia language.

# 3. Result and discussion

# 3.1. Chemical compounds of lavender essential oil

Study by de Groot and Schmidt (2016) analyzed lavender EO samples from France, Bulgaria, Australia, Ukraine, Moldavia, England, and China between 2001 and 2013 by GC/MS, and concluded

the following ten compounds that has the highest maximum concentrations found in the oil are as follows: linalool (26.0%-44.8%), linalyl acetate (26.1%-43.3%), (Z)-A-ocimene (0.3%-7.5%), lavandulyl acetate (0.4%-6.3%), terpinen-4-ol (0.07%-5.9%), acaryophyllene (1.8%-5.9%), (E)-A-ocimene (0.7%-4.7%), (E)-Afarnesene (0.4%-4.5%), borneol (0.3%-2.7%), and 1,8-cineole (0.01%-2.4%) (De Groot & Schmidt, 2016). Another test in 2014 also found that linalool (34.1%) and linalyl acetate (33.3%) were discovered to be the two primary ingredients of lavender oil (**Figure 1**.), while other notable constituents were ocymene and lavandulil acetate (3.2% each) (Sienkiewicz *et al.*, 2014). Other research by Vârban *et al.* (2022) using GC/MS analyzing lavender EO resulted in 38 of the 40 isolated chemicals that were identified using their mass spectra (29 terpenoids, 2 alcohols, 1 ketones and 5 esters, 1 hydrocarbon). The volatile profile was made up 94.41% by terpenes and terpenoids. Beta-linalool and linalool acetate were the two most prevalent volatile substances, followed by caryophyllene (5.66%) and beta-farnesene (6.45%), while camphor was only present in very trace amounts (0.18%). This kind of volatile character is said to be indicative of the highest-quality lavender EO (Vârban *et al.*, 2022).

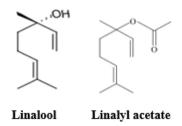


Figure 1. Two main compounds of lavender EO

# 3.2. Pharmacological activities

Viuda-Martos et al.

2011

Numerous articles were assessed to obtain data regarding the potential therapeutic activity of lavender EO as shown in **Table 1**.

**Table 1.** Studies on lavender EO therapeutic activity

Author(s) Year Therapeutic activity/response Disease Showed antimicrobial properties at Bacterial Soković et al. 2007 concentrations of 4.0-9.0 mg/ml infection Effective against gram-positive bacteria more than Bacterial Mayaud et al. 2008 gram-negative bacteria infection Diverse biological actions of antibacterial and Hanamanthagouda Bacterial and 2010 antifungal depends on the genus of Lavandula fungi infection et al. Bacterial Stanojevic et al. 2011 Inhibition of multiple strains of bacteria infection Inhibitory effect on the processes of fat oxidation Hui et al. 2010 Free radicals

Reduce 50% DPPH at multiple concentration of

Free radicals

and lipid peroxidation

Author(s)	Year	Therapeutic activity/response	Disease
		lavender EO	
Lin et al.	2009	Exhibit antioxidant properties akin to lime and marjoram EO in same study	Free radicals
Wattenberg	1991	Rats fed the lavender oil-containing diet had noticeably fewer tumors and adenomas per rat	Cancer
Teranishi <i>et al</i> .	1993	Containing compounds in trace amount that may have potent anticancer properties	Cancer
Zhang et al.	1999	Containing monoterpenoid perillyl alcohol inhibits	Cancer
Loutrari <i>et al</i> .	2004	the growth and division of angiogenic cells in vitro	dancer
Moteki <i>et al</i> .	2002	Contents of terpinen-4-ol and 1,8-cineole, have been shown to have anticancer properties in vitro	Cancer
Calcabrini <i>et al.</i>	2004	by inducing apoptosis in tumor cells	Gancer
Yamada et al.	1994	Inhaling or injecting lavender EO intraperitoneally can prevent convulsions caused by pentylenetetrazol or nicotine	Anxiety
Dunn et al.	1995	Lavender EO aromatherapy was found to reduce anxiety in comparison to receiving a massage without aromatherapy and to resting	Anxiety
Kritsidima et al.	2010	Used of lavender essential oil aromatherapy to reduce their anxiety about the uncomfortable feelings	Anxiety
Buchbauer et al.	1991	Linalool and terpineol, has been shown to reduce anxiety, encourage sleep, and weaken physical activity in both humans and animals	Central nervous system
Hudson	1995	Inhaling lavender oil increased sleep quality for 72% of patients, compared to only 11% of the control group	Central nervous system
Diego et al.	1998	Mice and rats given systemic injections of lavender EO exhibit sleepiness. Inhaling lavender EO improved arithmetic performance and increased wave activity of forty healthy individuals in brain wave research	Central nervous system
Styles	1997	Young HIV patients who had lavender EO massages required less painkillers overall	Pain
Lis-Balchin & Hart	1999	Lavender EO has an antispasmodic effect via increasing messenger cAMP levels	Pain
Ghelardini et al.	1999	In vitro studies have confirmed this EO's analgesic activity, and anaesthetic properties have been proven in rabbit experiments	Pain
Anderson <i>et al</i> .	2000	As an alternative of topical steroids to treat eczema, lavender EO showed substantial reduction in irritability and sleeping disruption	Eczema
Kim & Cho	2010	Using lavender oil topically may be able to block part of the allergic pathway	Skin allergic reaction
Koca Kutlu <i>et al</i> .	2013	Higher levels of both EGF (epidermal growth factor) and FGF (fibroblast growth factor)-2 in wounds treated with lavender EO	Wound
Mori et al.	2016	Lavender EO was found to significantly raise the levels of type I collagen and TGF- $\beta$ (transforming growth factor)- $\beta$	Wound

