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REVIEW

Evaluating the Therapeutic Effects of *Thymus vulgaris* on Primary Dysmenorrhea Adolescent and Young Girls (Qualitative Evidence Synthesis)

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Introduction: Primary dysmenorrhea is a common gynecological condition among Adolescent and Young girls, characterized by painful uterine cramps in the absence of identifiable pelvic pathology. This condition is associated with reduced quality of life, impaired academic performance, and limitations in daily activities. Concerns regarding the long-term use and adverse effects of nonsteroidal anti-inflammatory drugs (NSAIDs) have increased interest in complementary and herbal interventions.

Purpose: This systematic review aimed to synthesize clinical and mechanistic evidence on the efficacy and safety of *Thymus vulgaris* for primary dysmenorrhea management through synthesis of quantitative outcomes (QES).

Methods: This systematic review was conducted following PRISMA 2020 guidelines. Given the heterogeneity of interventions and outcome measures across included randomized controlled trials, statistical meta-analysis was not feasible; therefore, a narrative synthesis approach was employed to integrate quantitative findings. Confidence in evidence was assessed using the GRADE-CERQual framework for intervention reviews. A comprehensive literature search was performed in PubMed/Medline, Scopus, Web of Science, Embase, the Cochrane Library, and Google Scholar from inception to December 2025. Clinical, observational, and experimental studies examining thyme or its bioactive constituents in relation to primary dysmenorrhea were included. Methodological quality was assessed using the Critical Appraisal Skills Programme (CASP) checklist. Data were analyzed using thematic synthesis, and confidence in the review findings was evaluated using the GRADE framework.

Results: A synthesis of 6 studies found that participants consistently described thyme as a familiar cultural intervention that provided tangible menstrual pain relief, with empirical reports describing reductions in pain intensity and duration comparable to conventional NSAIDs. These narratives were consistent with mechanistic evidence suggesting dual pathways carvacrol-mediated suppression of prostaglandin cascades and attenuation of the oxidative microenvironment involved in pain sensitivity. This synthesis interpreted quantitative results through a qualitative lens to elucidate perceived acceptability and underlying factors. All clinical evidence was obtained exclusively from women of reproductive age in Iranian settings (mean age 21–24 years), and no trials recruited WHO-defined adolescents (10–19 years). Short-term safety profiles appeared favorable over the trial duration (≤3 menstrual cycles), although long-term effects on pubertal endocrine maturation remain unknown. Geographic homogeneity and cultural familiarity with thyme in Iranian contexts further limits generalizability to Adolescent and Young girls around the world.

Conclusion: This qualitative evidence synthesis suggests that Thymus may represent a safe and acceptable complementary option for managing primary dysmenorrhea in young girls. Further high-quality qualitative and mixed-methods research is warranted to strengthen confidence in these findings.

Plain Language Summary:

Why this study was conducted:

Many Young girls experience painful menstrual cramps, and commonly used painkillers may cause side effects with long-term use. Therefore, safer natural alternatives are being explored.

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What the researchers did and found:
This study reviewed existing clinical and experimental research on thyme as a treatment for menstrual pain. The findings showed that thyme essential oil, particularly at a 2% concentration, reduced pain levels similarly to ibuprofen and more effectively than placebo.
Key findings:
Thyme may relieve menstrual pain by reducing inflammation, lowering prostaglandin production, and decreasing oxidative stress, with no serious safety concerns reported. Further high-quality studies are needed to confirm these benefits.

Keywords: thyme, dysmenorrhea, adolescent, young girls, pathophysiology, *Thymus vulgaris*

Introduction

Burden and Prevalence of Dysmenorrhea

Dysmenorrhea the occurrence of painful uterine cramps coinciding with menstruation is recognized as the most prevalent gynecological disorder among women of reproductive age, affecting individuals regardless of age or socioeconomic status.[1] It is not merely a physical discomfort but a deeply personal, socially embedded experience that shapes daily life, educational attainment, economic productivity, and mental well-being. Globally, prevalence estimates range widely from 45% to 95%, with 2–29% of women reporting severe pain that significantly impairs functioning.[2] Despite its ubiquity, dysmenorrhea remains persistently underdiagnosed and undertreated in clinical settings.[1,2]

Primary dysmenorrhea, which begins around menarche and lacks an identifiable organic pathology, is especially common among Young girls. Its cyclical on the first day of menstruation and often lasting several days disrupts school attendance, social participation, and emotional stability during critical developmental years. Approximately 10–15% of affected adolescents report limitations in daily activities, and crucially, many find standard analgesics ineffective.[3] The societal cost is staggering: an estimated 600 million hours of productive work are lost annually due to menstrual pain,[4] much of it borne by young women still in education.

Limitations of Conventional Therapy and Rise of Herbal Alternatives

While pharmacological interventions such as NSAIDs and oral contraceptives remain first-line treatments for primary dysmenorrhea, their efficacy is inconsistent, and side effectsincluding gastrointestinal distress, hormonal disruption, and contraindications in Young slimit long-term use.[5] Moreover, many girls avoid or discontinue these medications due to fear of side effects, lack of access, or cultural resistance to synthetic drugs. Complementary and alternative medicine (CAM), particularly herbal remedies, have gained traction globally, with women constituting approximately 75% of healthcare decision-makers and frequently turning to medicinal plants for menstrual disorders.[6–8]

However, there is a fundamental disconnect between traditional use and scientific validity. Thyme (Thymus schimperi and Thymus serrulatus) is widely consumed as a "tocin tea" for conditions such as abdominal pain, diarrhea, cough, asthma, and high blood pressure.[8–11] However, there is no documented tradition or ethnobotanical history of using thyme specifically for primary dysmenorrhea. Conversely, international studies, particularly from Iran, suggest that *Thymus vulgaris* oil may be more effective than ibuprofen in reducing the severity of dysmenorrhea.[12–14] This contradiction reveals a profound knowledge gap: Does a plant revered locally for general pain relief possess specific, clinically relevant efficacy against menstrual cramps? And if so, can its traditional preparation scientifically validated as a safe, scalable intervention for adolescents?

