Nutrition and Dietary Supplements

REVIEW

A Narrative Review of *Foeniculum vulgare*: Mechanisms of Action, Biological and Chemical Properties, and Therapeutic Applications in Dysmenorrhea

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Introduction: Primary dysmenorrhea (PD) is a highly prevalent gynecological condition among adolescents and women of reproductive age, often inadequately managed by conventional analgesics due to side effects or contraindications.
Purpose: This review evaluates the efficacy, mechanisms, and safety of *Foeniculum vulgare* (fennel) as a phytotherapeutic alternative for PD.
Methods: This article is a narrative review that synthesizes the available evidence on the efficacy and safety of *Foeniculum vulgare* in primary dysmenorrhea. Owing to the heterogeneity of the available studies and the limited standardization of interventions and outcomes, a quantitative meta-analysis was not performed and reviews continued through to September 2025. Databases included PubMed, Scopus, and Google Scholar. Inclusion criteria were human studies on fennel for PD, reporting pain outcomes, safety, or biological mechanisms.
Results: Twelve randomized or quasi-experimental trials (n> 800) demonstrated that standardized fennel extract (30 mg three times daily, initiated premenstrually) significantly reduces pain intensity, duration, and systemic symptoms (nausea, fatigue) over 1–3 cycles, with efficacy comparable to ibuprofen or mefenamic acid. Mechanistically, fennel inhibits prostaglandin synthesis via COX-2 suppression, blocks voltage-dependent calcium channels, and exerts antioxidant and mild phytoestrogenic effects. Adverse events were rare and mild (transient dizziness), with no serious toxicity reported in adolescents or adults.
Conclusion: Fennel is a safe, effective, and culturally acceptable herbal intervention for primary dysmenorrhea. Its integration into clinical practice offers a viable alternative for NSAID-intolerant or hormone-averse individuals. Future research should prioritize standardized, multicenter trials with objective biomarkers to establish definitive dosing guidelines.

Plain Language Summary:

Why this study was conducted

Many young women suffer from painful periods (primary dysmenorrhea), but common painkillers can cause stomach problems or are not suitable for everyone. There is growing interest in safe, natural alternatives like fennel, which has been used traditionally for menstrual pain.

What the researchers did and found

We reviewed all high-quality studies on fennel for period pain. We found that taking fennel (usually as 30 mg capsules three times a day, starting a few days before the period) reduces pain and related symptoms like nausea, as effectively as ibuprofen—but with fewer side effects. Lab studies show fennel works by calming uterine contractions and reducing inflammation.

Implications of these results

Fennel can be a reliable, low-risk option for managing menstrual pain, especially for teenagers and women who cannot take NSAIDs. Healthcare providers, including nurses and midwives, can recommend it as part of comprehensive menstrual care based on individual conditions and expert opinion.

Keywords: primary dysmenorrhea, *Foeniculum vulgare*, phytotherapy, pain management, herbal medicine, fennel

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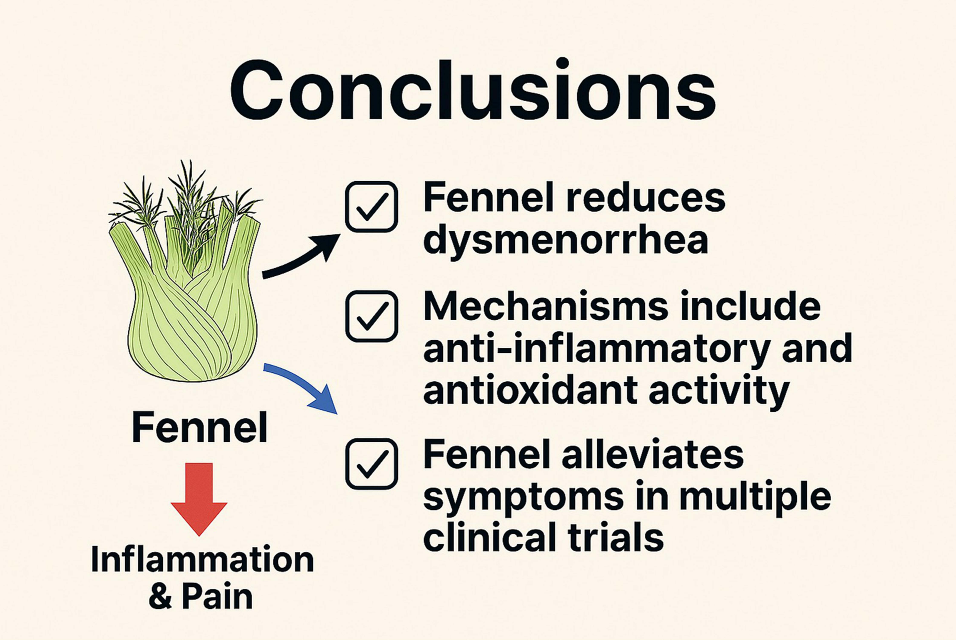
Graphical Abstract



