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Galaxy Publication

Comparative Evaluation of the Chemical Composition and Pharmacological Properties of Bulgarian Lavender Essential Oil Samples

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ABSTRACT

Lavender essential oil holds significant economic and therapeutic value, being extensively utilized in aromatherapy, perfumery, the food industry, and pharmaceuticals. In recent years, Bulgaria has emerged as the world's leading producer of lavender, surpassing countries like France, the United Kingdom, China, India, and Spain. This study aims to: (1) analyze the chemical composition of lavender essential oil sourced from an agricultural plantation near Pomorie, Bulgaria; (2) conduct a descriptive statistical evaluation using data from 13 samples reported in four different publications; (3) compare the concentrations of key constituents—particularly linalool and linalyl acetate—across different varieties; and (4) review the pharmacological properties of the principal compounds. Gas chromatography–mass spectrometry (GC/MS) analysis of the Pomorie oil sample identified 44 distinct compounds. The predominant constituents included linalyl acetate (27.5%), linalool (24.1%), E-β-ocimene (7.0%), terpinen-4-ol (5.1%), caryophyllene (4.5%), carvacrol (4.4%), lavandulyl acetate (3.5%), Z-β-farnesene (3.3%), and Z-β-ocimene (3.2%). The essential oil's quality is primarily assessed based on the content of linalool and linalyl acetate, which showed variations among different cultivars, influenced by the harvest year and geographic origin within Bulgaria. Certain varieties demonstrated a more consistent linalool-to-linalyl acetate ratio compared to others. The composition of both the Pomorie sample and other analyzed Bulgarian oils generally conformed to the standards set by ISO (2002) and the European Pharmacopoeia (10th ed., Council of Europe 2020), with only minor deviations. Lavender oil exhibits a wide spectrum of pharmacological actions, including anxiolytic, sedative, antioxidant, anti-inflammatory, antitumor, and antimicrobial effects. While linalool and linalyl acetate are the main contributors to these properties, the oil's overall bioactivity is attributed to synergistic interactions among its multiple constituents.

Keywords: Antimicrobial, Linalool, Lavandula angustifolia Mill, Synergy, Linalyl acetate, Anti-inflammatory activity

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Introduction

Lavender essential oil holds considerable economic and therapeutic importance, with extensive applications in aromatherapy, perfumery, pharmaceuticals, and the food industry [1-6]. Commercial production primarily utilizes lavender (L. angustifolia), spike lavender (L. latifolia L.), and lavandin—a sterile hybrid derived from L. angustifolia × L. latifolia. Among these, the essential oil of L. angustifolia is the most prized and expensive due to its superior fragrance and quality [3, 7, 8].

Lavandula angustifolia Mill. subsp. Angustifolia (synonyms: L. spica L. var. alpha, L. officinalis Chaix, L. fragrans Jord., L. vera DC) is a woody perennial shrub reaching up to 50 cm in height, featuring narrow linear-lanceolate leaves and dense inflorescences with numerous small flowers. The plant bears ovate to rhombic bracts, which serve as key diagnostic features. It is indigenous to mountainous regions of southwestern and south-central Europe, particularly in Italy, France, and Spain, typically thriving at altitudes above 1500 meters [9].

In recent years, Bulgaria has emerged as the world's leading producer of lavender, surpassing traditional producers such as France [8, 10, 11]. As of 2022, the country's lavender cultivation spanned over 11,145 hectares, yielding approximately 50,126 tons [12]. The crop was first introduced to Bulgaria in the early 20th century using French planting material. Large-scale cultivation began roughly three decades later, particularly in the Kazanlak and Karlovo regions, utilizing both locally propagated plants and imported seeds from England and France.

During the 1950s, breeding programs at the Institute of Roses and Aromatic Plants (IRAP), Kazanlak, under the direction of Dimitrova (1959) [13], significantly advanced lavender improvement through clonal selection, intraspecific hybridization, gamma irradiation, and chemical mutagenesis. These efforts led to the development of more than ten high-yielding varieties adapted to Bulgaria's environmental conditions [13-19]. Over the last decade, lavender cultivation has expanded beyond its traditional regions, yet in some newly established areas, suboptimal soil and climatic conditions have caused fluctuations in flower and essential oil yields, occasionally lowering oil quality. This variability underscores the need for region-specific selection and breeding programs that prioritize adaptability, yield stability, and essential oil quality [19].

At present, seven main lavender varieties dominate Bulgarian cultivation: 'Hemus,' 'Druzhba,' 'Karlovo,' 'Sevtopolis,' 'Jubileina,' 'Raya,' and 'Hebar.' The adoption of these selected varieties, as opposed to seed-derived or older heterogeneous populations, has substantially improved both flower and oil yields [10]. Nonetheless, recent trends in seed propagation have led to genetic mixing, diminishing varietal purity, and contributing to high genetic diversity among cultivated lavender [11]. This genetic variation, coupled with regional climatic influences, results in significant diversity in the chemical profiles of Bulgarian lavender essential oils [8, 11, 20].

According to the International Organization for Standardization (ISO 2002) [21], the essential oil of L. angustifolia must exhibit an ester value of 108–165 (equivalent to 38–58% ester content) and a minimum camphor concentration of 0.5% (m/m), along with specific chromatographic characteristics for key constituents. The European Pharmacopoeia [22] establishes similar yet slightly varied chromatographic standards for certain compounds.