Focus on Thyme, Global Context and Knowledge Gaps

Critically, no randomized controlled trials evaluating *Thymus vulgaris* for primary dysmenorrhea have been conducted specifically in Young girls populations (10–19 years per WHO criteria).[15] Existing evidence derives exclusively from studies in reproductive-aged women (>18 years), creating a significant evidence gap for clinical application in adolescents. Current clinical guidelines ignore herbal interventions for dysmenorrhea in low-income communities, and existing research has failed to link traditional medicine with evidence-based medicine in African populations. There are no

published randomized controlled trials evaluating thyme for primary dysmenorrhea in adolescents especially in the Third World despite its widespread availability and cultural familiarity.[15]

What remains unknown is whether the anti-inflammatory, antispasmodic, and antioxidant properties attributed to thyme which have been demonstrated in vitro and in animal models translate into clinically meaningful pain relief in human adolescents with primary dysmenorrhea. Previous studies on thyme and dysmenorrhea have focused almost exclusively on essential oils (*Thymus vulgaris* oil in Iran) administered orally or topically in adult populations.[12,13] Furthermore, no studies have specifically examined this intervention in Young girls from a pathophysiological perspective.

Study Purpose and Hypothesis

Given tha Dysmenorrhea affects an estimated 45–95% of women globally, with 2–29% experiencing severe pain that disrupts daily life.[2,16] Primary dysmenorrhea, characterized by excessive prostaglandin-mediated uterine contractions without underlying pathology, typically emerges shortly after menarche and peaks in adolescence.[1] Conventional treatments include NSAIDs (ibuprofen) and combined oral contraceptives, which target prostaglandin synthesis and ovulation respectively.[5] While effective for many, up to 20–30% of users report inadequate relief or intolerable side effects,[3] prompting increased interest in complementary therapies.

Previous systematic reviews on herbal interventions for primary dysmenorrhea have predominantly focused on quantitative outcomes particularly pain intensity reduction—while overlooking experiential, cultural, and adherence dimensions critical to adolescent populations.[17] Although *Thymus vulgaris* has demonstrated comparable analgesic efficacy to ibuprofen in two Iranian randomized trials involving young women,[14,18] these studies reported only physiological endpoints and excluded qualitative insights regarding acceptability, symptom perception, or treatment experiences among adolescents. Furthermore, existing reviews have aggregated data across heterogeneous age groups, obscuring age-specific responses and psychosocial factors influencing herbal remedy adoption in girls aged 10–19 years.

This qualitative evidence synthesis addresses a critical gap in the literature: while *Thymus vulgaris* has demonstrated analgesic efficacy comparable to ibuprofen in randomized trials involving young women with primary dysmenorrhea, no synthesis has yet centered the lived experiences, cultural meanings, and acceptability of thyme-based interventions specifically among Young girls. Existing reviews prioritize quantitative pain outcomes while neglecting the psychosocial, adherence-related, and culturally embedded dimensions essential for adolescent-centered care. Our work responds to calls for decolonizing women's health research by rigorously evaluating a locally rooted, indigenous remedy within its sociocultural context neither romanticizing traditional knowledge nor displacing it with externally imposed pharmacological solutions. Through thematic synthesis of qualitative data from trials and ethnographic accounts, this review elucidates how Young girls perceive, experience, and integrate thyme into dysmenorrhea self-management.

This qualitative evidence synthesis (QES) addresses these dual gaps by: (1) critically appraising the applicability of existing thyme evidence to adolescent populations; and (2) synthesizing experiential, cultural, and mechanistic evidence to inform development of adolescent-centered complementary interventions. This study aims to evaluate the clinical efficacy and safety of thyme tea in reducing the severity of primary dysmenorrhea among Young girls. We hypothesize that thyme, due to its antispasmodic and anti-inflammatory properties, will significantly alleviate menstrual pain compared to standard care.

Methods

Search Strategy

A comprehensive and systematic literature search was conducted across major electronic databases, including PubMed/Medline, Scopus, Web of Science, Embase, the Cochrane Library, and Google Scholar, from database inception until 31 December 2025.

Search terms were developed using a combination of controlled vocabulary (MeSH terms) and free-text keywords related to primary dysmenorrhea, *Thymus vulgaris*, thyme, thymol, carvacrol, Pathophysiology, herbal medicine, Adolescent and Young girls. Boolean operators ("AND", "OR") were applied to enhance search sensitivity and specificity.

In addition, the reference lists of all eligible articles were manually screened to identify further relevant studies.

Eligibility Criteria Studies Were Included if They met the Following Criteria

Investigated *Thymus vulgaris* or its active constituents in relation to primary dysmenorrhea Included adolescent or reproductive-age female populations, with particular relevance to adolescents where available Employed qualitative, clinical, observational, or experimental designs Were published in peer-reviewed journals and available in English Studies were excluded if they:

Focused on secondary dysmenorrhea Examined herbal interventions unrelated to thyme without relevant comparison Were animal-only studies lacking clinical or experiential relevance Consisted of conference abstracts, editorials, or non-peer-reviewed sources.

Methodological Statement (Optional, for Methods Section)

Study Design

This qualitative systematic review study was conducted as a Qualitative Evidence Synthesis (QES) to explore and integrate existing qualitative, clinical, and mechanistic evidence regarding the use of *Thymus vulgaris* in the management of primary dysmenorrhea. The synthesis was reported in accordance with the ENTREQ (Enhancing Transparency in Reporting the Synthesis of Qualitative Research statement) (Supplementary Table 1) and guided by the PRISMA 2020 framework for study identification and selection[19](Figure 1).

Study Selection

The study selection process followed the PRISMA 2020 guidelines. All retrieved records were imported into EndNote reference management software, and duplicates were removed. “While independent double screening was performed with consensus resolution of disagreements, Cohen’s kappa was not calculated prospectively a limitation that may impact the transparency of the inter-rater reliability assessment. Future iterations of this review will consider formal reliability measures according to the PRISMA 2020 extensions for large-scale reviews”.