Introduction

Dysmenorrhea, the medical term for painful menstruation is clinically categorized into two subtypes: *primary* (functional, without pelvic pathology) and *secondary* (attributable to underlying gynecological conditions such as endometriosis or adenomyosis).[1] Primary dysmenorrhea (PD) typically emerges 6–12 months after menarche and is pathophysiologically driven by excessive endometrial synthesis of prostaglandins (particularly $PGF_2\alpha$ and PGE_2) during the luteal phase.[2] These eicosanoids trigger intense myometrial contractions, ischemia, and heightened nociception culminating in cramping pelvic pain often accompanied by systemic symptoms like nausea, fatigue, headache, and diarrhea.[3,4]

Dysmenorrhea represents one of the most prevalent gynecological complaints worldwide, with prevalence estimates ranging from 45% to 95% among adolescents and reproductive-aged women.[5,6] A meta-analysis by Abdollahi et al (2018) reported that nearly 71% of female students experience some degree of menstrual pain, with up to 29% describing symptoms severe enough to disrupt daily activities.[7] The condition incurs substantial socioeconomic costs through school and work absenteeism, reduced productivity, and frequent healthcare utilization particularly in low-resource settings where access to effective pain management remains limited.[3]

Beyond physical discomfort, dysmenorrhea profoundly influences psychological, social, and academic domains. Chronic menstrual pain is associated with heightened anxiety, depressive symptoms, and impaired quality of life.[1,4] In adolescents, frequent absenteeism is associated with lower academic performance and social withdrawal.[6] Moreover, inadequate pain control may lead women to develop negative attitudes toward their reproductive health, potentially delaying care for more serious conditions like endometriosis.[5]

First-line pharmacological management of the disease relies heavily on nonsteroidal anti-inflammatory drugs (NSAIDs) such as ibuprofen and mefenamic acid and hormonal contraceptives.[1,8] While effective in many cases, these agents carry significant limitations. Up to 18% of women report inadequate pain relief with NSAIDs, and 20–50% experience adverse gastrointestinal, renal, or hepatic effects with chronic use.[9,10] Hormonal therapies, though potent, are contraindicated in women with thromboembolic risk, hypertension, or personal preference against exogenous hormones.[3] These challenges underscore the urgent need for safe, accessible, and culturally acceptable alternatives.

Despite the high burden of disease, research investment is disproportionately low compared with other chronic pain syndromes.[5] Notably absent are large-scale, mechanistically grounded clinical trials evaluating herbal medicines using standardized preparations, validated pain scales, and long-term safety monitoring. Furthermore, existing literature often neglects contextual factors such as patient preference, affordability, and cultural familiarity with plant-based remedies particularly in the Global South where traditional medicine remains integral to healthcare.[8,11] Fennel (*Foeniculum vulgare*), a widely used culinary and medicinal herb across Middle Eastern, South Asian, and Mediterranean cultures, represents a compelling candidate to address these gaps.

This narrative review advances beyond prior syntheses by integrating three interdependent dimensions of fennel research:

- Biological: Its antispasmodic, anti-inflammatory, and phytoestrogenic mechanisms relevant to uterine physiology.[12,13]
- Chemical: The pharmacologically active constituents including trans-anethole, fenchone, and estragole that modulate prostaglandin synthesis and calcium channel activity.[14,15]
- Therapeutic: A critical appraisal of clinical evidence, including head-to-head comparisons with NSAIDs, combination regimens (with vitamin E), and real-world outcomes on functional impairment.[16,17]

Unlike earlier reviews that catalogued ethnobotanical uses or phytochemistry in isolation,[11,18] our approach establishes a mechanism-to-bedside framework that clarifies *how* and *why* fennel alleviates PD and for whom it may be most beneficial.