Author(s)	Year	Therapeutic activity/response	Disease
Hay et al.	1998	Combination of oil containing thyme, rosemary, cedarwood and lavender EO showed hair growth improvement in randomized controlled study of alopecia areata patients	Alopecia
Lee et al.	2016	Lavender oil significantly promotes hair development, as seen both morphologically and histologically in female C57BL/6 mice	Alopecia

#### 3.2.1. Antimicrobial

At concentrations of 4.0–9.0 mg/ml, the lavender EO (*L. angustifolia*) exhibited antimicrobial properties (Soković *et al.*, 2007). Its antibacterial activities at doses of 0.94%–10% against 65 bacterial species were proven in the investigation by Mayaud *et al.*, (the effectiveness against Grampositive bacteria was higher than against Gram-negative) (Mayaud *et al.*, 2008). The growth of *S. enteritidis, K. pneumoniae, E. coli, S. aureus, P. aeruginosa, C. albicans,* and *A. niger* are all inhibited by lavender EO (Stanojevic *et al.*, 2011). The biological actions of the EOs produced by plants of the genus Lavandula are extremely diverse. The growth of germs like Salmonella, Enterobacter, Klebsiella, *E. coli, S. aureus,* and *L. monocytogenes* are inhibited by the EO of *Lavandula dentata*. At concentrations of 0.5-2.0 µg×ml-1 for bacteria and 2.0-4.0 µg×ml-1 for fungi, respectively, the EO of *L. bipinnata* demonstrates antibacterial activity (against *E. coli, P. aeruginosa, S. aureus, and B. subtilis*) and antifungal properties (against *A. niger, P. notatum,* and *C. albicans*) (Hanamanthagouda *et al.*, 2010).

# 3.2.2. Antioxidant

The antioxidant qualities of lavender EO protect cells from the damaging effects of free radicals. In a linoleic acid model system, Hui *et al.* (2010)'s research demonstrated this oil's inhibitory effect on the processes of fat oxidation and lipid peroxidation (Hui *et al.*, 2010). Studies examining this EO's ability to reduce 50% DPPH radicals yielded inconsistent findings; values ranged from 289  $\mu$ g×ml-1 to 48.7 mg×ml-1 (Viuda-Martos *et al.*, 2011). Another study used DPPH to examine the antioxidant properties of lavender essential oil (*L. angustifolia*) and how well it can counteract free radicals. At a concentration of 5 g×1-1, the reading of 15.18  $\pm$  0.009% indicates properties akin to those of lime and marjoram essential oils (Lin *et al.*, 2009). They discovered that the EO had a far lesser ability to neutralize free radicals at a comparable quantity (4.11%).

#### 3.2.3. Anticancer

To explore the anticancer potential of lavender oil components, numerous in vitro research has been conducted using rat, bovine, human, and bacterial cell lines. These investigations have shown that lavender oils contain compounds that, in trace amounts, may have potent anticancer properties (Teranishi *et al.*, 1993). Many lavender essential oils include nerolidol, a sesquiterpene

that is thought to have anticancer effects since rats fed the oil-containing diet had noticeably fewer tumors and adenomas per rat (Wattenberg, 1991). It also has been demonstrated that the monoterpenoid perillyl alcohol inhibits the growth and division of angiogenic cells *in vitro*, which makes it a viable candidate for use in anticancer treatment (Loutrari *et al.*, 2004; Zhang *et al.*, 1999). Later, perillyl alcohol's potential as a chemo preventive agent was explored through National Cancer Institute-sponsored Phase I, II, and III trials for colon, breast, and prostate cancers. Some constituents of lavender oil, such as terpinen-4-ol and 1,8-cineole, have been shown to have anticancer properties *in vitro* by inducing apoptosis in tumor cells (Calcabrini *et al.*, 2004; Moteki *et al.*, 2002).