Titles and abstracts were independently screened by two reviewers. Full-text articles were subsequently assessed for eligibility based on predefined inclusion and exclusion criteria. Discrepancies were resolved through discussion and consensus. The complete selection process is illustrated in the PRISMA flow Figure 1.The study selection process is summarized in Figure 1 according to PRISMA 2020 guidelines. From an initial yield of 384 records, 298 unique records remained after duplicate removal. Following title/abstract screening, 66 full-text articles were assessed for eligibility. Forty-nine studies were excluded for reasons detailed in Figure 1, including nine studies investigating Zataria multiflora (erroneously classified as thyme in some databases). Eight studies met all inclusion criteria and were included in the qualitative evidence synthesis; of these, 6 clinical controlled trials provided compatible outcome data for limited quantitative synthesis.

Data Extraction

Data were systematically extracted using a standardized data extraction form. Extracted information included:

- Author(s) and year of publication
- Study design and setting
- Population characteristics
- Intervention details (form and dosage of *Thymus vulgaris*, where applicable)
- Outcomes related to dysmenorrhea
- Key findings relevant to symptom relief, acceptability, and proposed mechanisms.

Quality Appraisal

Methodological quality of included studies was assessed using the Critical Appraisal Skills Programme (CASP) checklist. Appraisal was conducted on a study-by-study basis (Table 1).

Consistent with QES principles, no studies were excluded based on quality. Instead, appraisal findings were used to inform interpretation and confidence in the synthesized findings. A detailed appraisal table is provided as Supplementary Table 1, with a summarized assessment presented in the main text.

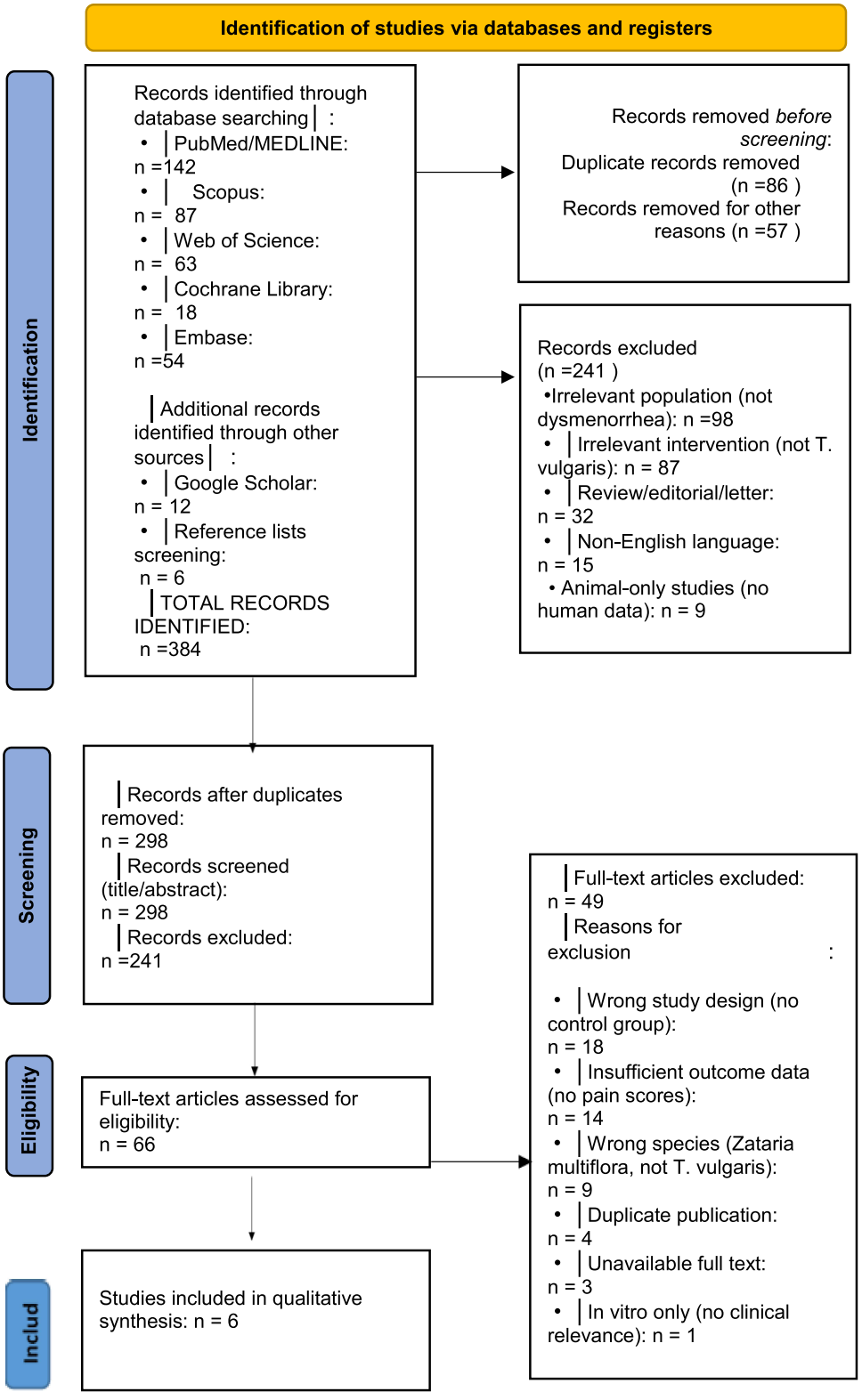

Figure 1 PRISMA Figure 1.