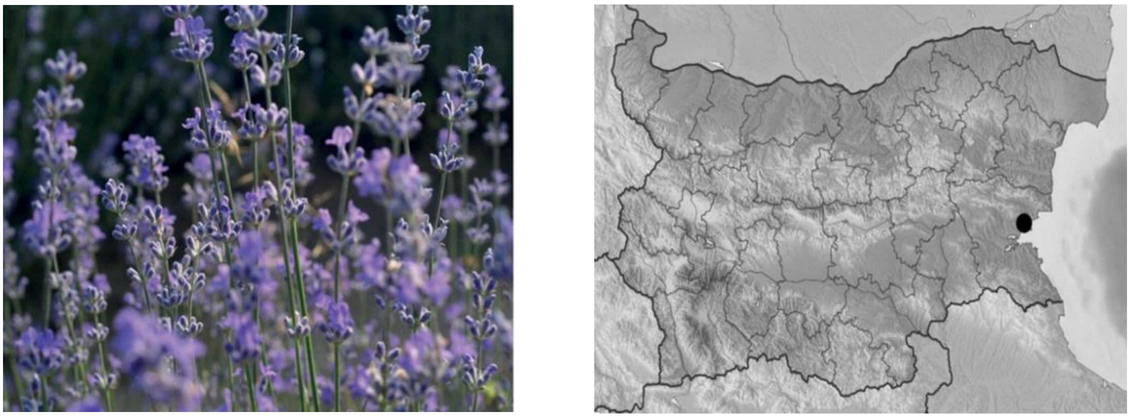
The objectives of the present study are to: (1) characterize a lavender essential oil sample obtained from an agricultural plantation near Pomorie, Bulgaria; (2) conduct comparative descriptive statistical analyses using data from 13 previously published samples; (3) evaluate inter-varietal differences in the levels of key compounds, particularly linalool and linalyl acetate; and (4) summarize the pharmacological activities of the principal components.

Materials and Methods

Essential oil extraction and analysis

Inflorescences of Lavandula angustifolia **(Figure 1a)** were collected during the third decade of June 2022 from a plantation near Pomorie on Bulgaria's Black Sea coast **(Figure 1b)**. The plantation owner reported the cultivated variety as 'Sevtopolis'; however, molecular marker confirmation was not conducted. Essential oil extraction was carried out by steam distillation for four hours using a Clevenger apparatus.

The chemical composition was analyzed through gas chromatography–mass spectrometry (GC/MS) following the guidelines of the European Pharmacopoeia (10th ed.). The diluted essential oil (1:1000) was examined using an Exactive Orbitrap GC-MS system (ThermoFisher Scientific) operating at 70 eV with an ion source temperature of 230 °C and interface temperature of 280 °C. Injections (1 µL, split ratio 20:1) were made at 270 °C, utilizing a fused silica capillary column coated with 5% phenyl/95% methyl polysiloxane (TG5SILMS, 30 m × 0.25 mm × 0.25 µm, Thermo).



a) b)

Figure 1. a) Agricultural plantation showing Lavandula angustifolia inflorescences; b) Geographic location of the plantation.

Data set and analysis preparation

A comprehensive literature search was performed using Google Scholar, Web of Science, and PubMed databases to locate studies published between 1900 and 2023, employing search terms such as "Lavandula angustifolia essential oil," "linalool," "linalyl acetate," "Bulgaria," and "pharmacological effect(s)." Four relevant publications were identified [23-26], collectively providing 13 samples that contained comprehensive GC or GC-MS compositional data for L. angustifolia essential oils obtained through hydrodistillation under various cultivation conditions and extraction durations (ranging from 40 minutes to 4 hours). To ensure consistency, synonymous compound names were standardized, duplicates were removed, and isomeric and coeluted compounds were merged into unified entries before arranging all components alphabetically.

Descriptive statistics

The concentrations of linalool and linalyl acetate in the Pomorie sample were compared with values reported in previous Bulgarian studies. Data covering a five-year period for southeastern Bulgaria were extracted from Stanev and Angelova (2022) [27]. The mean, minimum, and maximum percentages of these key constituents were computed for Bulgarian samples and evaluated against international standard specifications.

Results and Discussion

Chemical composition of lavender essential oil from pomorie

The essential oil yield from the Pomorie L. angustifolia sample was 1.15 ml per 100 g of plant material. A total of 44 constituents were identified **(Figure 2, Table 1).** The dominant compounds were linalyl acetate (27.52%), linalool (24.11%), E-β-ocimene (7.01%), terpinen-4-ol (5.11%), caryophyllene (4.46%), carvacrol (4.42%), lavandulyl acetate (3.52%), Z-β-farnesene (3.33%), and Z-β-ocimene (3.15%).

Table 1. Components detected in the *L. angustifolia* essential oil – Origin Pomorie.

Compound	% of total	Compound	% of total	Compound	% of total
tricyclene	0.02	*E*-β-ocimene	7.01	linalyl acetate	27.53
β-thujene	0.23	*Z*-β-ocimene	3.15	bornyl acetate	0.18
α-pinene	0.32	γ-terpinene	0.82	lavandulyl acetate	3.52
camphene	0.17	terpinolene	0.13	carvacrol	4.42
β-terpinene	0.04	linalool	24.11	nerol acetate	0.36
β-pinene	0.06	1-octen-3-yl-acetate	0.78	geranyl acetate	0.62
1-octen-3-ol 0.222 3-octanone	0.67	3-octanol,acetate 0.05 allo-ocimene	0.12	caryophyllene	4.46
β-myrcene	0.69	caren-4-ol	0.01	α-santalene	0.53
3-octanol	0.24	camphor	0.26	*E*-α-bergamotene	0.16
α-phellandrene	0.06	lavandulol	1.47	humulene	0.14

3-carene	0.11	terpinen-4-ol	5.11	β-sesquiphellandrene	0.12
acetic acid, hexyl ester	0.51	crypton	0.13	*Z*-β-farnesene	3.33
o-cymene	0.84	α-terpineol	1.36	germacrene D	0.52
limonene	0.53	butanoic acid,hexyl ester	0.36	caryophyllene oxide	0.24
eucalyptol	1.09	*Z*-geraniol	0.16		

