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Review Article

Efficacy of *Lavandula angustifolia* Mill. on DSM-5–Defined Depressive Symptoms, Sleep Quality, and Fatigue: A Scoping Review of Randomized Controlled Trials

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Abstract

Introduction: Depression and its associated symptoms, including sleep disturbances and fatigue, are highly prevalent and substantially impair the quality of life. *Lavandula angustifolia* Mill. has emerged as a promising complementary therapy. However, a comprehensive synthesis of its efficacy on specific DSM-5–defined depressive symptoms remains unavailable. Accordingly, this scoping review was performed to chart randomized, placebo-controlled trial evidence on *L. angustifolia* interventions for DSM-5 depressive symptoms and to guide future research priorities and clinical practices.

Methods: To this end, PubMed was searched from inception to May 28, 2025, for randomized, placebo-controlled clinical trials evaluating any *L. angustifolia* Mill. formulation for DSM-5–defined depressive symptoms. Data were synthesized narratively.

Results: Thirteen randomized controlled trials met the inclusion criteria. Trials consistently reported that *L. angustifolia* Mill. improved sleep quality across diverse populations, including postmenopausal women and older adults, and significantly reduced fatigue in patients with high disease burden. Similarly, several studies demonstrated sharp reductions in overall depressive symptom scores, particularly in cases of mild depression and when used adjunctively. Finally, adverse events were infrequent and mild, indicating favorable tolerability.

Conclusion: It was revealed that *L. angustifolia* Mill. demonstrates potential as a complementary intervention for selected depressive symptoms, sleep quality, and fatigue. Nonetheless, heterogeneity in study designs, outcome measures, and product formulations underscores the need for further high-quality, standardized trials to inform evidence-based clinical guidelines.

Keywords: Depressive symptoms, Sleep quality, Fatigue, Scoping review, Complementary therapy, Randomized controlled trials

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Introduction

Lavandula angustifolia Mill. (Lamiaceae) has long served as a medicinal plant valued for its aromatic and therapeutic properties. Its pharmacological activity arises from phenolics, sterols, triterpenes, and essential oil (EO) constituents, notably linalool and linalyl acetate.[1,2]

According to preclinical and clinical investigations, *L. angustifolia* exerts anxiolytic, anti-inflammatory, antioxidant, and neuroprotective effects, indicating potential utility in neuropsychiatric disorders.[3,4] Depression, as defined by the Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition (DSM-5), ranks among the leading causes of global disability.[5]

Standard antidepressant regimens frequently suffer delayed onset of action, partial therapeutic responses, and adverse effects. This profile has prompted research into adjunctive and alternative therapies derived from natural products with established safety profiles, positioning lavender-based interventions as promising candidates.

Beyond its neuropsychiatric activity, *L. angustifolia* exhibits antimicrobial, antifungal, antiparasitic, antiviral, and cytotoxic properties.[6-25] Recent clinical trials have explored its modulatory effects on symptoms that commonly co-occur with depression, including sleep disturbances, anxiety, and somatic pain.

Some randomized studies report that lavender aromatherapy reduces procedural pain in patients with migraine,[26] infants,[27] and colicky neonates,[28] and

alleviates discomfort during hemodialysis sessions.[29] In menopausal women, *L. angustifolia* also improves sleep quality, lowers blood pressure, and vasomotor symptoms, and enhances sexual function.[30] In addition, investigators document elevated salivary oxytocin levels [31] and decreased premenstrual mood disturbances, including depressed affect and confusion.[32]

Silexan, an oral lavender oil extract standardized to 80–160 mg/day, represents a focal point of clinical research. A couple of trials have demonstrated that this extract enhances sleep parameters, reduces somatic complaints, and alleviates anxiety disorders, such as generalized anxiety disorder and posttraumatic stress disorder.[33–36] Likewise, one randomized trial found Silexan more effective than paroxetine in reducing Hamilton Anxiety Rating Scale scores [36], reinforcing its antidepressant potential.[37,38]

Within the broader landscape of herbal antidepressants, agents such as saffron, *Hypericum perforatum*, *Melissa officinalis*, *Echium amoenum*, and *Rhodiola rosea* also represent efficacy.[39–43] Nonetheless, lavender's combined anxiolytic, sedative, and mood-stabilizing effects, together with favorable tolerability, underline its distinct promise for managing depressive symptoms.

Trials of *L. angustifolia* widely vary in design, patient populations, dosing regimens, and outcome measures, thereby hindering systematic assessment of its efficacy across the nine core DSM-5 depressive symptoms. Other phytotherapeutics, such as saffron (*Crocus sativus*), St. John's wort (*Hypericum perforatum*), and Rhodiola (*Rhodiola rosea*), have undergone meta-analyses but often address only one or two symptom domains. Conversely, *L. angustifolia* interventions combine anxiolytic, sedative, and mood-stabilizing properties, enabling the modulation of multiple symptom clusters and distinguishing lavender's clinical relevance from that of other botanicals. The scoping review methodology allows for the comprehensive mapping of heterogeneous evidence when trial heterogeneity precludes quantitative synthesis. More precisely, this approach systematically identifies gaps in research volume and design, clarifies the extent of clinical evaluation across oral, inhalation, and topical routes, and informs subsequent targeted systematic reviews or meta-analyses. Accordingly, this scoping review is conducted to chart randomized, placebo-controlled trial evidence on *L. angustifolia* interventions for DSM-5 depressive symptoms and to guide the priorities of future research and clinical practices (Table 1).