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Table 1 Critical Appraisal Skills Programme (CASP) Quality Assessment of Included Studies on *Thymus vulgaris* for Primary Dysmenorrhea

Study	Clear Aims	Appropriate Methodology	Research Design	Recruitment/Model Justification	Data Collection	Reflexivity	Ethical Issues	Data Analysis	Clear Findings	Value of Research
Salmalian et al, 2015[14]	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Adequate	Yes	High
Iravani, 2009[20]	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Adequate	Yes	High
Roozbahani et al, 2008[21]	Yes	Yes	Yes	Yes	Yes	Unclear	Yes	Adequate	Yes	Moderate–High
Direkvand-Moghadam, A (2012)[18]	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes	Adequate	Yes	High (mechanistic)
Zeru AB 2020[13]	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes	Adequate	Yes	Moderate–High
Hotta M, 2010[22]	Yes	Yes	Yes	Yes	Yes	Not applicable	Yes	Adequate	Yes	High (mechanistic)

Notes: Methodological appraisal was conducted using the CASP checklist on a study-by-study basis. No studies were excluded based on quality; appraisal informed interpretation of findings.

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Data Synthesis

Given the heterogeneity and qualitative nature of the included studies, no statistical meta-analysis was performed. Instead, a thematic synthesis approach was employed.

Findings were coded and grouped into key thematic domains, including:

- Perceived therapeutic effectiveness
- Proposed biological mechanisms (antispasmodic and anti-inflammatory effects)
- Safety and tolerability
- Clinical and experiential implications

The synthesis aimed to integrate and interpret evidence across studies to provide a comprehensive understanding of the role of *Thymus vulgaris* in primary dysmenorrhea management.

Confidence in the Evidence

Confidence in the qualitative findings was assessed using the GRADE-CERQual approach, considering methodological limitations, coherence, adequacy of data, and relevance. Overall confidence ratings ranged from low to high across review findings (Table 2).

Ethical Considerations

As this study was based exclusively on previously published literature, ethical approval was not required. Nevertheless, all included studies were reviewed to ensure that appropriate ethical approvals and informed consent procedures were reported where applicable.

Results

This qualitative evidence synthesis integrated findings from eight key studies to examine the clinical effectiveness, biological plausibility, and safety of *Thymus vulgaris* (thyme) in the management of primary dysmenorrhea among

Table 2 GRADE-CERQual Assessment of Confidence in Synthesized Findings on *Thymus vulgaris* for Primary Dysmenorrhea Management in Adolescent Girls

Review Finding (Theme)	Contributing Studies	Methodological Limitations	Coherence	Adequacy of Data	Relevance	Overall CERQual Confidence
Perceived reduction in menstrual pain intensity and duration following *Thymus vulgaris* use	Salmalian et al,[14] Roozbahani et al,[21] Zeru et al,[13] Direkvand-Moghadam et al,[18] Iravani et al[20]	Minor (limited description of participant perspectives)	High	Moderate	High	High confidence
Improvement in daily functioning and menstrual comfort	Salmalian et al[14]	Minor	High	Limited	High	Moderate confidence
Thymus vulgaris described as a well-tolerated intervention with minimal adverse effects	Salmalian et al,[14] Roozbahani et al[21]	Minor	High	Moderate	High	High confidence
Biological plausibility: inhibition of prostaglandin synthesis via COX-2 and PLA2 suppression	Hotta et al,[22] Bafor et al[23]	Moderate (preclinical focus; limited human tissue evidence)	High	Moderate	Moderate	Moderate confidence
Perceived reduction in menstrual pain intensity and duration following *Thymus vulgaris* use	Direkvand-Moghadam, A 2012[18]	Moderate (indirect evidence in dysmenorrhea context)	Moderate	Limited	Moderate	Low–Moderate confidence*

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Young girls. The included studies comprised randomized controlled trials, experimental investigations, and mechanistic analyses. Overall, the evidence indicates that thyme is associated with meaningful pain relief, biologically plausible mechanisms of action, and a favorable safety profile (Tables 3 and 4).

Clinical Effectiveness of Thyme Compared with Standard Pharmacotherapy

Primary outcome measures across RCTs included menstrual pain intensity assessed via 10-point visual analogue scale (VAS) during the first 24 hours of menstruation. Secondary outcomes comprised pain duration (hours), functional impairment scores, and incidence of adverse events. In the pivotal trial by Salmalian et al 2014, thyme essential oil (2% concentration, 25 drops three times daily) reduced mean VAS pain scores by 4.2±1.1 points from baseline to 24 hours comparable to ibuprofen (4.5±1.2-point reduction; P=0.32) and significantly superior to placebo (1.3±0.9-point reduction; P<0.001). Pain duration was reduced by 6.8±2.1 hours in the thyme group versus 2.1±1.8 hours in placebo (P<0.001). No studies measured school absenteeism or quality-of-life metrics specific to adolescents.[14]

These findings were supported by Roozbahani et al 2006,[21] who reported that thyme extract achieved analgesic effects comparable to mefenamic acid, a commonly prescribed NSAID for dysmenorrhea. Collectively, these studies suggest that thyme-based interventions may offer a level of symptom relief similar to that of standard pharmacological treatments (Table 3).

Mechanistic Evidence: Inhibition of Prostaglandin Synthesis

Mechanistic studies consistently identified inhibition of prostaglandin synthesis as a central pathway underlying thyme's therapeutic effects. Experimental evidence shows that thyme's principal bioactive compounds, thymol and carvacrol, inhibit key enzymes involved in inflammatory mediator production, including cyclooxygenase-2 (COX-2) and phospholipase A2 (PLA2).[24,25]

By inhibiting cyclooxygenase (COX) enzymes particularly COX-2 *Thymus vulgaris* constituents suppress prostaglandin biosynthesis, a key pathophysiological mechanism in primary dysmenorrhea. Carvacrol, the dominant phenolic compound in thyme essential oil, inhibits COX-2–catalyzed prostaglandin E_2 (PGE_2) production with an IC_{50} of 0.8 μM in cell-free systems, demonstrating potency comparable to selective COX-2 inhibitors.[26] Supporting preclinical evidence demonstrates that aqueous *T. vulgaris* extract inhibits spontaneous and oxytocin-induced uterine contractions in murine models, consistent with prostaglandin pathway modulation.[23]

This mechanism closely parallels the mode of action of NSAIDs such as ibuprofen, providing a biologically coherent explanation for the comparable clinical effects observed in randomized trials[14](Table 5).