#### 3.2.4. Anti-anxiety

In a randomized clinical experiment with 122 critically ill patients, EO aromatherapy was found to reduce anxiety in comparison to receiving a massage without aromatherapy and to resting. Blood pressure and respiratory system health did not differ between the two groups (Dunn *et al.*, 1995). According to other research, inhaling or injecting lavender EO intraperitoneally can prevent convulsions caused by pentylenetetrazol or nicotine (Yamada *et al.*, 1994). Another study on people waiting at dentist clinics used lavender essential oil aromatherapy to reduce their anxiety about the uncomfortable feelings they expected (Kritsidima *et al.*, 2010).

# 3.2.5. Central nervous system

A study by Buchbauer *et al.* (1991) found that specific EO components, including linalool and terpineol, have an impact on the central nervous system. This has been shown to reduce anxiety, encourage sleep, and weaken physical activity in both humans and animals (Buchbauer *et al.*, 1991). A 245-person clinical experiment found that inhaling lavender oil increased sleep quality for 72% of patients, compared to only 11% of the control group. Four out of every five patients who took the medicine reported feeling generally well, compared with only 25% of individuals in the control group (Hudson, 1995). Mice and rats given systemic injections of lavender essential oil exhibit sleepiness. Inhaling lavender essential oil (EO) improved arithmetic performance and increased wave activity of forty healthy individuals in brain wave research. In addition to being sleepy, patients have also allegedly reported feeling relaxed and having a positive attitude on life (Diego *et al.*, 1998).

# 3.2.6. Pain relieves

Young HIV patients who had lavender essential oil massages required less painkillers overall and, in certain cases, felt no discomfort at all (Styles, 1997). Lavender essential oil (EO) has an antispasmodic effect via increasing messenger cAMP levels, while the exact mechanism is unclear (Lis-Balchin & Hart, 1999). *In vitro* studies have confirmed this EO's analgesic activity, and anaesthetic properties have been proven in rabbit experiments. Anaesthetic activity was measured

using both *in vivo* testing on the rabbit conjunctival reflex and *in vitro* testing on a rat phrenic nervehemidiaphragm preparation. The *L. angustifolia* EO, linally acetate, and linalool (0.01 - 10 g/ml) substantially and dose-dependently decreased the electrically induced contractions of the rat phrenic-hemidiaphragm. In the rabbit conjunctival reflex test, the addition of 30–2500 g/ml of linally acetate and linalool to solution of *L. angustifolia* EO increases the number of shocks needed to induce the response in a dose-dependent manner, confirming in vivo the local anaesthetic effect found in vitro (Ghelardini *et al.*, 1999).

# 3.2.7. Dermatological activities

Lavender and other essential oils have been evaluated for their efficacy as an alternative of conventional drugs, like topical steroids, which are often found to be ineffective. The usefulness of several EOs, including lavender, in the treatment of eczema was investigated by Anderson *et al.* (2000) by employing both massage with the oils and the addition of the oils (6 drops of a blend of three oils in a 1:1:1 ratio) to bath water. The 8-week course of treatment led to a substantial reduction in irritability and sleeping disruption in both the massage alone and EO groups, despite the small sample size of 16 children (Anderson *et al.*, 2000). Furthermore, it has been suggested that using lavender oil topically may be able to block part of the allergic pathway (Kim & Cho, 2010).

# 3.2.8. Wound healing

Lavender essential oil was found to significantly raise the levels of type I collagen and TGF- $\beta$  (transforming growth factor)- $\beta$  in one investigation. This result supports the clinical observation of faster and greater wound contraction in the lavender-treated group as compared to the control group because TGF- $\beta$  is known to induce fibroblast proliferation and differentiation into myofibroblasts, which are crucial for wound contraction via tissue shrinkage (Mori *et al.*, 2016). Another study discovered considerably higher levels of both EGF (epidermal growth factor) and FGF (fibroblast growth factor)-2 in wounds treated with lavender EO (Koca Kutlu *et al.*, 2013). As its name would suggest, FGF-2 is crucial for the proliferation of fibroblasts. EGF is being researched as a possible topical treatment for chronic wounds since it is a signalling molecule that promotes fibroblast and epithelial cell migration, which causes wound contraction and epithelialization (Bodnar, 2013).

# 3.2.9. Hair growth

It is claimed that thyme, rosemary, cedarwood, and lavender EO promote hair growth in alopecia individuals. A randomized, double-blind, controlled study was conducted by Hay *et al.* (1998) to look at this effect, where 86 alopecia areata patients had their scalps massaged nightly with a combination of oil containing 114 mg of *Rosmarinus officinalis*, 94 mg of *Cedrus atlantica*, 108 mg of *Thyme vulgaris*, and 108 mg of *L. angustifolia*. Hair growth was assessed at 3- and 7-month

intervals. When EOs were administered, 19 out of 35 patients reported an improvement in hair growth, compared to just 6 out of 28 controls. This indicates that the treated group's area of alopecia was much smaller than that of the control group (Hay *et al.*, 1998). Another study was conducted to investigate the effects of lavender oil (LO) on hair growth in female C57BL/6 mice. In comparison to the normal group (saline solution), the experimental group that received lavender oil at concentrations of 3% and 5%, respectively, had considerably more hair follicles, deeper hair follicles, thicker dermal layer, and fewer mast cells. These findings demonstrated that LO significantly promotes hair development, as seen both morphologically and histologically (Lee *et al.*, 2016).