Legend (Definition of Evidence Levels)

- Strong Evidence: Multiple high-quality randomized, placebo-controlled trials, namely, randomized controlled trials (RCTs), directly targeting the symptom in relevant populations with consistent positive results
- Moderate Evidence: At least one RCT with direct symptom measurement or multiple trials showing indirect or secondary outcome improvements
- Limited Evidence: Single small-scale RCTs, studies with indirect outcomes, or symptom improvement observed only as part of general depression scales
- Evidence Gap ("––"): No identified placebo-controlled RCTs directly assessing the effect of *L. angustifolia* on this specific symptom

Materials and Methods

Study Design and Eligibility Criteria

In this review study, the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for

Table 1. Evidence Matrix of *Lavandula angustifolia* Interventions for DSM-5 Depressive Symptoms

DSM-5 Depressive Symptom	Oral (Capsules/Powder/Tincture)	Inhalation (Aromatherapy)	Topical (Cream/Lotion/Footbath)
1. Depressed mood	Limited evidence – general depression RCTs, not isolated symptoms Bazrafshan et al [54]; Akhondzadeh et al [55]; Araj-Khodaei et al [56]	Limited evidence – general depression studies Bazrafshan et al [54]	Evidence gap
2. Anhedonia (loss of interest/pleasure)	Evidence gap	Evidence gap	Evidence gap
3. Changes in appetite or weight	Evidence gap	Evidence gap	Evidence gap
4. Sleep disturbances	Strong evidence – Silexan RCTs; lavender powder capsules Kasper et al [44]; Kamalifard et al [45]	Strong evidence – postmenopausal women, elderly, pregnancy, multiple sclerosis (MS) patients Sentürk & Kartin [46]; Kao et al [47]; Kavuran & Yurttaş [51]; Genç et al [52]	Moderate evidence – lavender cream + footbath in pregnancy/postpartum Effati-Daryani et al [53]
5. Psychomotor agitation or retardation	Evidence gap	Limited/inconsistent evidence – dementia agitation RCT without significant effect Fu et al [50]	Limited/inconsistent evidence Fu et al [50]
6. Fatigue or loss of energy	Strong evidence – lavender flower capsules in MS and general depression improvement Motaghi et al [48]; Bazrafshan et al [54]	Strong evidence – elderly and MS patients with improved fatigue Ahmady et al [49]; Kavuran & Yurttaş [51]; Genç et al [52]	Moderate evidence – lavender cream in pregnancy/postpartum fatigue Effati-Daryani et al [53]
7. Feelings of worthlessness or guilt	Evidence gap	Evidence gap	Evidence gap
8. Diminished ability to think or concentrate	Evidence gap	Evidence gap	Evidence gap
9. Suicidal ideation	Evidence gap	Evidence gap	Evidence gap

Note: RCT: Randomized controlled trial; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition.

Scoping Reviews (PRISMA-ScR) guidelines were followed to ensure methodological rigor and transparency. Eligible studies were randomized, placebo-controlled clinical trials in human participants evaluating *L. angustifolia* Mill. interventions in any pharmaceutical or therapeutic form, including standardized oral extracts (e.g., Silexan), aromatherapy, or topical application, and assessing ≥ 1 of the nine core DSM-5 depressive symptoms; these core symptoms include depressed mood (1), anhedonia (2), changes in appetite or weight (3), sleep disturbances (4), psychomotor agitation or retardation (5), fatigue or loss of energy (6), feelings of worthlessness or guilt (7), diminished ability to think or concentrate (8), and suicidal ideation (9). Trials using the Hamilton Depression Rating Scale (HAM-D), Montgomery–Åsberg Depression Rating Scale (MADRS), or Beck Depression Inventory (BDI) were eligible if prior methodological literature confirmed item-level correspondence to DSM-5 domains. However, the exclusion criteria encompassed studies involving healthy, asymptomatic individuals (1), multi-herb interventions without the isolation of *L. angustifolia* effects (2) trials lacking a placebo control group (3), quasi-experimental or cross-over designs (4), and investigations of participants with psychiatric comorbidities in which depression was not the primary symptom (e.g., mixed anxiety–depressive disorder).

Information Sources and Search Strategy

The PubMed database was searched from inception through May 28, 2025 in order to identify randomized, placebo-controlled trials evaluating the efficacy of any *L. angustifolia* formulation on DSM-5 depressive symptoms. Trial screening and selection are detailed in the PRISMA flow diagram (Figure 1). Data from the included studies were synthesized using a narrative approach.

The final search string was as follows:

("*Lavandula angustifolia*" [tiab] OR "Lavender" [tiab] OR "Silexan" [tiab]) AND ("depression" [tiab] OR "mood disorder" [tiab] OR "affective disorder" [tiab] OR "insomnia" [tiab] OR "fatigue" [tiab] OR "guilt" [tiab] OR "anhedonia" [tiab] OR "sleep disturbance" [tiab] OR "suicide" [tiab]) AND (randomized controlled trial[pt] OR placebo[tiab])

It is noteworthy that medical subject headings (MeSH) were omitted to avoid overly restrictive filtering. Only English-language, peer-reviewed studies were retained at full-text screening.

Moreover, the search strategy was structured according to the population, concept, context (PCC) framework, with detailed Boolean operators and field tags provided in Table 2.