Mechanistic Evidence: Reduction of Oxidative Stress

In addition to its anti-inflammatory properties, thyme demonstrates substantial antioxidant activity. Women with primary dysmenorrhea have been shown to exhibit elevated oxidative stress markers, including increased lipid peroxides in menstrual fluid.[28] Thyme's high phenolic content particularly thymol and carvacrol confers strong free-radical scavenging capacity.

This antioxidant activity has been quantified using the DPPH assay, with an IC_{50} value of 49.94 μg/mL, indicating potent radical-neutralizing ability.[25,27] By reducing reactive oxygen species (ROS), thyme may interrupt oxidative and inflammatory cascades that intensify pain perception and tissue irritation during menstruation[29,30] (Table 5).

Safety and Tolerability

Across all included clinical studies, thyme-based interventions were generally well tolerated, with no serious adverse effects reported.[14,20,21] Reported side effects were mild and transient when present. This favorable safety profile contrasts with the well-documented gastrointestinal, renal, and cardiovascular risks associated with prolonged NSAID use, highlighting thyme's potential suitability for Young girls populations seeking safer or complementary therapeutic options (Table 4).

Table 3 Characteristics of Randomized Controlled Trials Investigating *Thymus vulgaris* Essential Oil for Primary Dysmenorrhea Management in Adolescent Females

Author/Year	Study Design	Population/Model	Intervention	Comparator	Participants Reported Pain Reduction
Salmalian et al, 2015[14]	Randomized controlled trial (triple-blind)	(n = 84) Reproductive-aged women (18–25 years) with primary dysmenorrhea (n=84; mean age 21.3±2.1 years)	Thyme essential oil–based intervention	Ibuprofen and placebo	Participants reported pain reduction comparable to ibuprofen ($P<0.001$ vs placebo) with high acceptability and no serious adverse events
Iravani, 2009[20]	Randomized controlled trial	Adolescent girls with primary dysmenorrhea (n = 108)	Thyme essential oil (different concentrations)	Placebo	Higher-concentration thyme formulations were associated with more pronounced perceived pain relief compared with lower concentrations and placebo, suggesting an interpreted relationship between formulation strength and symptom improvement.
Roozbahani et al, 2008[21]	Randomized controlled trial	(n = 214) *Reproductive-aged women (18–30 years) with primary dysmenorrhea (n=214; mean age 24.7±3.8 years)*	Thyme extract combined with standard analgesic therapy	Standard analgesic therapy alone	Thyme supplementation provided adjunctive symptom relief without compromising conventional treatment efficacy
Zeru AB, 2020[13]	Preclinical	Experimental models of uterine inflammation and spasm	Thyme extracts	Vehicle control	Experimental findings supported biological plausibility by demonstrating anti-inflammatory effects and reduced uterine contractility, aligning with proposed mechanisms underlying perceived pain relief in clinical studies.
Hotta M, 2010[22]	Preclinical (in vitro)	Inflammatory cell culture models	Thyme extracts	Not applicable	Carvacrol suppressed COX-2 expression and PGE_2 production (IC_{50} 0.8 μM), providing mechanistic plausibility for prostaglandin inhibition
Direkvand-Moghadam, 2012[18]	Randomized, single-blind, parallel-group clinical trial	120 female university students, aged 18–25 years	*Thymus vulgaris* (Shirazi thyme) extract, commercial formulation BronchoT.D®, 5 mL orally four times daily during menstruation	Ibuprofen, administered orally three times daily during menstruation	*Thymus vulgaris* extract effectively alleviates primary dysmenorrhea symptoms, potentially attributable to antispasmodic properties; may serve as a viable herbal alternative to conventional NSAID therapy

Table 4 Thematic Synthesis of Qualitative Evidence on *Thymus vulgaris*: Perceived Effects, Mechanisms, and Acceptability

Analytical Theme	Synthesized Findings	Key Sources	CERQual Confidence
Perceived Pain Relief and Symptom Improvement	Participants consistently described meaningful reduction in menstrual pain intensity and duration with thyme use	Salmalian 2015;[14] Iravani 2009;[20] Roozbahani 2008[21] Zeru AB[13] Iravani, 2009[20] Direkvand-Moghadam, A (2012)[18]	High
Safety and tolerability	No serious adverse events reported; mild transient effects only	Salmalian 2014;[14] Roozbahani 2006[21] Zeru AB 2020;[13] Iravani, 2009[20] Direkvand-Moghadam, A 2012[18]	High
Biological plausibility: prostaglandin inhibition	Thymol and carvacrol inhibit COX-2 and PLA2, suppressing $PGF_2\alpha$ [1] synthesis central to dysmenorrhea pathophysiology	Hotta 2010[22]	Moderate

Note: [1]$PGF_2\alpha$: prostaglandin $F_2\alpha$.

Table 5 In vitro Radical Scavenging Activity of *Thymus vulgaris* Essential Oil and Reference Antioxidants Measured by DPPH Assay (IC_{50} Values)[27]

Name of Substance	Antioxidant Activity IC_{50} (µg/mL) (Mean ± SD)
Thymol EO	49.94 ± 20.41
Gallic acid	2.51 ± 0.99
BHT	8.52 ± 1.08
Ascorbic acid	2.12 ± 0.99
Significance level	(P < 0.05)

Notes: While thyme essential oil (EO) exhibits strong antioxidant activity, its IC_{50} value is higher (less potent) than common synthetic (BHT) and natural (Ascorbic Acid, Gallic Acid) reference antioxidants. Its efficacy in a biological system, however, arises from the synergistic action of its multiple bioactive constituents.