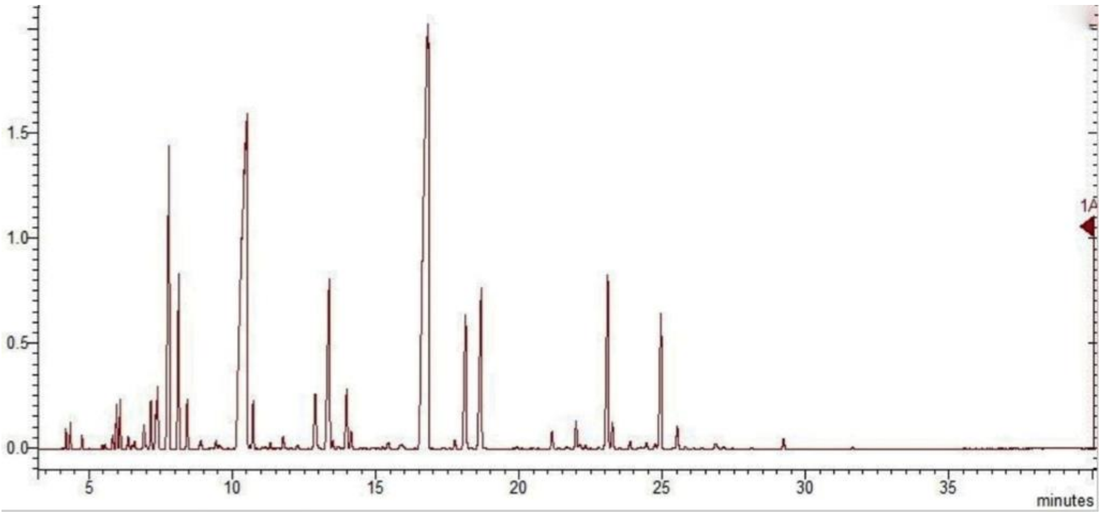


Figure 2. GC/MS chromatogram showing the chemical composition of L. angustifolia essential oil from Pomorie.

Descriptive statistics and comparative analysis

Linalool and linalyl acetate serve as the primary quality indicators for lavender essential oil. In the Pomorie sample, their concentrations were 26.84% and 30.64%, respectively **(Table 1).** These values were compared with data from multiple samples representing seven different lavender varieties cultivated in various regions and harvested across different years **(Figure 3).**

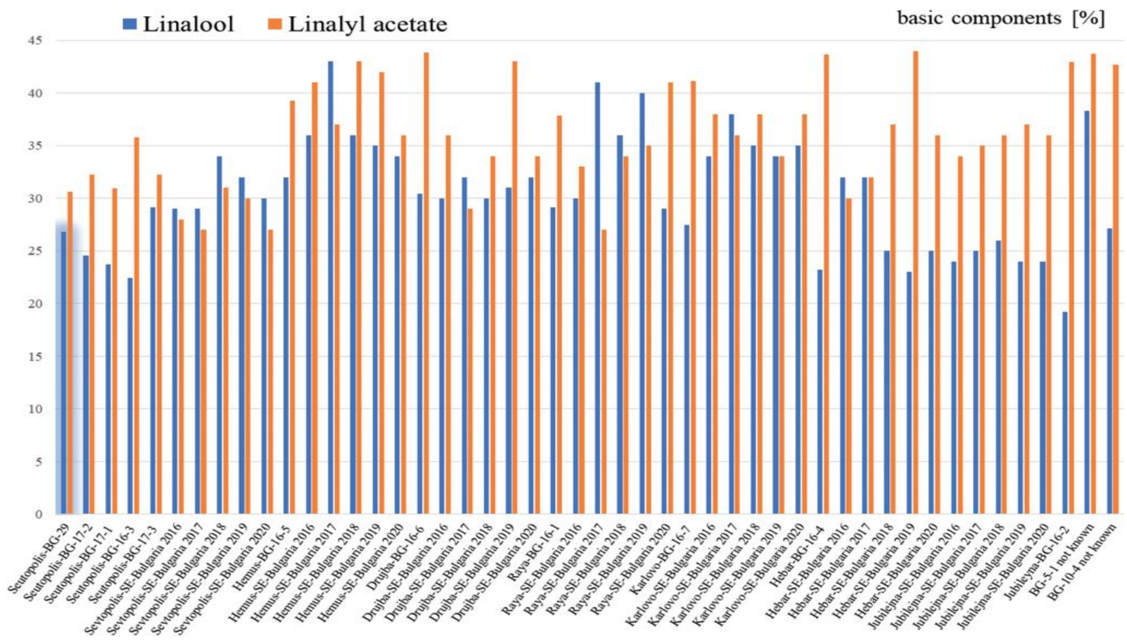


Figure 3. Concentrations of linalool and linalyl acetate in the Pomorie sample (Sevtopolis-BG-29) compared with those of the 'Sevtopolis,' 'Hemus,' 'Druzhba,' 'Raya,' 'Karlovo,' 'Hebar,' and 'Jubileina' varieties originating from different regions and harvest years.

The proportions of linalool and linalyl acetate exhibit noticeable variation both among different lavender varieties and across years and cultivation regions within Bulgaria. Previous studies have shown that the 'Hemus' and 'Hebar' cultivars maintain a relatively consistent linalool-to-linalyl acetate ratio, unlike 'Karlovo,' 'Druzhba,' 'Raya,' and 'Sevtopolis,' while 'Jubileina' demonstrates the highest stability in this regard [27]. Our descriptive statistical analysis aligns with these earlier observations, confirming that Bulgarian lavender essential oils from different sources conform to the quality specifications set by ISO and the European Pharmacopoeia (10th ed., **Table 2**).