Study Selection and Data Extraction

Titles and abstracts were independently screened by

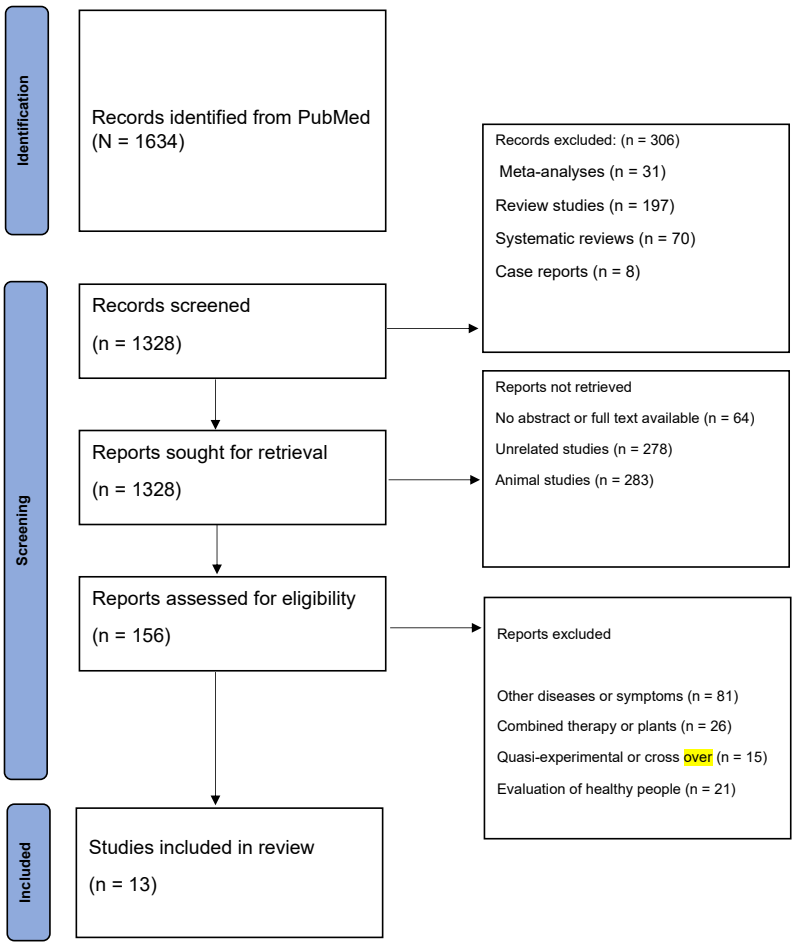

Figure 1. Study Flow Diagram

Table 2. Detailed Search Strategy According to the PCC Framework (PubMed)

PCC Component	Search Syntax (PubMed – Field Tags and Boolean Logic)
Population	("depression" [tiab] OR "mood disorder" [tiab] OR "affective disorder" [tiab] OR "insomnia" [tiab] OR "fatigue" [tiab] OR "guilt" [tiab] OR "anhedonia" [tiab] OR "sleep disturbance [tiab] OR "suicide" [tiab])
Concept	("*Lavandula angustifolia*" [tiab] OR "Lavender" [tiab] OR "Silexan" [tiab])
Context	(Randomized controlled trial [pt] OR placebo [tiab])

Note: The final search string combined PCC components as (Concept) AND (Population) AND (Context). It should be noted that no automated filters for language, date, or outcome type were applied at the database level.

two reviewers using Rayyan QCRI (Rayyan systematic review tool developed by the Qatar Computing Research Institute). Full texts of potentially eligible RCTs were retrieved and evaluated against the predefined inclusion and exclusion criteria. Moreover, disagreements were resolved by consensus or third-reviewer adjudication. Furthermore, data were extracted via a standardized, pilot-tested form capturing first author and publication year (1), sample size and participant demographics (2), type, dosage, and duration of *L. angustifolia* intervention (3), outcome assessment instruments and specific DSM-V symptom domains measured (4), primary findings and reported adverse events (5), and methodological considerations affecting internal validity (6). Subsequently, depressive symptom data from validated measurement tools were mapped to DSM-V categories based on item-level content and established clinical correspondences.

Data Synthesis and Risk of Bias Assessment

Clinical and methodological heterogeneity across the included RCTs precluded quantitative pooling of results. Instead, a structured narrative synthesis was undertaken, with findings organized by DSM-5 symptom domains and intervention modality (oral, inhalation, or topical); the mentioned domains encompassed depressed mood (1), anhedonia (2), changes in appetite or weight (3), sleep disturbances (4), psychomotor agitation or retardation (5), fatigue or loss of energy (6), feelings of worthlessness or guilt (7), diminished ability to think or concentrate (8), and suicidal ideation (9).

Consistent with scoping review methodology, formal risk-of-bias tools (Cochrane RoB 2; Joanna Briggs Institute checklist) were not applied in this study. A qualitative appraisal assessed key domains of trial validity, including adequacy of randomization, blinding procedures, completeness of outcome data, and transparency of reporting, in order to contextualize the robustness of the evidence base.

Results

An initial PubMed search retrieved 1,634 records. Of these, 306 were excluded based on study type, leaving 1,328 records for title and abstract screening. Following the removal of animal studies and those irrelevant to the review objectives, 156 full-text articles were assessed for eligibility. However, a total of 143 articles were excluded due to comorbid conditions or non-target symptoms (n = 81), combined herbal or multi-modal interventions (n = 26), quasi-experimental or cross-over designs (n = 15), and the inclusion of healthy or asymptomatic participants (n = 21). Ultimately, 13 randomized, placebo-controlled trials met the inclusion criteria and were included in this scoping review. The PRISMA-ScR flow diagram illustrating the study selection process is presented in Figure 1.