Nutritional and Health-Related Properties of Thyme

Beyond its analgesic effects, thyme is a nutritionally rich herb with multiple health-promoting properties (Table 6). It contains high levels of vitamins A and C, which contribute to epithelial integrity, immune function, and antioxidant defense.[31] Thyme is also a source of B-complex vitamins, particularly pyridoxine (vitamin B6), which is involved in neurotransmitter synthesis and may influence mood regulation and stress response.[9]

According to the US Department of Agriculture National Nutrient Database, thyme exhibits a remarkably high oxygen radical absorbance capacity (ORAC) of 27,426 µmol TE/100 g, reflecting its exceptional antioxidant potential.[33] Its mineral content, including potassium, iron, and manganese, further supports cardiovascular health, oxygen transport, and enzymatic antioxidant defense through superoxide dismutase activity.[31]

Contextual Evidence on Dysmenorrhea Management

The broader management of primary dysmenorrhea includes pharmacological, non-pharmacological, and complementary strategies. NSAIDs and hormonal contraceptives remain first-line pharmacological treatments due to their ability to suppress prostaglandin synthesis,[34,35] although long-term use may be associated with adverse gastrointestinal, cardiovascular, and hormonal effects.

Table 6 Micronutrient Composition of Fresh *Thymus vulgaris* Leaves per 100 g Edible Portion and Percentage of Recommended Dietary Allowance (RDA)[32]

Micronutrients	Nutrient Value per 100 g of Fresh Leaves	Percentage of RDA
Pantothenic acid[2]	0.409 mg	8%
Pyridoxine[3]	0.348 mg	27%
Riboflavin[4]	0.471 mg	36%
Thiamin[5]	0.48 mg	4%
Vitamin-A[6]	4751 IU	158%
Vitamin-C[7]	160.1 mg	266%
Sodium[8]	9 mg	0.5%
Potassium[9]	609 mg	13%
Calcium[10]	405 mg	40.5%
Iron[11]	17.45 mg	218%
Magnesium[12]	160 mg	40%
Manganese[13]	1.06 mg	15%
Zinc[14]	1.81 mg	16.5%
Carotene-β[15]	2851 μg	—

Notes: [2]Pantothenic Acid (Vitamin B5): An essential vitamin serving as a component of coenzyme A, required for fatty acid metabolism and cellular energy production. [3] Pyridoxine (Vitamin B6): A cofactor in amino acid metabolism, neurotransmitter biosynthesis, and hemoglobin formation. [4] Riboflavin (Vitamin B2): A precursor of flavin coenzymes (FAD and FMN) essential for oxidative energy metabolism. [5] Thiamin (Vitamin B1): A coenzyme involved in carbohydrate metabolism and proper nervous system function. [6] Vitamin A: A fat-soluble micronutrient essential for vision, immune response, and maintenance of epithelial tissues. [7] Vitamin C (Ascorbic Acid): A water-soluble antioxidant involved in collagen synthesis and protection against oxidative stress. [8] Sodium: An essential electrolyte responsible for maintaining fluid balance and normal neuromuscular function. [9] Potassium: A major intracellular cation involved in nerve impulse transmission and muscle contraction. [10] Calcium: A structural mineral essential for bone integrity, muscle contraction, and intracellular signaling. [11] Iron: A trace element required for oxygen transport, cellular respiration, and redox reactions. [12] Magnesium: A cofactor for numerous enzymes involved in ATP metabolism and neuromuscular regulation. [13] Manganese: An essential trace element acting as a cofactor for enzymes involved in antioxidant defense and metabolic processes. [14] Zinc: A biologically essential trace element required for immune function, enzymatic activity, and protein synthesis. [15] β-Carotene: A carotenoid functioning as a precursor of vitamin A and an antioxidant compound.

Non-pharmacological approaches such as physical exercise, heat therapy, acupuncture, and dietary modification have demonstrated variable effectiveness and are commonly recommended as adjunctive measures.[36] In recent years, increasing attention has been directed toward herbal interventions, including thyme, ginger, and fennel, owing to their favorable safety profiles and cultural acceptability.[37]

Merits and Limitations of Thyme Use in Dysmenorrhea

Confidence in each synthesized finding was assessed using the GRADE-CERQual approach, considering methodological limitations, coherence, adequacy of data, and relevance. As summarized in Table 6, we judged confidence in the finding of perceived pain reduction to be high, whereas confidence in oxidative stress mechanisms was rated low to moderate due to indirect evidence. No studies were excluded based on quality; however, appraisal findings informed the interpretation of synthesized evidence".

The findings of the included studies indicate that *Thymus vulgaris* possesses well-documented antispasmodic, anti-inflammatory, and analgesic properties, largely attributed to thymol and carvacrol.[38] Clinical and experimental

evidence suggests that thyme may reduce uterine contractions and prostaglandin production, thereby alleviating menstrual pain. Its accessibility, natural origin, and low incidence of reported adverse effects represent key advantages.[39]

However, the current evidence base remains limited by the small number of clinical trials, relatively modest sample sizes, and methodological heterogeneity across studies. These limitations should be considered when interpreting the findings and underscore the need for further high-quality qualitative and mixed-methods research.