Table 2. Content of the main lavender essential oil components in the sample from Pomorie, Average, Minimum and Maximum values calculated for 13 samples from Bulgarian and compared to the standards.

Components	Sample from Pomorie	Samples from Bulgaria (n = 13)			ISO and/or European Pharmacopoeia (10th edn.)	
		Average [%]	Min [%]	Max [%]	Min [%]	Max [%]
Camphor	0.26	0.12	0.00	0.29	–	1.20 or 1.50
1,8-Cineole	1.21	0.35	0.00	3.06	–	2.50 or 3.00
1,8-Cineole + Phellandrene	–	0.65	0.00	2.21	–	–
Phellandrene	0.06	–	–	–	–	1.00
D-Limonene	0.53	0.38	0.00	0.80	–	1.00
Z-β-Ocimene	3.15	5.18	0.00	9.04	1.00	10.00
E-β-Ocimene	7.01	2.78	0.90	8.71	0.50	6.00
Lavandulol	1.47	0.82	0.00	1.64	0.1	3.00
Lavandulyl acetate	3.52	3.78	0.00	5.83	0.20	8.00
Linalool	24.11	27.20	19.22	38.32	20.00	45.00
Linalyl acetate	27.53	38.24	30.64	43.84	25.00	47.00
3-Octanone	0.74	0.96	0.00	2.61	0.10	5.00
Terpinen-4-ol	1.51	2.58	0.00	6.84	0.10	8.00
α-Terpineol	1.36	0.68	0.00	1.51	–	2.00

The other predominant constituents identified in the Pomorie sample, along with those found in the analyzed Bulgarian lavender oils, generally met the chemical composition criteria established by ISO (2002) [21] and the European Pharmacopoeia [22], except for a few minor deviations **(Table 2).**

Pharmacological effects of lavender essential oil

Insomnia, anxiety, and pain relief

Lavender essential oil is extensively applied in aromatherapy owing to its calming and sleep-inducing qualities. These effects are mainly attributed to its dominant monoterpenes, linalool and linalyl acetate, which exhibit sedative, antispasmodic, and relaxing properties [28]. Clinical observations among female students have demonstrated that inhaling lavender aroma improves sleep quality and reduces depressive symptoms [29]. Moreover, lavender oil aromatherapy has been shown to alleviate agitation and restlessness in patients with dementia [30]. Experimental studies also confirmed its ability to reduce preoperative anxiety, perceived pain, and enhance patient comfort during surgery [31]. The oil has further been reported to lessen the severity of primary dysmenorrhea—menstrual pain with normal ovulatory cycles and no pelvic disorder [32]. Additionally, Sanna *et al*. (2019) [33] revealed that oral administration of lavender oil in animal models not only produced antidepressant and anxiolytic effects but also mitigated neuropathic pain symptoms caused by spared nerve injury (SNI).

Anti-allergic properties

Lavender essential oil has demonstrated the ability to suppress allergic responses by inhibiting mast cell degranulation, thereby reducing immediate-type hypersensitivity reactions both in vitro and in vivo [34]. However, certain oxidation by-products of its main constituents—linalool and linalyl acetate—have been recognized as potential allergens capable of triggering skin sensitization [35-37].

Anti-inflammatory activity

Lavender oil also exhibits strong anti-inflammatory potential and is widely used in topical formulations for massage therapy and wound treatment. Its mechanism of action is thought to involve the regulation of inflammatory mediators, including prostanoids, nitric oxide (NO), histamine, and proinflammatory cytokines [38]. Furthermore, experimental evidence has indicated that lavender oil, along with linalool and linalyl acetate, can alleviate psoriasis-like inflammation induced by Imiquimod in mouse models [39].

Antimicrobial properties

Research by Lodhia *et al*. (2009) [40] highlighted the antibacterial potential of lavender essential oil, particularly its effectiveness against Gram-negative bacteria. Subsequent investigations confirmed that it can inhibit the growth of pathogenic bacteria isolated from pet turtles, suggesting its applicability as a natural antimicrobial alternative [41].

Insect repellent and pest management effects

Lavender essential oil is well recognized for its insect-repelling and pest-deterrent abilities [42]. It is commonly incorporated into repellents targeting mosquitoes, fleas, and ticks. Beyond domestic use, the oil has demonstrated effectiveness against storage pests such as Tyrophagus longior (a mite) [43] and Sitophilus oryzae (a grain beetle) [44], indicating its potential as a sustainable and natural pest control agent.

Pharmacological effects of main components

Linalool and linalyl acetate are the key bioactive constituents of lavender essential oil, both recognized for their significant anti-inflammatory [45] and sedative [37] actions.

Linalool, a naturally occurring monoterpene alcohol, is present in numerous aromatic plant species, predominantly in its (–)-enantiomeric form, (–)-linalool. Inhalation of linalool vapor has been shown to elicit beneficial psychopharmacological effects in humans [37] and is considered the primary component responsible for the anxiolytic activity of lavender oil [46]. This compound demonstrates local anesthetic potential through its interaction with voltage-gated Na^+ channels, effectively inhibiting action potential generation in sensory neurons [47]. In murine models, Peana *et al*. (2003) [48] reported that (–)-linalool reduces inflammatory pain by significantly lowering acetic acid-induced abdominal contractions, while higher doses exert supraspinal analgesic effects in the hot-plate test. The same research group later proposed that linalool's antinociceptive properties involve modulation of nitric oxide (NO) pathways and interactions with both cholinergic and glutamatergic neurotransmission systems [49].