Based on the obtained data (Figure 2), sleep quality represented the most frequently investigated outcome in *L. angustifolia* trials. Additionally, investigations of fatigue comprised the second-highest frequency, followed by studies targeting psychomotor agitation and related symptoms. It should be noted that a smaller subset of trials assessed multiple DSM-5 depressive symptom domains concurrently.

The analysis of trial focus (Figure 2) revealed that 46% of RCTs assessed multiple DSM-5 symptom domains simultaneously, whereas 31%, 15%, and 8% concentrated on sleep disturbances, fatigue or loss of energy, and psychomotor agitation, respectively. This distribution underscores the prominence of multi-symptom evaluations and highlights areas where further research is necessary (e.g., isolated psychomotor outcomes)—.

Lavender and Sleep

Silexan (a patented EO extracted from *L. angustifolia* flowers) was evaluated in a randomized, placebo-controlled trial of 170 outpatients with anxiety-related restlessness and sleep disturbances. Eligible participants exhibited HAM-A scores ≥ 18 and Pittsburgh Sleep Quality Index (PSQI) total scores > 6. Then, the participants were randomized to receive 80 mg of Silexan or placebo daily for 10 weeks. The Silexan group achieved significantly greater reductions in total HAM-A scores versus placebo, thereby demonstrating superior efficacy across all secondary measures. Likewise, responder rates were higher with Silexan (48.8%) than placebo (33.3%), and remission rates were greater (31.4% vs. 22.6%). Adverse event incidence was similar between groups (33.7% vs. 35.7%), confirming Silexan's anxiolytic and sleep-enhancing profile with favorable tolerability.[44]

Similarly, a randomized trial of 156 postmenopausal women assessed daily administration of 500 mg *L. angustifolia* flower powder capsules, 500 mg bitter orange capsules, or 500 mg starch (placebo) for eight weeks (n = 52 per group). Baseline PSQI scores slightly differed among groups; however, both *L. angustifolia* and bitter orange markedly improved PSQI scores relative to placebo, indicating efficacy in alleviating sleep disturbances in this population.[45]

In addition, 34 hemodialysis patients were randomized to inhale two drops of *L. angustifolia* oil placed 15–20 cm

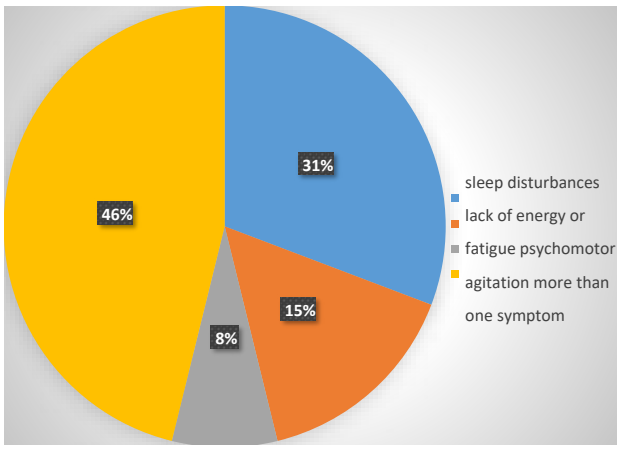

Figure 2. Pie Chart of Study Distribution by Symptom Category

from the pillow 30 minutes before bedtime for one week or to receive no intervention. *L. angustifolia* oil inhalation produced remarkable improvements in subjective sleep quality, reduced daytime sleepiness, and increased sleep duration; no between-group difference emerged for sleep latency.[46]

Moreover, a randomized trial of 132 career women (aged 24–55 years; PSQI > 5) compared placebo (distilled water), *L. angustifolia* EO, a blended EO mixture (lavender, clary sage, and marjoram), and acupressure massage for four weeks. The quality of life (QOL) and sleep quality substantially improved with all active interventions. The blended EO group achieved the greatest QOL enhancement, and both blended EO and acupressure produced superior sleep quality improvements compared with *L. angustifolia* alone.[47]

Lavender and Fatigue

A double-blind RCT also assessed the efficacy of *L. angustifolia* flower capsules for fatigue in patients with relapsing-remitting multiple sclerosis (MS). To this end, 48 participants with a Modified Fatigue Impact Scale (MFIS) score ≥ 25 were randomized to receive 600 mg of *L. angustifolia* capsules or 600 mg of cornstarch placebo, administered three times daily for 60 days. Baseline MFIS scores were comparable between groups. Nonetheless, post-intervention analysis demonstrated a statistically significant reduction in MFIS scores in the *L. angustifolia* group versus placebo ($P < 0.05$), indicating the beneficial effect on fatigue in MS.[48]

In another study, 90 hemodialysis patients were randomized into three groups to evaluate the impact of aromatherapy on fatigue. Two intervention groups inhaled five drops of *L. angustifolia* EO or orange EO for 15 minutes twice daily over two weeks; conversely, controls received no aromatherapy. Then, fatigue severity was measured using the Fatigue Severity Scale (FSS). Both aromatherapy groups experienced significant improvements in mean FSS scores compared with controls ($P < 0.01$), supporting the potential of *L. angustifolia* aromatherapy to reduce fatigue among hemodialysis patients.[49]