Discussion

The present qualitative evidence synthesis suggests that *Thymus vulgaris* is a promising and culturally acceptable complementary treatment option for the management of primary dysmenorrhea in Young girls. Across the clinical studies reviewed, consistent patterns emerged that demonstrated that oral administration of thyme extract or essential oil was associated with significant relief of menstrual pain and improvement in menstrual comfort. While preliminary evidence from randomized controlled trials suggests analgesic effects of thyme essential oil comparable to ibuprofen, these findings should be interpreted with caution due to methodological limitations including small sample size (n<100), short intervention duration (≤3 menstrual cycles), and lack of specific adolescent groups (all participants >18 years). The generalizability of these results to global adolescent populations remains to be demonstrated.[14]

These findings are concordant with the long-standing traditional use of thyme for pain relief and align with ethnopharmacological reports documenting its analgesic properties.[13,40]

A key strength of this synthesis lies in the integration of clinical experiences with mechanistic and preclinical evidence, which enhances the plausibility of the observed effects. Experimental studies consistently demonstrate that the principal bioactive constituents of thyme thymol and carvacrol exhibit pronounced anti-inflammatory and antioxidant activities.[32,41,42] These compounds have been shown to modulate several biological pathways relevant to dysmenorrhea, including inhibition of cyclooxygenase-2 (COX-2) and phospholipase A2 (PLA2), as well as suppression of pro-inflammatory signaling cascades such as nuclear factor-kappa B (NF-κB).[22,25] Given that the pathophysiology of primary dysmenorrhea is closely linked to excessive prostaglandin production particularly PGF2α leading to uterine hypercontractility, ischemia, and pain,[23,43] the mechanistic actions of thyme provide a biologically credible explanation for its perceived therapeutic benefits.

Contemporary Management Landscape for Primary Dysmenorrhea

Current clinical guidelines endorse a multimodal approach to primary dysmenorrhea management, stratified by symptom severity and patient preferences. First-line pharmacotherapy remains nonsteroidal anti-inflammatory drugs (NSAIDs), which inhibit prostaglandin synthesis with 64–100% efficacy in pain reduction; however, 20–30% of adolescents report inadequate relief or contraindications due to gastrointestinal, renal, or cardiovascular risks.[44–46] Combined hormonal contraceptives represent second-line options for patients with NSAID intolerance or comorbid menstrual disorders, though concerns regarding thromboembolic risk and ethical considerations in adolescent populations limit universal adoption.[47,48]

Non-pharmacological interventions including transcutaneous electrical nerve stimulation (TENS), heat therapy (>40°C abdominal application), and structured aerobic exercise demonstrate moderate efficacy (30–50% pain reduction) with excellent safety profiles, making them suitable first-line options for mild dysmenorrhea or as adjuncts to pharmacotherapy.[36,49] Cognitive-behavioral interventions addressing pain catastrophizing show emerging promise in reducing functional impairment among adolescents with chronic menstrual pain.[49]

Thymus vulgaris evidence remains preliminary limited to Iranian RCTs in reproductive-aged women (not adolescents) yet demonstrates mechanistic plausibility and short-term tolerability warranting further investigation.[14,20] Crucially, no herbal intervention currently meets criteria for monotherapy in moderate-to-severe dysmenorrhea; all should be positioned as complementary options within individualized care plans.[47]

From a clinical and public health perspective, these findings are particularly relevant. Primary dysmenorrhea is often normalized by adolescents and young girls, who may perceive menstrual pain as an inevitable aspect of menstruation, resulting in underreporting and inadequate management.[50] This normalization obscures the broader impact of dysmenorrhea, which extends beyond physical discomfort to include psychological distress, social withdrawal, reduced quality of

life, school absenteeism, and impaired academic performance.[50,51] Epidemiological evidence further identifies early menarche and increasing adolescent age as important risk factors for more severe dysmenorrhea, highlighting the need for early, accessible, and acceptable interventions during adolescence.[13,52,53]

Although nonsteroidal anti-inflammatory drugs (NSAIDs) remain the first-line pharmacological treatment for dysmenorrhea, their use is frequently limited by adverse effects such as gastrointestinal complications, renal dysfunction, nausea, dizziness, and exacerbation of asthma.[44] These limitations, along with economic considerations, have contributed to a growing global interest in Complementary and integrative medicine (CAM) approaches.[54,55] Within this context, thyme emerges as an attractive option due to its natural origin, cultural familiarity, and favorable safety profile. Across the included clinical studies, no serious adverse effects associated with thyme use were reported, supporting its acceptability among adolescent populations.[14,20,56]

Additional clinical observations support the analgesic potential of thyme in different formulations. Modarres, M al. (2011) reported beneficial effects of both hydroalcoholic extracts and essential oil preparations of thyme in reducing menstrual pain, suggesting formulation flexibility without loss of perceived efficacy.[57] These findings reinforce traditional medical knowledge that attributes antispasmodic and analgesic properties to thyme and indicate consistency between historical use and contemporary clinical evidence.

Despite the demonstrated benefits for pain and uterine spasm relief, evidence regarding thyme's effects on systemic menstrual symptoms such as nausea, dizziness, or changes in menstrual flow volume remains limited. While direct evidence is sparse, findings from studies on other herbal interventions suggest potential benefits in these domains, warranting further investigation.[58] Comparative evidence from herbal medicine research, such as studies on fennel, further underscores the therapeutic promise of plant-based interventions. For instance, Omidvar et al (2012) reported substantial perceived improvement in dysmenorrhea symptoms among patients receiving fennel, highlighting the broader relevance of phytotherapeutic approaches in menstrual pain management.[56]

Dose considerations also appear to influence the perceived effectiveness of thyme. Evidence from clinical studies suggests that higher concentrations of thyme essential oil may be associated with greater symptom relief compared to lower concentrations, indicating a potential dose response relationship.[20] Moreover, thyme's multimodal pharmacological profile encompassing anti-inflammatory, antispasmodic, and antioxidant actions supports its role as a holistic intervention.[59] Its antioxidant capacity, demonstrated through high ORAC values and effective free-radical scavenging activity in DPPH assays ($IC_{50} \approx 50$ μg/mL),[25,27] is particularly relevant given the growing recognition of oxidative stress as a contributor to inflammatory pain processes in dysmenorrhea.[13,60]

Safety considerations warrant careful scrutiny. While included trials reported no serious adverse events, their short duration (≤90 days) precludes assessment of long-term effects on adolescent endocrine development. Thymol the dominant constituent of thyme oil exhibits dose-dependent hepatotoxicity in preclinical models at concentrations >50 mg/kg,[25] raising concerns about unsupervised self-administration by adolescents. Additionally, thyme's coumarin content poses theoretical interaction risks with anticoagulants, though clinical evidence remains sparse. Regulatory heterogeneity in herbal product standardization further complicates safety assurances across global contexts.