# 3.3. Application of nanotechnology on essential oil

Due to their traditional uses, plant-based products such as EO have several disadvantages when used as medications, including reduced solubility and bioavailability of the ingredient, increased dosage requirements, volatile and low stability, as well as prone to oxidation and polymerization (Mukherjee, 2015; Turek & Stintzing, 2013). These drawbacks can be addressed and enhanced using nanotechnology to produce better herbal dosage forms, such as liposomes, gold nanoparticles, and self-nano emulsifying drug delivery systems (SNEDDS). Active compounds' solubility, stability, and bioavailability can all be enhanced by formulations based on nanoparticles. Nanoparticle sizes can vary from 20 to 200 nm, depending upon its components and the method of production. Particle size reduction will increase a preparation's surface area and facilitate the entry of active components into hard-to-reach action locations, such as the blood-brain barrier, and their passage across cell and other membranes to the target of action. The creation of a more intricate drug delivery system has significantly improved thanks to the application of nanotechnology (Alexander *et al.*, 2016; Harwansh *et al.*, 2011b, 2011a; Porter *et al.*, 2008). Recent studies have been conducted to assess the possibility of nanotechnology applications in formulating lavender EO into a more potent dosage form, as shown in **Table 2**.

**Table 2.** Recent examples of nanotechnology applications in lavender EO formulation

Author(s)	Year	Formulation	Therapeutical uses
Sofi et al.	2019	Composite electrospun wound-dressing nanofibers made of polyurethane containing lavender oil and silver nanoparticles	Antibacterial/Wound healing
Fadel et al.	2023	Nano system made of gold nanoparticles and nano-lavender EO using ultrasonic nanoemulsifying techniques	Antibacterial/Wound healing
Rahayu <i>et al</i> .	2024	Lavender EO-loaded polyurethane nanoparticles via a facile swelling-diffusion method as hydrocolloid agents	Antibacterial/Wound healing

238 | Trianloka *et al.* / Jurnal Ilmiah Farmasi (Scientific Journal of Pharmacy) 20(2) August-December 2024, 231-242

Author(s)	Year	Formulation	Therapeutical uses
Fahimnia <i>et al</i> .	2024	Topical gel containing lavender oil loaded solid lipid nanoparticles	Antibacterial/Anti- inflammatory
Sanei-Dehkordi <i>et al</i> .	2023	Lavender and Geranium EO-Loaded nanogels using nanoemulsion-based gel method	Antibacterial/Repellent

A study employed a unique approach to create composite electrospun wound-dressing nanofibers made of polyurethane containing lavender oil and silver (Ag) nanoparticles (NP). The Ag NPs and lavender oil enhanced the hydrophilicity of the nanofibers and facilitated the proliferation of chicken embryo fibroblasts grown *in vitro* on these fiber dressings. The antibacterial efficacy of the nanofiber dressings was assessed using *E. coli* and *S. aureus*, resulting in inhibition zones of  $16.2 \pm 0.8$  mm and  $5.9 \pm 0.5$  mm, respectively, demonstrating the dressings' superior bactericidal capabilities (Sofi *et al.*, 2019).

In order to aid in wound healing and fight bacterial infection, another current study sought to create a unique nano system made of gold nanoparticles and nano-lavender EO using ultrasonic nanoemulsifying techniques. Unlike lavender EO, the newly created nano-gold/nano-lavender completely eradicated the microbial cells by penetrating the generated *P. mirabilis biofilm*. The MIC and MBEC (minimum biofilm eradication concentration) values were 8 and 16  $\mu$ g/mL, respectively. Higher results, compared to lavender EO, were obtained when the cytotoxic effect of the innovative nano-gold and nano-lavender formulas was evaluated against WI-38 fibroblasts Vero (normal) cells (IC<sub>50</sub> = 0.529 and 0.209 mg/mL, respectively). With a 96.78% wound closure rate, the nano-gold/nano-*Lavandula angustifolia* mixture demonstrated potent wound healing ability (Fadel *et al.*, 2023).

Other study also sought to formulate wound healing applications where the hydrocolloid-based preformed polyurethane (PU) NPs were used as a template for the simple swelling-diffusion of lavender EO. PU hydrocolloid was carefully combined with the Lavender EO phase that had been dissolved in an ethanol/water mixture at various volume ratios. Lavender EO diffused and became trapped in the PU NPs as a result of the high miscibility between Lavender EO and the PU matrix. Using ethanol/water at a ratio of 0/100, stable lavender EO-loaded PU NPs with high 59.67% entrapment efficiency 27.98% loading capacity were created. In phosphate buffer at pH 8.5, the release behaviour of lavender EO from the lavender EO-loaded PU NPs demonstrated sustained release for 192 hours. The biocompatibility of the NPs was demonstrated by the high cell survival of around 80% in the cytotoxicity assay employing fibroblast cells at the maximum dose of 1 mg/ml. A

transparent soft film formed from the encapsulated PU NPs demonstrated antibacterial efficacy against *E. coli* and *S. aureus* (Rahayu *et al.*, 2024).