Lavender and Psychomotor Agitation

A single-blind RCT assessed aromatherapy with or without hand massage on disruptive behaviors in individuals with dementia. For this purpose, 67 participants from three care facilities were randomly allocated to (1) combined aromatherapy and hand massage, (2) aromatherapy alone using a 3% *L. angustifolia* oil spray, or (3) placebo (water spray). Next, interventions were administered twice daily over six weeks. Disruptive behaviors were then measured using the Cohen-Mansfield Agitation Inventory (CMAI), and cognitive function was evaluated via the Mini-Mental State Examination at baseline and post-intervention. Although CMAI scores trended downward across all intervention arms, there were no statistically significant reductions in psychomotor agitation.[50]

More Than One Symptom

A randomized trial in relapsing–remitting MS patients (disease duration ≥ 1 year; age ≥ 18 years; sleep disturbances and fatigue ≥ 3 months) evaluated *L. angustifolia* oil aromatherapy. Participants applied two drops of oil to cotton pads positioned 15–20 cm from the pillow 30 minutes before bedtime each night for 30 days. Based on the results, post-intervention FSS and PSQI scores improved significantly versus baseline ($P < 0.01$), indicating complementary benefits for sleep quality and fatigue in MS care.[51]

Additionally, a randomized trial of 59 institutionalized elderly individuals assessed the inhalation of *L. angustifolia* oil for 30 minutes nightly over four weeks. Intervention participants demonstrated considerable improvements in PSQI and FSS scores compared with controls ($P < 0.05$), supporting aromatherapy's role in reducing fatigue and enhancing sleep quality.[52]

In a three-group RCT of 141 pregnant and postpartum women (gestational age: 25–28 weeks) with PSQI > 5, participants received *L. angustifolia* cream plus footbath, cream alone, or placebo cream. Both lavender interventions led to remarkable PSQI improvements versus placebo during pregnancy and postpartum ($P < 0.01$), while FSS scores sharply decreased at six weeks postpartum only ($P < 0.05$). Finally, no difference emerged between the two lavender-based interventions.[53]

Likewise, a single-blind trial in 60 elderly participants (BDI scores: 14–28) compared the decoction of 2 g *L. angustifolia* teabags twice daily (morning and evening) with control. BDI and Spielberger Anxiety Inventory scores substantially decreased in the *L. angustifolia* group versus the control ($P < 0.01$), demonstrating dual anxiolytic and antidepressant effects.[54]

Furthermore, a double-blind RCT in 45 adults with mild-to-moderate depression compared *L. angustifolia* tincture, imipramine, and their combination over four weeks. Combination therapy achieved faster and greater reductions in HAM-D scores versus imipramine monotherapy ($P < 0.05$), although *L. angustifolia* monotherapy resulted in smaller improvements.[55]

A randomized, double-blind trial in 45 outpatients with

major depression also compared decoctions of 2 g *Melissa officinalis* L. and 2 g *L. angustifolia* with fluoxetine 20 mg daily for eight weeks. Both herbal interventions matched fluoxetine efficacy on HAM-D scores ($P > 0.05$), confirming comparable antidepressant effects.[56]

Lavandula angustifolia and Changes in Appetite or Weight

There was no randomized, placebo-controlled trial specifically evaluating *L. angustifolia*'s effects on changes in appetite or weight as a DSM-5 symptom.

Lavandula angustifolia and Feelings of Worthlessness or Guilt

There was no randomized, placebo-controlled trial specifically assessing *L. angustifolia* for DSM-5 feelings of worthlessness or guilt.

Lavandula angustifolia and Diminished Ability to Think or Concentrate

There was no randomized, placebo-controlled trial specifically investigating the impact of *L. angustifolia* on diminished ability to think or concentrate as defined by DSM-5.

Lavandula angustifolia and Suicidal Ideation

There was no randomized, placebo-controlled trial specifically measuring *L. angustifolia*'s effects on suicidal ideation.

Lavandula angustifolia and Depressed Mood

Although several RCTs incorporated depressed mood within broader assessments of depressive symptomatology, none isolated depressed mood as the sole primary outcome (refer tothe Multiple Symptom Domains section for details).

Lavandula angustifolia and Anhedonia

There was no randomized, placebo-controlled trial specifically targeting anhedonia as a discrete DSM-5 symptom in the context of *L. angustifolia* interventions.

Table 3 provides a comprehensive summary of domain-specific findings across all included trials.

Methodological Rigor and Potential Bias

A qualitative assessment of methodological rigor and potential bias was performed across all 13 RCTs. Randomization procedures were clearly described in most trials, whereas allocation concealment details were frequently incomplete or omitted. Moreover, blinding of