In vitro studies have shown that linalool induces dose-dependent sedative effects on the central nervous system, producing hypnotic, anticonvulsant, and hypothermic outcomes. Re *et al*. (2000) [50] demonstrated its inhibitory action on acetylcholine (ACh) release and the shortening of ion channel opening time at the mouse neuromuscular junction. Moreover, Camargo *et al.* (2016) [51] highlighted its antihypertensive potential, reporting that linalool reduces cardiac hypertrophy, decreases vascular responsiveness to the vasoconstrictor phenylephrine, and enhances sensitivity to the vasodilator sodium nitroprusside—indicating synergistic cardiovascular effects.

Regarding antimicrobial properties, linalool exhibits notable antifungal activity against Candida species, with the strongest effect against Candida tropicalis (MIC = 500 mg/mL), followed by C. albicans (MIC = 1,000 mg/mL) and C. krusei (MIC = 2,000 mg/mL) [52]. It also acts against dermatophytes such as Microsporum canis and M. gypseum [53]. Sato *et a*l. (2007) [54] reported that vaporized (R)-(–)-linalool reduced airborne microbial counts by more than 40% when dispersed via an air washer. In addition, linalool's antioxidant capacity has been linked to its anticancer potential, as it induces apoptosis in human colon cancer cells through oxidative stress mechanisms [55] and causes apoptotic morphological changes—such as cell shrinkage and membrane blebbing—in prostate cancer cells [56]. Its repellent efficiency has also been established, with linalool diffusers providing 93% protection indoors and 58% outdoors, indicating its promise as an eco-friendly substitute for conventional insecticides [57]. Toxicological evaluations classify linalool as a mild irritant with low acute oral and dermal toxicity in rodent models [58].

Linalyl acetate, the acetate ester derivative of linalool, frequently coexists with it and exhibits similar pharmacological functions. Both compounds contribute prominently to the anti-inflammatory response of essential oils, demonstrated by their ability to suppress Carrageenan-induced edema in rats [45]. Moon *et al*. (2018) [59] proposed its therapeutic potential in managing atopic and inflammatory disorders through inhibition of thymic stromal lymphopoietin expression. Seo *et al*. (2021) [60] further indicated that lavender oil, particularly linalyl acetate, may help prevent rheumatoid arthritis–related muscle atrophy in rats chronically exposed to nicotine.

Linalyl acetate has also been found to counteract olmesartan-induced intestinal hypermotility by modulating the sympathetic inhibitory pathway in hypertensive rats [61] and to function as a vascular smooth muscle relaxant in rabbits [62]. Its cosmeceutical relevance lies in its ability to inhibit melanin synthesis, providing anti-hyperpigmentation effects [63]. Moreover, it displays antihypertensive properties that can protect against ischemic damage related to high blood pressure [64]. According to Shin *et al*. (2020) [65], linalyl acetate may also prevent type 2 diabetes mellitus by improving mitochondrial function, alleviating stress, and reducing insulin resistance in male rats subjected to a high-fat diet and chronic stress conditions.

Synergism

While individual constituents of lavender essential oil exhibit distinct pharmacological actions, the oil as a complete mixture frequently demonstrates enhanced overall efficacy due to synergistic interactions among its components. Numerous investigations have confirmed that such synergy amplifies the antimicrobial potency of lavender oil. For instance, its combination with piperacillin significantly increases the permeability of the Escherichia coli outer membrane relative to untreated controls [66]. Likewise, pairing lavender essential oil with standard β-lactam antibiotics has been shown to mitigate bacterial resistance mechanisms [67]. The joint application of gentamicin and linalool produces a pronounced bactericidal effect against methicillin-resistant Staphylococcus aureus [68]. Beyond antibiotics, synergistic outcomes have also been recorded when lavender oil is used in conjunction with other essential oils—for example, combining lavender and tea tree oils results in improved antifungal activity [69]. Similarly, a blend of Artemisia herba-alba, Lavandula angustifolia, and Rosmarinus officinalis essential oils demonstrates synergism at concentrations far lower than their individual MIC values [70].

Conclusion

The key constituents linalool and linalyl acetate, which determine the quality of lavender essential oil, display variability among samples, yet the Bulgarian specimens analyzed in this study largely conform to international quality benchmarks, with only minor deviations. The principal pharmacological actions of lavender oil encompass relief of insomnia, anxiety, and pain, alongside anti-inflammatory, anti-allergic, and antimicrobial effects, as well as insect-repellent and acaricidal properties. Among its components, linalool contributes predominantly to the sedative, analgesic, and anti-inflammatory actions and exhibits strong antioxidant, antitumor, and antimicrobial potential. Linalyl acetate is particularly associated with potent anti-inflammatory activity and demonstrates protective roles against hypertension-induced ischemic damage and type 2 diabetes mellitus. Despite these distinct individual effects, the collective bioactivity of lavender essential oil is often superior, reflecting the synergistic interplay of its multiple constituents.

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Ethics Statement: None

References

1. Clarke S. Essential Chemistry for Safe Aromatherapy. Edinburgh: Churchill Livingstone; 2002. 231 p.
2. Clarke S, editor. Essential Chemistry for Aromatherapy. 2nd ed. Elsevier Health Sciences; 2009. 301 p.
3. Lis-Balchin M. Lavender essential oil standardisation, ISO; adulteration and its detection using GC, enantiomeric columns and bioactivity. In: Lis-Balchin M, editor. Lavender: The Genus Lavandula. London: CRC Press; 2002. p. 131–7. doi:10.1201/9780203216521-16
4. Lawless J. The Encyclopedia of Essential Oils. San Francisco: Conari Press; 2013. 224 p.