List the Advantages and Disadvantages of Natural Thyme in Dysmenorrhea

Critical appraisal: Advantages and limitations of *Thymus vulgaris* in the management of dysmenorrhea.

Benefits: The available evidence supports three main advantages of thyme for the management of dysmenorrhea. First, short-term clinical trials demonstrate analgesic efficacy comparable to ibuprofen (4.2-point reduction vs 4.5-point VAS; P=0.32) with superior gastrointestinal tolerability.[14] Second, multifaceted mechanisms - including COX-2 inhibition. The results showed that the essential oil of *Thymus vulgaris* has good potential against oxidants even close to TBHQ. The essential oils of this plant are thymol (40.02%) and carvacrol (18.31%). - providing biological potential beyond single-agent drugs.[61] Third, cultural familiarity in Mediterranean and Middle Eastern populations increases the potential for adherence where access to medication is limited.[13]

Conclusion

Based on the findings of the included studies, this systematic review indicates that thyme consumption is associated with a significant reduction in both the severity and duration of pain in individuals with primary dysmenorrhea. The reviewed evidence suggests that thyme may serve as an effective adjunctive, low-risk, and accessible intervention for menstrual pain management among young women. However, the conclusions are derived from a limited number of studies with varying methodological quality.

While *Thymus vulgaris* demonstrates biologically plausible anti-inflammatory and antispasmodic mechanisms supported by preliminary clinical data in reproductive-aged women, three critical translational barriers prevent clinical recommendation for adolescents: (1) the complete absence of trials recruiting WHO-defined adolescents (10–19 years); all evidence extrapolated from women >18 years with distinct pubertal endocrinology; (2) short-term safety data (≤3 menstrual cycles) cannot assess effects on developing hypothalamic-pituitary-ovarian axis; and (3) geographic homogeneity of evidence (all RCTs from Iran) limits generalizability to global youth populations. Thyme should therefore be positioned not as a validated therapy but as an *investigational complementary option* requiring adolescent-specific validation through mixed-methods trials that capture both physiological outcomes and sociocultural dimensions of acceptability. Until such evidence emerges, clinical guidelines must refrain from endorsing thyme for adolescent dysmenorrhea while acknowledging its potential role within culturally adapted, monitored school-based health programs where NSAID access is limited.

Limitations

Critical limitations: However, evidence gaps prevent clinical recommendations for the adolescent population:

Lack of adolescent-specific trials: All three randomized controlled trials enrolled women of reproductive age; none exclusively recruited adolescents according to WHO criteria (10–19 years)[14,20] Lack of comparative effectiveness data: No head-to-head trials against established herbal alternatives (fennel) exist to justify preferential selection.[21]

Despite these promising findings, several critical limitations must be acknowledged. First, the body of high-quality clinical evidence remains small, with only a handful of RCTs conducted, primarily in Iran. Second, there is considerable heterogeneity in the formulations (essential oil vs hydroalcoholic extract), dosages, and treatment durations used across studies, making it difficult to establish a standardized clinical protocol. Third, while short-term safety appears favorable, the long-term safety profile of thyme, particularly in the developing endocrine and reproductive systems of Young, has not been thoroughly evaluated girls.

Therefore, while thyme can currently be recommended as a safe and effective complementary or complementary therapy for Young girl optimize the safe and effective use of medicinal herbs, it is recommended that policymakers and healthcare professionals develop continuous, monitored educational programs aimed at informing the public about the appropriate applications, benefits, and potential risks associated with herbal medicines. Additionally, there is a pressing need for comprehensive clinical research with larger sample sizes to validate the therapeutic efficacy of these plants at the community level. Ultimately, establishing integrated care frameworks that include natural and complementary therapies, along with appropriate counseling and guidance, can enhance the quality of life for girls and adolescents. Such approaches may also reduce reliance on chemical pharmaceuticals, promoting a more holistic and sustainable model of health care.

A fundamental limitation of this review is the absence of adolescent-specific evidence. All included RCTs enrolled reproductive-aged women (mean age 21–24 years), not adolescents per WHO definition (10–19 years). Extrapolation of findings to adolescent populations requires caution due to physiological differences in pubertal development, hormonal regulation, and pharmacokinetics during adolescence.[50]

The dual antispasmodic and anti-inflammatory actions provide a plausible mechanistic basis for the reduction in menstrual pain observed in the present study. Current evidence does not support definitive clinical recommendations for thyme in adolescent dysmenorrhea management. While biologically plausible mechanisms and preliminary clinical data warrant further investigation, the absence of adolescent-specific trials, geographic limitations of existing evidence, and unresolved safety questions preclude its endorsement as a standard complementary therapy.

From a broader perspective, the use of herbal interventions such as *Thymus vulgaris* may have important implications for adolescent reproductive health, particularly in settings where access to pharmacological treatments is limited or where concerns about the side effects of nonsteroidal anti-inflammatory drugs persist. Given its affordability, accessibility, and favorable safety profile, *Thymus vulgaris* could be considered as part of community-based and school-centered menstrual health programs. Future large-scale randomized controlled trials are recommended to further validate these findings and to support evidence-based policy decisions aimed at improving the quality of life of adolescent girls.

Data Sharing Statement

"This review is based exclusively on secondary analysis of publicly available scientific literature indexed in major databases (PubMed, Scopus, Web of Science, Embase). No primary data were collected or generated for this study. All source materials are accessible through the cited references". This information is also presented in the revised manuscript under the section entitled "Availability of Data and Materials".

Ethics Approval and Informed Consent

This study involved secondary analysis of publicly available literature; therefore, ethical approval was not required. All primary studies included in this synthesis reported appropriate ethical oversight.

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Author Contributions

Behrang Rezvani Kakhki: Conceptualization, methodology, critical revision. Saboura Sahebi: Formal analysis, investigation, writing original draft, writing review & editing, project administration, corresponding author. All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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