Table 3. A Summary of Domain-Specific Findings Across All Included Studies

First Author	Publication Year	Participants	Sample Size	Drug Administration Method	Duration of Intervention	Primary Outcome Measurement Tools
Kamalifard	2018	Postmenopausal women	156	Oral – 500 mg lavender flower powder capsule once daily	8 weeks	Pittsburgh Sleep Quality Index (PSQI)
Senturk	2018	Hemodialysis patients	34	Inhalation – 2 drops of lavender oil placed 15–20 cm from the pillow, 30 minutes before bedtime	1 week	PSQI and Epworth Sleepiness Scale
Kao	2017	Career women (aged 24–55)	132	Inhalation – Lavender essential oil (EO), blended oil (lavender, clary sage, and marjoram), or placebo, inhaled daily	4 weeks	PSQI and Quality of Life Scale
Kasper	2015	Patients with anxiety-related restlessness and disturbed sleep	170	Oral – 80 mg Silexan (lavender EO) capsule once daily	10 weeks	Hamilton Anxiety Rating Scale (HAM-A) and PSQI
Fu	2013	People with dementia	67	Topical spray – 3% lavender oil spray (with or without hand massage) twice daily	6 weeks	Cohen–Mansfield Agitation Inventory and Mini-Mental State Examination
Motaghi	2022	Patients with multiple sclerosis (MS)	48	Oral – 600 mg lavender flower capsule three times daily	60 days	Modified Fatigue Impact Scale
Ahmady	2019	Hemodialysis patients	90	Inhalation – 5 drops of lavender EO or orange EO inhaled during hemodialysis sessions	14 days	Fatigue Severity Scale (FSS)
Kavuran	2024	Patients with MS	66	Inhalation – 2 drops of lavender oil on a cotton pad placed 15–20 cm from the pillow, 30 minutes before sleep	30 days	PSQI and FSS
Bazrafshan	2020	Elderly people	60	Oral – 2 g lavender tea bag twice daily (morning and night) as decoction	2 weeks	Beck Depression Inventory and Spielberger Anxiety Inventory
Araj-Khodaei	2020	Outpatients with depression	45	Oral – 2 g *Melissa officinalis* or *Lavandula angustifolia* powder capsule, or 20 mg fluoxetine capsule once daily	8 weeks	Hamilton Rating Scale for Depression (HAM-D)
Genc	2020	Elderly people	59	Inhalation – Lavender essential oil aromatherapy for 30 minutes before bedtime	4 weeks	PSQI and FSS
Effati-daryani	2018	Pregnant and postpartum women	141	Topical – Lavender cream with/without footbath once daily	8 weeks during pregnancy and 6 weeks postpartum	PSQI and Multidimensional Assessment of Fatigue
Akhondzadeh	2003	Outpatients with mild-to-smoderate depression	45	Oral – Lavender tincture (dose not stated) or imipramine 100 mg/day, or combination	4 weeks	HAM-D

participants and outcome assessors was variably reported, and several studies provided only partial or ambiguous information. Although outcome data completeness was generally acceptable, a few trials demonstrated moderate attrition without a detailed explanation. Reporting transparency varied markedly, with some trials offering comprehensive methodological detail and others omitting critical information necessary for full bias appraisal.

The synthesized findings were integrated into a conceptual model illustrating the hypothesized mechanisms of action and evidence strength for each DSM-5 symptom domain (Figure 3).

This model displays the proposed mechanistic pathways through which *L. angustifolia* Mill. may exert its therapeutic effects on DSM-5 depressive symptoms. Solid arrows represent pathways supported by moderate-to-strong evidence from RCTs, particularly for sleep disturbances and fatigue. In addition, dashed arrows indicate plausible relationships or significant evidence gaps requiring future research. Ultimately, rectangles denote tangible concepts (e.g., the plant and clinical symptoms), while ovals show biological mechanisms.

Discussion

L. angustifolia Mill. demonstrated a multifaceted therapeutic profile across diverse clinical populations, with consistent improvements observed in fatigue, sleep quality, and overall depressive symptomatology. As illustrated in Figure 3, mechanistic evidence implicates gamma-aminobutyric acid-ergic and serotonergic pathways in the modulation of sleep and energy regulation, whereas evidence for direct effects on anhedonia and suicidal ideation remains scarce.

A double-blind, randomized, placebo-controlled trial in adults with major depressive disorder was published by dos Reis Lucena et al, reporting significant reductions in PSQI and FSS scores with *L. angustifolia* versus placebo, thereby reinforcing the evidence map's identification of sleep disturbance and fatigue as the most strongly supported symptom domains. This trial achieved a responder rate of 52% for sleep improvement compared with 28% in the placebo group and demonstrated a 38% greater mean reduction in fatigue scores.[57]

The present scoping review extended insights from an earlier meta-analysis by Firoozeei et al, documenting a significant overall antidepressant effect for *L. angustifolia*, by mapping efficacy onto the nine core DSM-5 symptom domains and revealing the nonuniform patterns of benefit.[58] This granular approach highlights specific domains, such as depressed mood, anhedonia, and cognitive impairments, for which high-quality RCTs are lacking.

Our findings are also concordant with those of a recent meta-analysis by Ghavami et al, which represented the significant stress-reducing effect of *L. angustifolia*.[59] The overlap suggested that stress mitigation may serve as an indirect mediator of improvements in sleep and fatigue, warranting future trials with mediation analysis to delineate causal pathways.