5. Buckle J. Clinical aromatherapy: essential oils in healthcare. 3rd ed. Elsevier Health Sciences; 2014. 412 p. doi:10.1016/B978-0-7020-5440-2.00002-4
6. Ramsey JT, Shropshire BC, Nagy TR, Chambers KD, Li Y, Korach KS. Essential oils and health. Yale J Biol Med. 2020;93(2):291.
7. Lesage-Meessen L, Bou M, Sigoillot JC, Faulds CB, Lomascolo A. Essential oils and distilled straws of lavender and lavandin: current use and potential in white biotechnology. Appl Microbiol Biotechnol. 2015;99(8):3375–85. doi:10.1007/s00253-015-6511-7
8. Giray FH. An analysis of world lavender oil markets and lessons for Turkey. J Essent Oil Bear Plants. 2018;21(6):1612–23. doi:10.1080/0972060X.2019.1574612
9. Upson T. The taxonomy of the genus Lavandula L. In: Lis-Balchin M, editor. Lavender: the genus lavandula. London: CRC Press; 2002. p. 16–48. doi:10.1201/9780203216521-7
10. Stanev S, Zagorcheva T, Atanassov I. Lavender cultivation in Bulgaria – 21st century developments, breeding challenges and opportunities. Bulg J Agric Sci. 2016;22(4):584–90.
11. Zagorcheva T, Stanev S, Rusanov K, Atanassov I. SRAP markers for genetic diversity assessment of lavender (Lavandula angustifolia Mill.) varieties and breeding lines. Biotechnol Biotechnol Equip. 2020;34(1):303–8. doi:10.1080/13102818.2020.1742788
12. Anonymous. Operational analysis for major agricultural crops 30. Ministry of Agriculture of Bulgaria; 2022. Bulgarian. Available from: https://www.mzh.government.bg/media/filer_public/2022/07/28/operativen_analiz_2022-07-27_ZiA805x.pdf
13. Dimitrova E. Nature of inheritance during seed propagation of Lavandula vera L. Use of seedling generation obtained by free pollination in selection and seed production. C R Inst Hortic. 1959;8:12–23.
14. Topalov V. On the diversity of lavender population. Agricultural Science. 1962;6:623–30.
15. Topalov V. Newly developed lavender cultivar Venetsh. Scientific Works of the High Agricultural Institute V. Kolarov, Plovdiv. 1969;18(1):47–50.
16. Raev R, Boyadzhieva B. Newly developed lavender cultivars Sevtopolis and Yubilejna. In: proceedings of the Scientific Conference, Stara Zagora; 1988.
17. Staikov V, Boyadzhieva B. Hemus: Newly developed highly productive lavender cultivar. Hort Sci. 1989;26(1):31–4.
18. Stanev S. Alternative approach for vegetative propagation of lavender. In: scientific conference: 100 Years of experimental and scientific work with essential oil bearing and medicinal crops in Bulgaria; 2007. p. 206–10.
19. Stanev S. Evaluation of the stability and adaptability of the Bulgarian lavender (*lavandula angustifolia* mill.) sorts yield. Agric Sci Technol. 2010;2(3):121–3.
20. Zagorcheva T, Stanev S, Rusanov K, Atanassov I. Comparative GC/MS analysis of lavender (Lavandula angustifolia Mill.) inflorescence and essential oil volatiles. Agric Sci Technol. 2013;5(4):459–62.
21. ISO. ISO 3515:2002. Oil of lavender *(*Lavandula angustifolia Mill*.)*. Geneva: international organization for standardization; 2002. Reviewed and confirmed 2018. Available from: https://www.iso.org/standard/36253.html
22. Council of Europe. European pharmacopoeia 10.0. Strasbourg: European directorate for the quality of medicines; 2020.
23. Schmidt E. The characteristics of lavender oils from eastern Europe. Perfumer & flavorist. 2003;28(4):48–61.
24. Prusinowska R, Śmigielski KB. Composition, biological properties and therapeutic effects of lavender (Lavandula angustifolia L.): a review. Herba Polonica. 2014;60(2):56–66. doi:10.2478/hepo-2014-0010
25. Konaktchiev A. Essential oils from Lavandula angustifolia Mill varieties and species of the genus Achillea L. PhD thesis. Sofia: IOCCPC, BAS; 2015. Bulgarian.
26. Zagorcheva T, Rusanov K, Stanev S, Atanassov I. A simple procedure for comparative GC–MS analysis of lavender (Lavandula angustifolia Mill.) flower volatile composition. IOSR J Pharm Biol Sci. 2016;11(4):9–14. doi:10.9790/3008-1104030914
27. Stanev S, Angelova D. Stability of the ratio between linalool and linalyl acetate in the essential oil of Bulgarian lavender varieties. In: proceedings of the scientific forum with international participation*:* ecology and agrotechnologies – fundamental science and practical realization. 2022;3:225–62.