This manuscript presents a narrative review rather than a systematic review. The objective is to critically synthesize the current evidence on the use of *Foeniculum vulgare* for primary dysmenorrhea, highlighting efficacy, safety, and the methodological limitations of the existing literature. Given the heterogeneity of study designs, fennel formulations, dosages, treatment durations, and outcome measures, a formal meta-analysis was not considered appropriate.

Narrative reviews can provide important interpretive and clinically meaningful syntheses, particularly in areas where the literature is heterogeneous and not readily amenable to formal quantitative pooling.[19]

By synthesizing high-quality clinical data with molecular insights, this review equips clinicians with evidence-based guidance for recommending fennel as a first- or second-line option particularly for NSAID-intolerant or hormone-averse patients. For women, it validates culturally resonant, low-risk self-management strategies that align with holistic health preferences. At the health policy level, fennel represents a scalable, low-cost intervention that could reduce reliance on pharmaceutical analgesics in resource-constrained settings.[3,20] Ultimately, this work contributes to a paradigm shift: from viewing herbal medicine as "alternative" to recognizing it as an integral component of evidence-informed, patient-centered gynecological care.

Materials and Methods

This study was designed as a narrative review. Unlike a systematic review, the purpose of this approach was to provide a broad, critical, and interpretive synthesis of the available literature on *Foeniculum vulgare* for primary dysmenorrhea.[21] No protocol was registered in PROSPERO, as the review was not intended to follow a formal systematic review framework. However, to enhance methodological transparency, the review was structured according to recognized quality principles for narrative review articles. The methodological approach followed general principles for transparent reporting and evidence synthesis recommended by the International Committee of Medical Journal Editors (ICMJE) and commonly applied in narrative and integrative reviews in women's health research.

Because the objective of this review was to provide an integrative overview of pharmacological mechanisms and clinical evidence rather than to generate pooled quantitative estimates, a narrative synthesis approach was adopted. Therefore, a formal protocol was not registered in PROSPERO and a meta-analysis was not performed. Nevertheless, to enhance transparency and reproducibility, the literature search process, eligibility criteria, and study selection procedures were explicitly defined and documented.

Literature Search Strategy

A structured search of PubMed, MEDLINE, Scopus, Web of Science and Google Scholar was conducted to September 2025. Search terms included a combination of "Foeniculum vulgare", "fennel", "primary dysmenorrhea", "menstrual pain" and "clinical trial". Reference lists of relevant reviews and eligible articles were also manually screened by two authors to identify additional studies.

The search strategy combined controlled vocabulary (MeSH terms) with free-text keywords related to the population, intervention, and outcomes of interest. The key concepts included:

Population: primary dysmenorrhea, menstrual pain, adolescent women, reproductive-age women.

Intervention: *Foeniculum vulgare*, fennel, fennel extract, fennel essential oil.

Outcomes: pain intensity, uterine contraction, prostaglandin inhibition, adverse effects, safety.

An example of the PubMed search string was:

("fennel" OR "Foeniculum vulgare") AND ("primary dysmenorrhea") AND ("pain relief" OR "safety" OR "randomized trial")

No language restrictions were initially applied during the search stage. However, due to feasibility considerations and the predominance of clinical research on fennel conducted in Iran, only full-text articles published in English or Persian were included in the final analysis.

Eligibility Criteria

We included original clinical studies evaluating *Foeniculum vulgare* in women with primary dysmenorrhea. Case reports, editorials, conference abstracts without full data, and non-peer-reviewed theses were excluded.
Studies were considered eligible if they met the following criteria:

- Investigated *Foeniculum vulgare* (including aqueous extract, ethanolic extract, or essential oil) as a monotherapy or as part of a combination therapy for the management of primary dysmenorrhea.
- Reported quantitative outcomes related to pain intensity (VAS, VRS), duration of pain, associated systemic symptoms, or safety outcomes.
- Were original clinical studies involving human female participants aged 12–45 years. Eligible study designs included randomized controlled trials, quasi-experimental studies, and controlled before-after studies.
- Were published up to September 2025.

Data Extraction

A standardized data extraction framework was used to ensure consistent collection of relevant information from eligible studies. Extracted variables included:

- Study characteristics (author, year of publication, country, and study design).
- Participant characteristics (sample size, age range, and diagnostic criteria for primary dysmenorrhea).
- Intervention details (formulation of fennel, dosage, treatment duration, and comparator interventions).
- Outcome measures (pain assessment scales, timing of measurement, and associated symptoms).
- Safety outcomes and reported adverse events.