A separate investigation involved the preparation of lavender oil-loaded Solid Lipid Nanoparticles (Lav-SLN) utilizing cholesterol and lecithin as natural lipids, followed by the characterization of the generated SLNs. Next, Carbopol 940 was used to create a topical gel (Lav-SLN-G) that contained 3% SLN. The antibacterial properties of Lav-SLN and Lav-SLN-G against *S. aureus* were evaluated. Lav-SLNs showed an % entrapment efficiency of 75.46%, a zeta potential of -21.6 mv, and a particle size of 19.24 nm. The pH and textural characteristics of the topical gel formulation were satisfactory. Lavender oil, Lav-SLN, and Lav-SLN-G had the following minimum inhibitory/bactericidal concentrations (MIC/MBC) against *S. aureus*: 0.12 and 0.24 mgml<sup>-1</sup>, 0.05 and 0.19 mgml<sup>-1</sup>, and 0.045 and 0.09 mgml<sup>-1</sup>, respectively (Fahimnia *et al.*, 2024).

Different study attempted to create lavender and geranium ( $Pelargonium\ graveolens\ L'Hér.$ ) EO nanogels (NGs) with potential antibacterial and repellent properties. A nanoemulsion-based gel method was used to formulate the NGs; the zeta potentials and nanoemulsion droplet sizes were found to be  $146\pm7$  and  $106\pm6$  nm and  $-23.2\pm0.7$  and  $-17.4\pm1$  mV, respectively. The successful loading of EOs in NGs was validated by the ATR-FTIR analysis. *Anopheles stephensi* Liston mosquitoes were employed in repellent bioassays, which showed that geranium NG (140 min) was just as efficient as the commonly used repellent DEET (140 min). According to antibacterial testing, the nanogels successfully inhibited the development of bacteria; against *E. coli* Migula, the geranium NG demonstrated a reduction of over 90%. Higher effectiveness against *S. aureus* Rosenbach was demonstrated by the lavender NG (Sanei-Dehkordi *et al.*, 2023).

The findings of the studies mentioned above imply that lavender EOs could be developed into nanoparticle medication delivery systems. This goes to show that other therapeutic properties of lavender EO could also be beneficial from the application of nanotechnology in future studies, to improve its efficacy and stability as a pharmaceutical dosage form.

# 4. Conclusion

Lavender (*Lavandula angustifolia*), one of the most popular garden herbs in the world, contains EO with major constituents like linalool and linalyl acetate. Antimicrobial, antioxidant, anticancer, anti-anxiety, central nervous system, pain-relieving, dermatological, wound-healing, and hair-growth qualities are only a few of its many medical benefits. Recent research has focused on using nanotechnology to increase the effectiveness of lavender EO. Future research is needed to

create drug delivery methods using nanoparticles for the numerous medicinal advantages of lavender essential oil.

# Acknowledgement

We are grateful to Department of Pharmacy, Master of Pharmacy Study Program, and Directorate of Research and Community Services of Universitas Islam Indonesia, as well as Ministry of Education, Culture, Research, and Technology for providing the facilities and financial support through Master's Thesis Research grants 2024 number 073/ST-DirDPPM/70/DPPM/PTM-KEMDIKBUDRISTEK/VI/2024 to allow this review article to be completed as the initial study for our research. The authors declare no conflict of interest.