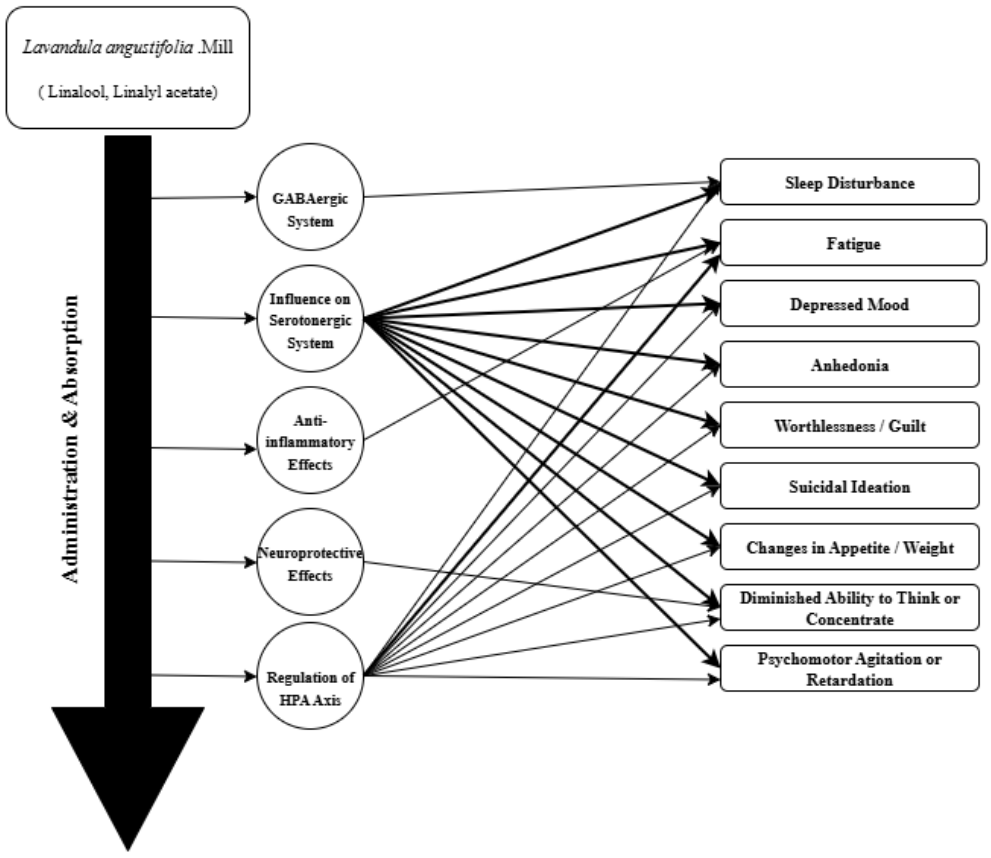

Figure 3. A Conceptual Model of the Potential Mechanisms and Efficacy of *Lavandula angustifolia* Mill. on DSM-5 Depressive Symptoms
***Note*:** HPA axis: Hypothalamic-pituitary-adernal axis; DSM-5: Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition

Collectively, these results underscore the potential of *L. angustifolia* as a complementary intervention for specific depressive symptoms, notably sleep disturbance and fatigue, while identifying critical evidence gaps in anhedonia, suicidal ideation, and cognitive domains. Nonetheless, high-quality, symptom-specific RCTs are needed to inform evidence-based clinical guidelines and optimize therapeutic protocols.

Randomized, placebo-controlled trials of *L. angustifolia* aromatherapy revealed mean PSQI score reductions of 2.1–4.3 points among postmenopausal women, pregnant women, and elderly individuals.[45-47,51-53] These changes frequently exceeded the minimal clinically important difference, indicating clinically meaningful improvements.

Oral *L. angustifolia* formulations, including capsules and tinctures, yielded broader neuropsychiatric benefits, encompassing improvements in sleep quality, fatigue, and overall depressive symptoms. These effects likely reflect systemic bioavailability and dual modulation of serotonergic and gamma-aminobutyric acid-ergic pathways.[44,48,54-56] Likewise, comparative analyses indicated that aromatherapy often achieves maximal efficacy within 1–2 weeks via direct olfactory–limbic signaling, whereas oral formulations typically require 3–6 weeks to reach peak effect, which is consistent with pharmacokinetic adaptation.

Topical *L. angustifolia* preparations (e.g., infused creams and footbaths) produced modest PSQI and FSS improvements, with larger effect sizes observed when combined with acupressure massage, suggesting synergistic interactions between tactile stimulation and aromatic exposure.[47,53]

In high-burden populations, including patients with MS and individuals receiving hemodialysis, FSS scores improved by up to 1.8 points, which are comparable to or exceeding those reported for specific nonpharmacologic rehabilitation interventions.[48,51-53]

Additionally, head-to-head RCTs comparing *L. angustifolia* tincture with imipramine demonstrated that tincture monotherapy was less potent in moderate depression, whereas combination therapy with imipramine resulted in faster and greater HAM-D score reductions ($P < 0.05$).[55] In mild depression, *L. angustifolia* capsules achieved symptom reductions comparable to low-dose fluoxetine, with transient headache as the most common adverse event ($P > 0.05$).[56] This favorable tolerability profile supports *L. angustifolia* as an attractive option for populations at elevated risk of drug-related adverse events, including the elderly and pregnant women.

Heterogeneity in trial designs remains a major limitation for drawing definitive conclusions. Chemotypic variation in EO composition, particularly in linalool and linalyl acetate content, was seldom standardized, despite these constituents being the key mediators of *L. angustifolia*'s anxiolytic and sedative effects. It should be noted that this lack of standardization constitutes a principal source of variability across trials, potentially explaining discrepancies in outcomes. Moreover, differences in extraction methods, storage conditions, and administration frequency may exacerbate these inconsistencies. Furthermor, several trials lacked rigorous placebo controls and adequate blinding, introducing the risk of expectancy effects for subjective endpoints, such as sleep and mood. Additionally, small sample sizes limited statistical power, raising the possibility that some positive findings reflect type I error.