Data Synthesis

Because this work was conducted as a narrative review rather than a systematic review, full adherence to PRISMA 2020 was not applicable. Nevertheless, key principles of transparent reporting were incorporated, including explicit description of the literature sources, search terms, eligibility criteria, and narrative synthesis approach. Under such circumstances, narrative synthesis is a more appropriate method for summarizing and interpreting the evidence.[22]

Due to the expected heterogeneity across studies in terms of fennel formulations, dosing regimens, study designs, and outcome measures, quantitative meta-analysis was not considered appropriate. Instead, the findings were synthesized using a structured narrative approach.
The evidence was organized thematically into the following domains:

- Biological mechanisms of action (anti-inflammatory, antispasmodic, and phytoestrogenic effects).
- Clinical efficacy in reducing menstrual pain and associated symptoms.
- Safety profile and reported adverse events.

The synthesis focused on studies involving adolescent and adult women with primary dysmenorrhea, while pediatric populations were excluded to maintain consistency with the defined scope of the review.

Results

Clinical investigations into the therapeutic application of *Foeniculum vulgare* (fennel) for primary dysmenorrhea reveal consistent efficacy, favorable safety, and multifaceted symptomatic benefits beyond mere pain reduction. While numerous trials confirm analgesic effects comparable to conventional NSAIDs, a deeper examination of trial reports uncovers nuanced therapeutic dimensions (Table 1).

The potential mechanism, Biological and Chemical of efficacy of some pharmacologic properties of *Foeniculum vulgare* Mill (Table 2).

Table 1 Clinical Evidence on Fennel (*Foeniculum vulgare*) for Primary Dysmenorrhea

Study (Year) Reference	Population & Design	Fennel Intervention/ Exposure	Duration	Key Outcomes
Ghodsi & Asltoghiri 2014[4]	80 students female; quasi-experimental	Fennel capsules (30 mg, three times daily)	Three cycles	Relieves symptoms of dysmenorrhea and ↓ menstrual duration
Delaram & Foroozandeh 2011[23]	60 students female; clinical trial	Fennel extract capsules (30 mg, three times daily)	Two cycles	↓severity of dysmenorrhea reported pain relief.
Manochehri Tarshizi et al 2005[16]	90 high school students with primary dysmenorrhea; randomized controlled trial	Fennel extract capsules (30 mg, every 8 hours) vs. ibuprofen (400 mg TDS)	One cycle	↓severity of dysmenorrhea reported pain relief.
Modaress Nejad & Asadipour 2006[9]	55 girls; randomized clinical trial	Fennel extract vs. mefenamic acid (500 mg TDS)	Two menstrual cycles	↓Pain dysmenorrhea
Namavar Jahromi et al 2003[10]	70 female and girls; double-blind RCT	Fennel essential oil capsules (30 mg TDS) vs.	Two cycles	Improve dysmenorrhea
Nasehi et al 2013[17]	68 female students; triple-arm RCT	Capsule/daily	Two menstrual cycles	↓ The severity of primary dysmenorrhea pain
Moslemi et al 2012[24]	65 female students; RCT	Fennel extract (30 mg TDS) vs. placebo	Two cycles	↓Pain dysmenorrhea
Omidvar et al 2012[25]	50 female students; placebo-controlled trial	Fennel extract capsules (30 mg TDS)	Two cycles	↓Pain dysmenorrhea

(*Continued*)

Table 1 (Continued).

Study (Year) Reference	Population & Design	Fennel Intervention/ Exposure	Duration	Key Outcomes
Akhavan Amjadi et al 2010[26]	90 female; clinical trial	Capsules, 46 mg/daily	Two cycles	Inhibiting uterine contractions and increasing menstrual bleeding
Torkzahrani et al 2007[27]	90 female students; RCT	Five capsules daily, 46 mg	Two cycles	↓severity of dysmenorrhea
Nesa et al 2019[28]	100 female; RCT	Fennel supplementation 10 mL three times daily.	One cycle	↓ The severity of primary dysmenorrhea pain
Bokaie et al 2013[29]	60 female students, double-blind, randomized, placebo-controlled trial	Oral fennel drops (2% concentration, 30 drops twice daily)	Two menstrual cycles	↓severity of dysmenorrheareported pain relief.