#### References

- Adaszyńska, M., Swarcewicz, M., Dzięcioł, M., & Dobrowolska, A. (2013). Comparison of Chemical Composition and Antibacterial Activity of Lavender Varieties from Poland. *Natural Product Research*, 27(16), 1497–1501. https://doi.org/10.1080/14786419.2012.724408
- Alexander, A., Ajazuddin, Patel, R.J., Saraf, Swarnlata, & Saraf, Shailendra. (2016). Recent Expansion of Pharmaceutical Nanotechnologies and Targeting Strategies In The Field of Phytopharmaceuticals For The Delivery of Herbal Extracts and Bioactives. *Journal of Controlled Release*, 241, 110–124. https://doi.org/10.1016/j.jconrel.2016.09.017
- 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 Pacific Journal of Tropical Biomedicine*, 5(8), 601–611. https://doi.org/10.1016/j.apjtb.2015.05.007
- Anderson, C., Lis-Balchin, M., & Kirk-Smith, M. (2000). Evaluation of Massage With Essential Oils On Childhood Atopic Eczema. *Phytotherapy Research*, 14(6), 452–456. https://doi.org/10.1002/1099-1573(200009)14:6<452::AID-PTR952>3.0.CO;2-4
- Bodnar, R.J. (2013). Epidermal Growth Factor and Epidermal Growth Factor Receptor: The Yin and Yang in the Treatment of Cutaneous Wounds and Cancer. *Advances in Wound Care*, 2(1), 24–29. https://doi.org/10.1089/wound.2011.0326
- Buchbauer, G., Jirovetz, L., & Jäger, W. (1991). Aromatherapy: Evidence for Sedative Effects of the Essential Oil of Lavender after Inhalation. *Zeitschrift für Naturforschung C*, 46c, 1067–1072. https://doi.org/10.1515/znc-1991-11-1223
- Calcabrini, A., Stringaro, A., Toccacieli, L., Meschini, S., Marra, M., Colone, M., Arancia, G., Molinari, A., Salvatore, G., & Mondello, F. (2004). Terpinen-4-ol, The Main Component of *Melaleuca Alternifolia* (Tea Tree) Oil Inhibits the In Vitro Growth of Human Melanoma Cells. *Journal of Investigative Dermatology*, 122(2), 349–360. https://doi.org/10.1046/j.0022-202X.2004.22236.x
- Cavanagh, H.M.A., & Wilkinson, J.M. (2002). Biological Activities of Lavender Essential Oil. *Phytotherapy Research*, 16(4), 301–308. https://doi.org/10.1002/ptr.1103
- De Groot, A., & Schmidt, E. (2016). Essential Oils, Part V: Peppermint Oil, Lavender Oil, and Lemongrass Oil. *Dermatitis*, 27(6), 325–332. https://doi.org/10.1097/DER.000000000000218
- Diego, M.A., Jones, N.A., Field, T., Hernandez-reif, M., Schanberg, S., Kuhn, C., Galamaga, M., McAdam, V., & Galamaga, R. (1998). Aromatherapy Positively Affects Mood, Eeg Patterns of Alertness and Math Computations. *International Journal of Neuroscience*, 96(3-4), 217–224. https://doi.org/10.3109/00207459808986469
- Dunn, C., Sleep, J., & Collett, D. (1995). Sensing An Improvement: An Experimental Study To Evaluate The Use of Aromatherapy, Massage and Periods of Rest In An Intensive Care Unit. *Journal of Advanced Nursing*, 21(1), 34–40. https://doi.org/10.1046/j.1365-2648.1995.21010034.x
- Dunning, T. (2013). Aromatherapy: Overview, Safety and Quality Issues. *OA Alternative Medicine*, 1(1). https://doi.org/10.13172/2052-7845-1-1-518