28. Buchbauer G, Jirovetz L, Jäger W. Aromatherapy: evidence for sedative effects of the essential oil of lavender after inhalation. Z Naturforsch C. 1991;46(11–12):1067–72. doi10.1515/znc-1991-11-1223
29. Lee IS, Lee GJ. Effects of lavender aromatherapy on insomnia and depression in women college students. J Korean Acad Nurs. 2006;36(1):136–43. doi:10.4040/jkan.2006.36.1.136
30. van der Ploeg ES, Eppingstall B, O'Connor DW. Study protocol of a blinded randomized controlled cross-over trial of lavender oil as a treatment of behavioural symptoms in dementia. BMC Geriatr. 2010;10:49. doi:10.1186/1471-2318-10-49
31. Karaman T, Karaman S, Dogru S, Tapar H, Sahin A, Suren M, et al. Evaluating the efficacy of lavender aromatherapy on peripheral venous cannulation pain and anxiety: a prospective, randomized study. Complement Ther Clin Pract. 2016;23:64–8. doi:10.1016/j.ctcp.2016.03.008
32. Zayeri F, Raisi Dehkordi Z, Hosseini-Baharanchi FS. Clinical efficacy of lavender oil inhalation on intensity of menstrual pain from primary dysmenorrhea. J HerbMed Pharmacol. 2019;8:218–23. doi10.15171/jhp.2019.32
33. Sanna MD, Les F, Lopez V, Galeotti N. Lavender (Lavandula angustifolia Mill.) essential oil alleviates neuropathic pain in mice with spared nerve injury. Front Pharmacol. 2019;10:472. doi:10.3389/fphar.2019.00472
34. Kim HM, Cho SH. Lavender oil inhibits immediate-type allergic reaction in mice and rats. J Pharm Pharmacol. 1999;51(2):221–6. doi:10.1211/0022357991772178
35. Karlberg A-T. Fragrance allergy: caused by oxidation of common fragrances: diagnosis and prevention. Abstract presented at: 14th International Congress of Contact Dermatitis. Seoul, Korea; 2003.
36. Sköld M, Hagvall L, Karlberg AT. Autoxidation of linalyl acetate, the main component of lavender oil, creates potent contact allergens. Contact Dermatitis. 2008;58(1):9–14. doi:10.1111/j.1600-0536.2007.01262.x
37. Woronuk G, Demissie Z, Rheault M, Mahmoud S. Biosynthesis and therapeutic properties of Lavandula essential oil constituents. Planta Med. 2011;77(1):7–15. doi:10.1055/s-0030-1250136
38. Cardia GFE, Silva-Filho SE, Silva EL, Uchida NS, Cavalcante HAO, Cassarotti LL, et al. Effect of lavender (Lavandula angustifolia) essential oil on acute inflammatory response. Evid Based Complement Alternat Med. 2018;2018:1413940. doi:10.1155/2018/1413940
39. Rai VK, Sinha P, Yadav KS, Shukla A, Saxena A, Bawankule DU, et al. Anti-psoriatic effect of Lavandula angustifolia essential oil and its major components linalool and linalyl acetate. J Ethnopharmacol. 2020;261:113127. doi:10.1016/j.jep.2020.113127
40. Lodhia MH, Bhatt KR, Thaker VS. Antibacterial activity of essential oils from palmarosa, evening primrose, lavender and tuberose. Indian J Pharm Sci. 2009;71(2):134–6. doi:10.4103/0250-474X.54278
41. Hossain S, Heo H, De Silva BCJ, Wimalasena SHMP, Pathirana HNKS, Heo GJ. Antibacterial activity of essential oil from lavender (Lavandula angustifolia) against pet turtle-borne pathogenic bacteria. Lab Anim Res. 2017;33(3):195–201.
42. Erland LA, Mahmoud SS. Lavender (Lavandula angustifolia) oils. In: preedy V, editor. *Essential oils in food preservation, flavor and safety*. London: academic press; 2016. p. 501–8. doi:10.1016/B978-0-12-416641-7.00057-2
43. Perrucci S. Acaricidal activity of some essential oils and their constituents against Tyrophagus longior, a mite of stored food. J Food Prot. 1995;58(5):560–3. doi:10.4315/0362-028X-58.5.560
44. Al-Harbi NA, Al Attar NM, Hikal DM, Mohamed SE, Abdel Latef AAH, Ibrahim AA, et al. Evaluation of insecticidal effects of plants essential oils extracted from basil, black seeds and lavender against Sitophilus oryzae. Plants. 2021;10(5):829. doi:10.3390/plants10050829
45. Peana AT, D'Aquila PS, Panin F, Serra G, Pippia P, Moretti MD. Anti-inflammatory activity of linalool and linalyl acetate constituents of essential oils. Phytomedicine. 2002;9(8):721–6. doi:10.1078/094471102321621322
46. Umezu T, Nagano K, Ito H, Kosakai K, Sakaniwa M, Morita M. Anticonflict effects of lavender oil and identification of its active constituents. Pharmacol Biochem Behav. 2006;85(4):713–21. doi:10.1016/j.pbb.2006.10.026
47. Leal-Cardoso JH, da Silva-Alves KS, Ferreira-da-Silva FW, dos Santos-Nascimento T, Joca HC, de Macedo FHP, et al. Linalool blocks excitability in peripheral nerves and voltage-dependent Na^+ current in dissociated dorsal root ganglia neurons. Eur J Pharmacol. 2010;645(1–3):86–93. doi:10.1016/j.ejphar.2010.07.014