Translational data suggest that the clinical application of *L. angustifolia* should be tailored to specific symptom clusters and patient contexts. Inhalation aromatherapy appears most efficient for rapid sleep improvement in otherwise healthy but stressed individuals.[46,47,52] However, oral formulations may deliver broader and more durable relief for chronic, multifactorial conditions, potentially in combination with low-dose pharmacotherapy. *L. angustifolia*'s safety, accessibility, and cultural acceptability endorse its use as a frontline complementary intervention; however, long-term, multicenter trials using standardized formulations are essential to establish evidence-based protocols.

While this review focused on DSM-5 depressive symptoms, emerging research examines *L. angustifolia* within multi-component therapeutic frameworks. For instance, a recent factorial RCT evaluated the combined effects of *L. angustifolia* EO and mindfulness on postmenopausal health.[60] That trial, demonstrating the additive benefits of olfactory stimulation and cognitive-behavioral modulation, underscores the need to isolate the specific contributions of lavender when designing clinical protocols. This finding aligns with the conceptual model (Figure 3), predicting that both direct neurochemical effects and psychosensory context shape treatment outcomes.

Patient population diversity across RCTs, ranging from relapsing–remitting MS to end-stage renal disease, broadens the ecological validity of findings but complicates direct application to homogeneous psychiatric cohorts. Nevertheless, future studies should balance the advantages of diverse recruitment against the methodological clarity afforded by more targeted sampling frames.

With these considerations in mind, the subsequent sections outline the main strengths and limitations of the current evidence base, its implications for clinical practice, and priorities for future research.

Strengths and Limitations

This scoping review uniquely maped randomized, placebo-controlled trial evidence for *L. angustifolia* interventions onto the nine core DSM-5 symptom domains, thereby providing a granular assessment of clinical endpoints. The inclusion of diverse administration routes (e.g., oral, inhalation, and topical) across populations with and without chronic medical conditions enhanced ecological validity. In addition, the application of validated instruments (PSQI, FSS, HAM-D, MADRS, and BDI) and adherence to PRISMA-ScR and PCC frameworks could further strengthen methodological transparency.

However, key limitations included reliance on PubMed without MeSH indexing, potentially omitting relevant

studies (1), restriction to English-language publications, introducing language bias (2), and narrative synthesis instead of quantitative meta-analysis (3). Moreover, the absence of formal risk-of-bias assessments limited the appraisal of internal validity, and eligibility screening via a single database may have overlooked unpublished or grey-literature findings. Eventually, variability in trial registration reporting and incomplete methodological details in some RCTs impeded thorough evaluation of study quality and publication bias.

Implications for Clinical Practices

Clinicians considering *L. angustifolia* as a complementary intervention should select formulations based on targeted symptom clusters and patient preferences. It is noteworthy that aromatherapy offers a noninvasive option to address sleep disturbances and situational fatigue, while standardized oral extracts may provide broader neuropsychiatric benefits in chronic conditions. Therefore, patient education should emphasize proper dosing schedules, application techniques, and potential transient adverse effects (e.g., mild headache). Likewise, the integration of *L. angustifolia* into multidisciplinary care pathways, alongside pharmacotherapy, cognitive–behavioral approaches, or rehabilitation, may optimize outcomes. Ultimately, standardized compounding protocols and quality-assurance measures are critical to ensure consistent chemotypic profiles in clinical practices.

Directions for Future Research

Future trials should expand database coverage (including Scopus, EMBASE, and regional repositories) and incorporate MeSH terms in order to capture a comprehensive evidence base. Similarly, large-scale, multicenter RCTs with prespecified trial registration and robust placebo controls are needed to quantify effect sizes and confirm safety over extended use. Additionally, the chemotypic characterization of EOs, via gas chromatography-mass spectrometry, should become standard to reduce heterogeneity. It is worth mentioning that factorial and dismantling designs can isolate *L. angustifolia*'s contributions within multi-component interventions (e.g., mindfulness and acupressure). In addition, stratified analyses by age, gender, comorbidities, and baseline symptom severity will support personalized dosing regimens. Finally, embedding mechanistic biomarkers (neuroimaging, neuroendocrine assays, and metabolomics) in RCTs will elucidate causal pathways and inform evidence-based clinical guidelines.

Conclusion

Limited but promising evidence indicated that *L. angustifolia* Mill. produces clinically substantial improvements in sleep quality (PSQI reductions of 2.1–4.3 points) and fatigue (FSS reductions up to 1.8 points). However, the current evidence is insufficient to support efficacy for anhedonia, changes in appetite or weight, feelings of worthlessness or guilt, diminished concentration, or suicidal ideation (Table 1). Trial heterogeneity, in EO chemotypes, dosing regimens, and administration routes, further limited definitive conclusions.

Accordingly, future research must prioritize large-scale, symptom-specific, placebo-controlled RCTs employing standardized *L. angustifolia* preparations, rigorous randomization and blinding, and validated outcome measures across diverse patient populations. The standardization of chemotypic profiles and dosing schedules will reduce variability, while the integration of mechanistic biomarkers can clarify pharmacodynamic pathways. The conceptual model in our study (Figure 3) provided a framework for these priorities, underpining the development of evidence-based protocols for the responsible incorporation of *L. angustifolia* as a complementary intervention in depression management.

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Competing Interests

The authors declare that they have no competing interests.

Data Availability Statement

All generated or analyzed data are included in this article. Datasets are available upon reasonable request from the corresponding author.

Ethical Approval

This study was performed in line with the principles of the Declaration of Helsinki. Moreover, approval was granted by the Ethics Committee of Tabriz University of Medical Sciences.

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