- Fadel, B.A., Elwakil, B.H., Fawzy, E.E., Shaaban, M.M., & Olama, Z.A. (2023). Nanoemulsion of Lavandula angustifolia Essential Oil/Gold Nanoparticles: Antibacterial Effect against Multidrug-Resistant Wound-Causing Bacteria. *Molecules*, 28(19), 6988-7004. https://doi.org/10.3390/molecules28196988
- Fahimnia, F., Nemattalab, M., & Hesari, Z. (2024). Development and Characterization of A Topical Gel, Containing Lavender (*Lavandula angustifolia*) Oil Loaded Solid Lipid Nanoparticles. *BMC Complement Medicine and Therapies*, 24(155), 1-12. https://doi.org/10.1186/s12906-024-04440-2
- Ghelardini, C., Galeotti, N., Salvatore, G., & Mazzanti, G. (1999). Local Anaesthetic Activity of the Essential Oil of *Lavandula angustifolia. Planta Medica*, 65(8), 700–703. https://doi.org/10.1055/s-1999-14045
- Hanamanthagouda, M.S., Kakkalameli, S.B., Naik, P.M., Nagella, P., Seetharamareddy, H.R., & Murthy, H.N. (2010). Essential Oils of *Lavandula bipinnata* and Their Antimicrobial Activities. *Food Chemistry*, 118(3), 836–839. https://doi.org/10.1016/j.foodchem.2009.05.032
- Harwansh, R.K., Patra, K.C., & Pareta, S.K. (2011a). Nanoemulsion As Potential Vehicles For Transdermal Delivery of Pure Phytopharmaceuticals and Poorly Soluble Drug. *International Journal of Drug Delivery*, 3, 209-218.
- Harwansh, R.K., Patra, K.C., Pareta, S.K., Singh, J., & Rahman, M.A. (2011b). Nanoemulsions As Vehicles For Transdermal Delivery of Glycyrrhizin. *Brazilian Journal of Pharmaceutical Sciences*, 47(4), 769–778. https://doi.org/10.1590/S1984-82502011000400014
- Hay, I.C., Jamieson, M., & Ormerod, A.D. (1998). Randomized Trial of Aromatherapy: Successful Treatment for Alopecia Areata. *Arch Dermatol*, 134(11), 1349-1352. https://doi.org/10.1001/archderm.134.11.1349
- Hudson, R., 1995. Use of Lavender In A Long-Term Elderly Ward. Nursing Times 91, 12.
- Hui, L., He, L., Huan, L., XiaoLan, L., & AiGuo, Z. (2010). Chemical Composition of Lavender Essential Oil and Its Antioxidant Activity and Inhibition Against Rhinitis-Related Bacteria. *African Journal of Microbiology Research*, 4(4), 309–313.
- Kim, H.-M., & Cho, S.-H. (2010). Lavender Oil Inhibits Immediate-type Allergic Reaction in Mice and Rats. *Journal of Pharmacy and Pharmacology*, 51(2), 221–226. https://doi.org/10.1211/0022357991772178
- Koca Kutlu, A., Çeçen, D., Gürgen, S.G., Sayın, O., & Çetin, F. (2013). A Comparison Study of Growth Factor Expression Following Treatment with Transcutaneous Electrical Nerve Stimulation, Saline Solution, Povidone-Iodine, and Lavender Oil in Wounds Healing. Evidence-Based Complementary and Alternative Medicine, 2013, 1–9. https://doi.org/10.1155/2013/361832
- Kritsidima, M., Newton, T., & Asimakopoulou, K. (2010). The Effects of Lavender Scent On Dental Patient Anxiety Levels: A Cluster Randomised-Controlled Trial. *Community Dentistry and Oral Epidemiology*, 38(1), 83–87. https://doi.org/10.1111/j.1600-0528.2009.00511.x
- Lee, B.H., Lee, J.S., & Kim, Y.C. (2016). Hair Growth-Promoting Effects of Lavender Oil in C57BL/6 Mice. *Toxicological Research*, 32(2), 103–108. https://doi.org/10.5487/TR.2016.32.2.103
- Lin, C.-W., Yu, C.-W., Wu, S.-C., & Yih, K.-H. (2009). DPPH free-Radical Scavenging Activity, Total Phenolic Contents and Chemical Composition Analysis of Forty-Two Kinds of Essential Oils. *Journal of Food and Drug Analysis*, 17(5), 386-395. https://doi.org/10.38212/2224-6614.2594
- Lis-Balchin, M., & Hart, S. (1999). Studies On The Mode of Action of The Essential Oil of Lavender *Lavandula angustifolia* P. Miller). *Phytotherapy Research*, 13(6), 540–542. https://doi.org/10.1002/(SICI)1099-1573(199909)13:6<540::AID-PTR523>3.0.CO;2-I
- Loutrari, H., Hatziapostolou, M., Skouridou, V., Papadimitriou, E., Roussos, C., Kolisis, F.N., & Papapetropoulos, A. (2004). Perillyl Alcohol Is an Angiogenesis Inhibitor. *The Journal of Pharmacology and Experimental Therapeutics*, 311(2), 568–575. https://doi.org/10.1124/jpet.104.070516
- Mayaud, L., Carricajo, A., Zhiri, A., & Aubert, G. (2008). Comparison of Bacteriostatic and Bactericidal Activity of 13 Essential Oils Against Strains With Varying Sensitivity To Antibiotics. *Letters in Applied Microbiology* 47(3), 167–173. https://doi.org/10.1111/j.1472-765X.2008.02406.x
- Miastkowska, M., Kantyka, T., Bielecka, E., Kałucka, U., Kamińska, M., Kucharska, M., Kilanowicz, A., Cudzik, D., & Cudzik, K. (2021). Enhanced Biological Activity of a Novel Preparation of *Lavandula angustifolia* Essential Oil. *Molecules*, 26(9), 2458-2479. https://doi.org/10.3390/molecules26092458
- Mori, H.-M., Kawanami, H., Kawahata, H., & Aoki, M. (2016). Wound Healing Potential of Lavender Oil By Acceleration of Granulation and Wound Contraction Through Induction of TGF-β In A Rat Model. *BMC Complementary and Alternative Medicine*, 16(144), 1-11. https://doi.org/10.1186/s12906-016-1128-