48. Peana AT, Paolo SD, Chessa ML, Moretti MD, Serra G, Pippia P. (–)-Linalool produces antinociception in two experimental models of pain. Eur J Pharmacol. 2003;460(1):37–41. doi:10.1016/S0014-2999(02)02856-X
49. Peana AT, Marzocco S, Popolo A, Pinto A. (–)-Linalool inhibits in vitro NO formation: probable involvement in the antinociceptive activity of this monoterpene compound. Life Sci. 2006;78(7):719–23. doi:10.1016/j.lfs.2005.05.065
50. Re L, Barocci S, Sonnino S, Mencarelli A, Vivani C, Paolucci G, et al. Linalool modifies the nicotinic receptor–ion channel kinetics at the mouse neuromuscular junction. Pharmacol Res. 2000;42(2):177–81. doi:10.1006/phrs.2000.0671
51. Camargo SB, Simões LO, de Azevedo Medeiros CF, de Melo Jesus A, de Jesus Silva J, Fregoneze JB, et al. Cardiovascular effects induced by linalool after subchronic treatment of spontaneously hypertensive rats. FASEB J. 2016;30:941–7.
52. Dias IJ, Trajano ERIS, Castro RD, Ferreira GLS, Medeiros HCM, Gomes DQC. Antifungal activity of linalool in cases of Candid*a* spp. isolated from individuals with oral candidiasis. Braz J Biol. 2017;78:368–74. doi:10.1590/1519-6984.171054
53. Silva KV, Lima MI, Cardoso GN, Santos AS, Silva GS, Pereira FO. Inhibitory effects of linalool on fungal pathogenicity of clinical isolates of Microsporum canis and Microsporum gypseum. Mycoses. 2017;60(6):387–93. doi:10.1111/myc.12606
54. Sato K, Krist S, Buchbauer G. Antimicrobial effect of vapours of geraniol, (R)-(–)-linalool, terpineol, γ-terpinene and 1,8-cineole on airborne microbes using an airwasher. Flavour Fragr J. 2007;22:435–7. doi:10.1002/ffj.1818
55. Iwasaki K, Zheng YW, Murata S, Ito H, Nakayama K, Kurokawa T, et al. Anticancer effect of linalool via cancer-specific hydroxyl radical generation in human colon cancer. World J Gastroenterol. 2016;22(44):9765–75. doi:10.3748/wjg.v22.i44.9765
56. Sun XB, Wang SM, Li T, Yang YQ. Anticancer activity of linalool terpenoid: apoptosis induction and cell cycle arrest in prostate cancer cells. Trop J Pharm Res. 2015;14(4):619–25. doi:10.4314/tjpr.v14i4.9
57. Müller GC, Junnila A, Butler J, Kravchenko VD, Revay EE, Weiss RW, et al. Efficacy of the botanical repellents geraniol, linalool, and citronella against mosquitoes. J Vector Ecol. 2009;34(1):2–8. doi:10.1111/j.1948-7134.2009.00002.x
58. Kamatou GP, Viljoen AM. Linalool–a review of a biologically active compound of commercial importance. Nat Prod Commun. 2008;3(7):1183–92. doi:10.1177/1934578X0800300727
59. Moon PD, Han NR, Lee JS, Kim HM, Jeong HJ. Effects of linalyl acetate on thymic stromal lymphopoietin production in mast cells. Molecules. 2018;23(7):1711. doi:10.3390/molecules23071711
60. Seo E, Shin YK, Hsieh YS, Lee JM, Seol GH. Linalyl acetate as a potential preventive agent against muscle wasting in rheumatoid arthritis rats chronically exposed to nicotine. J Pharmacol Sci. 2021;147(1):27–32. doi:10.1016/j.jphs.2021.05.003
61. Kwon S, Hsieh YS, Shin YK, Kang P, Seol GH. Linalyl acetate prevents olmesartan-induced intestinal hypermotility mediated by interference of the sympathetic inhibitory pathway in hypertensive rat. Biomed Pharmacother. 2018;102:362–8. doi:10.1016/j.biopha.2018.03.095
62. Koto R, Imamura M, Watanabe C, Obayashi S, Shiraishi M, Sasaki Y, et al. Linalyl acetate as a major ingredient of lavender essential oil relaxes the rabbit vascular smooth muscle through dephosphorylation of myosin light chain. J Cardiovasc Pharmacol. 2006;48(1):850–6. doi:10.1097/01.fjc.0000238589.00365.42
63. Peng HY, Lin CC, Wang HY, Shih Y, Chou ST. The melanogenesis alteration effects of Achillea millefolium L. essential oil and linalyl acetate: involvement of oxidative stress and the JNK and ERK signaling pathways in melanoma cells. PLoS ONE. 2014;9(4):e95186. doi:10.1371/journal.pone.0095186
64. Hsieh YS, Kwon S, Lee HS, Seol GH. Linalyl acetate prevents hypertension-related ischemic injury. PLoS ONE. 2018;13(5): 0198082. doi:10.1371/journal.pone.0198082
65. Shin YK, Hsieh YS, Han AY, Kwon S, Kang P, Seol GH. Sex-specific susceptibility to type 2 diabetes mellitus and preventive effect of linalyl acetate. Life Sci. 2020;260:118432. doi:10.1016/j.lfs.2020.118432
66. Yap PSX, Krishnan T, Yiap BC, Hu CP, Chan KG, Lim SHE. Membrane disruption and anti-quorum sensing effects of synergistic interaction between *Lavandula angustifolia* (lavender oil) in combination with antibiotic against plasmid-conferred multi-drug-resistant *Escherichia coli*. J Appl Microbiol. 2014;116(5):1119–28. doi:10.1111/jam.12444

67. Yap PSX, Lim SHE, Hu CP, Yiap BC. Combination of essential oils and antibiotics reduce antibiotic resistance in plasmid-conferred multidrug resistant bacteria. Phytomedicine. 2013;20(8–9):710–3. doi:10.1016/j.phymed.2013.02.013
68. Adaszyńska-Skwirzyńska MI, Szczerbińska DA, Zych SŁ. Antibacterial activity of lavender essential oil and linalool combined with gentamicin on selected bacterial strains. Medycyna Weterynaryjna. 2019;75(05):6279. doi:10.21521/mw.6279
69. Cassella S, Cassella JP, Smith I. Synergistic antifungal activity of tea tree (Melaleuca alternifolia) and lavender (Lavandula angustifolia) essential oils against dermatophyte infection. Int J Aromather. 2002;12(1):2–15. doi:10.1054/ijar.2001.0127
70. Moussii IM, Nayme K, Timinouni M, Jamaleddine J, Filali H, Hakkou F. Synergistic antibacterial effects of Moroccan Artemisia herba alba, lavandula angustifolia and rosmarinus officinalis essential oils. Synergy. 2020;10:e100057. doi:10.1016/j.synres.2019.100057