- Moteki, H., Hibasami, H., Yamada, Y., Katsuzaki, H., Imai, K., & Komiya, T. (2002). Specific Induction of Apoptosis By 1,8-cineole In Two Human Leukemia Cell Lines, But Not A In Human Stomach Cancer Cell Line. *Oncology Reports*, 9(4), 757-760. https://doi.org/10.3892/or.9.4.757
- Mukherjee, P.K. (2015). Evidence-Based Validation of Herbal Medicine. Elsevier, Amsterdam.
- Porter, C.J.H., Pouton, C.W., Cuine, J.F., & Charman, W.N. (2008). Enhancing Intestinal Drug Solubilisation Using Lipid-Based Delivery Systems. *Advanced Drug Delivery Reviews*, 60(6), 673–691. https://doi.org/10.1016/j.addr.2007.10.014
- Rahayu, S.S., Kaewsaneha, C., Opaprakasit, P., Wongngam, Y., & Polpanich, D. (2024). Fabrication of Lavender Essential Oil-Loaded Polyurethane Nanoparticles Via A Facile Swelling-Diffusion Method As Hydrocolloid Agents For Wound Healing Applications. *Emergent Materelias*. https://doi.org/10.1007/s42247-024-00887-8
- Sanei-Dehkordi, A., Abdollahi, A., Montaseri, Z., Safari, M., Rostami Chaijan, M., & Osanloo, M. (2023). Lavender and Geranium Essential Oil-Loaded Nanogels with Promising Repellent and Antibacterial Effects. *Psyche: A Journal of Entomology*, 2023, 1–9. https://doi.org/10.1155/2023/9911066
- Sienkiewicz, M., Głowacka, A., Kowalczyk, E., Wiktorowska-Owczarek, A., Jóźwiak-Bębenista, M., & Łysakowska, M. (2014). The Biological Activities of Cinnamon, Geranium and Lavender Essential Oils. *Molecules*, 19(12), 20929–20940. https://doi.org/10.3390/molecules191220929
- Sofi, H.S., Akram, T., Tamboli, A.H., Majeed, A., Shabir, N., & Sheikh, F.A. (2019). Novel Lavender Oil and Silver Nanoparticles Simultaneously Loaded Onto Polyurethane Nanofibers For Wound-Healing Applications. *International Journal of Pharmaceutics*, 569(2019), 118590-118602. https://doi.org/10.1016/j.ijpharm.2019.118590
- Soković, M., Petar, D.M., Dejan, B., & van Griensven, L.J.L.D. (2007). Chemical Composition and Antibacterial Activity of Essential Oils of Ten Aromatic Plants against Human Pathogenic Bacteria. *Food, Global Science Books*, 1(1), 1-7.
- Stanojevic, L., Stankovic, M., Cakic, M., Nikolic, V., Nikolic, L., Ilic, D., & Radulovic, N. (2011). The Effect of Hydrodistillation Techniques On Yield, Kinetics, Composition And Antimicrobial Activity of essential Oils From Flowers of *Lavandula officinalis* L. *Hemijska Industrija*, 65(4), 455–463. https://doi.org/10.2298/HEMIND110129047S
- Styles, J.L. (1997). The Use of Aromatherapy In Hospitalized Children With HIV Disease. *Complementary Therapies in Nursing and Midwifery*, 3, 16–20. https://doi.org/10.1016/S1353-6117(97)80029-7
- Teranishi, R., Buttery, R.G., & Sugisawa, H. (Eds.). (1993). *Bioactive Volatile Compounds from Plants, ACS Symposium Series*. American Chemical Society, Washington, DC. https://doi.org/10.1021/bk-1993-0525
- Turek, C., & Stintzing, F.C. (2013). Stability of Essential Oils: A Review. *2 Comprehensive Reviews in Food Science and Food Safety*, 12(1), 40–53. https://doi.org/10.1111/1541-4337.12006
- Vârban, D., Zăhan, M., Pop, C.R., Socaci, S., Ştefan, R., Crişan, I., Bota, L.E., Miclea, I., Muscă, A.S., Deac, A.M., & Vârban, R. (2022). Physicochemical Characterization and Prospecting Biological Activity of Some Authentic Transylvanian Essential Oils: Lavender, Sage and Basil. *Metabolites*, 12(10), 962-983. https://doi.org/10.3390/metabo12100962
- Viuda-Martos, M., Mohamady, M.A., Fernández-López, J., Abd ElRazik, K.A., Omer, E.A., Pérez-Alvarez, J.A., & Sendra, E. (2011). In Vitro Antioxidant and Antibacterial Activities of Essentials Oils Obtained From Egyptian Aromatic Plants. *Food Control*, 22(11), 1715–1722. https://doi.org/10.1016/j.foodcont.2011.04.003
- Wattenberg, L.W. (1991). Inhibition of Azoxymethane-Induced Neoplasia of The Large Bowel By 3-hydroxy-3,7,11-trimethyl-l,6,10-dodecatriene (nerolidol). *Carcinogenesis*, 12(1), 151–152. https://doi.org/10.1093/carcin/12.1.151
- Yamada, K., Mimaki, Y., & Sashida, Y. (1994). Anticonvulsive Effects of Inhaling Lavender Oil Vapour. *Biological & Pharmaceutical Bulletin* 17(2), 359–360. https://doi.org/10.1248/bpb.17.359
- Zhang, Z., Chen, H., Chan, K.K., Budd, T., & Ganapathi, R. (1999). Gas Chromatographic-Mass Spectrometric Analysis of Perillyl Alcohol and Metabolites In Plasma. *Journal of Chromatography B: Biomedical Sciences and Applications*, 728(1), 85–95. https://doi.org/10.1016/S0378-4347(99)00065-1