Notes: ↓ indicates a decrease in the reported outcome (reduced pain intensity, decreased menstrual duration, or diminished severity of dysmenorrhea).

Table 2 Pharmacological Effects of *Foeniculum vulgare* and Their Proposed Mechanisms of Action[30]

Pharmacological Effect	Proposed Mechanism of Efficacy
Anti-microbial activity	Presence of bioactive compounds such as oleic acid and coumarin in aqueous and alcoholic extracts.
Antioxidant activity	Rich in flavonoids and phenolic compounds in aqueous and ethanolic extracts that scavenge free radicals and enhance endogenous antioxidant defenses.
Anti-inflammatory activity	Methanolic extract exerts preventive effects against acute and subacute inflammation and type IV hypersensitivity reactions via inhibition of cyclooxygenase (COX) and lipoxygenase (LOX) pathways.
Anti-anxiety activity	Anxiolytic effects mediated through modulation of GABAergic neurotransmission and interaction with estrogen receptors.
Gastro-protective activity	Regulation of intestinal motility; relief of gastrointestinal spasms and chronic colitis; protection against gastric ulceration; reduction in gastric mucosal damage.
Estrogenic activity	Presence of compounds such as anethole, which mimic estrogenic effects—enhancing lactation, reducing menstrual pain, facilitating labor, and alleviating symptoms of primary dysmenorrhea and infertility.
Anti-lipid (Hypolipidemic) activity	Reduction in plasma triglycerides and total cholesterol; lowering of LDL and apolipoprotein B; elevation of HDL and apolipoprotein A-1.

Chemical Composition and Key Bioactive Constituents

Foeniculum vulgare Mill. (fennel), a perennial herb of the Apiaceae family, is phytochemically rich in volatile and non-volatile compounds that underpin its therapeutic versatility. The essential oil of fennel seeds comprising 2–6% of dry weight is dominated by trans-anethole (60–80%), a phenylpropene derivative responsible for its characteristic aroma and primary pharmacological actions.[11,14] Additional constituents include fenchone (3–20%), estragole (methyl chavicol, ≤10%), limonene, and α-pinene, each contributing to its antimicrobial, antioxidant, and spasmolytic properties.[11,14] Non-volatile fractions contain flavonoids (quercetin, apigenin), phenolic acids (rosmarinic acid), and coumarins, which synergistically enhance its anti-inflammatory and estrogenic activities.[14,31]

The chemical profile varies by cultivar, geography, and extraction method, with sweet fennel (low estragole) preferred for medicinal use due to safety concerns about estragole's potential genotoxicity at high doses.[11,32] Standardization of trans-anethole content is thus critical for reproducible clinical outcomes.[14,15]

Anti-Inflammatory and Antioxidant Mechanisms (Figure 1)

Fennel exerts potent anti-inflammatory effects through multiple pathways relevant to dysmenorrhea pathophysiology. Trans-anethole suppresses the production of prostaglandins ($PGF_2\alpha$ and PGE_2) key mediators of uterine hypercontractility and pain by inhibiting cyclooxygenase-2 (COX-2) expression and phospholipase A_2 activity, without significantly affecting COX-1, thus reducing gastrointestinal toxicity risk.[11,33] In animal models, fennel extract significantly lowers serum levels of pro-inflammatory cytokines (IL-6, TNF-α) and reactive oxygen species (ROS), while enhancing endogenous antioxidants such as superoxide dismutase (SOD) and glutathione peroxidase.[13,14]

Notably, Imran et al (2019) demonstrated that fennel ameliorates oxidative stress in neural and systemic tissues, suggesting broad cellular protection that may extend to endometrial tissue during menstruation.[13] The flavonoid fraction further contributes by scavenging free radicals and modulating NF-κB signaling a master regulator of inflammation implicated in menstrual pain.[11,33] Choi et al examined the anti-inflammatory potential of a fennel methanol extract and demonstrated that its activity operates via dual pathways engaging both central nervous system and peripheral physiological mechanisms.[34]

Uterine Modulatory Effects and Antispasmodic Action

The therapeutic efficacy of fennel in dysmenorrhea is largely attributed to its direct antispasmodic effect on uterine smooth muscle. In an ex vivo pharmacological model using rat uterine tissue, Ostad et al (2001) demonstrated that fennel essential oil (0.5–2 mg/mL) dose-dependently inhibited both spontaneous and oxytocin-induced contractions an effect

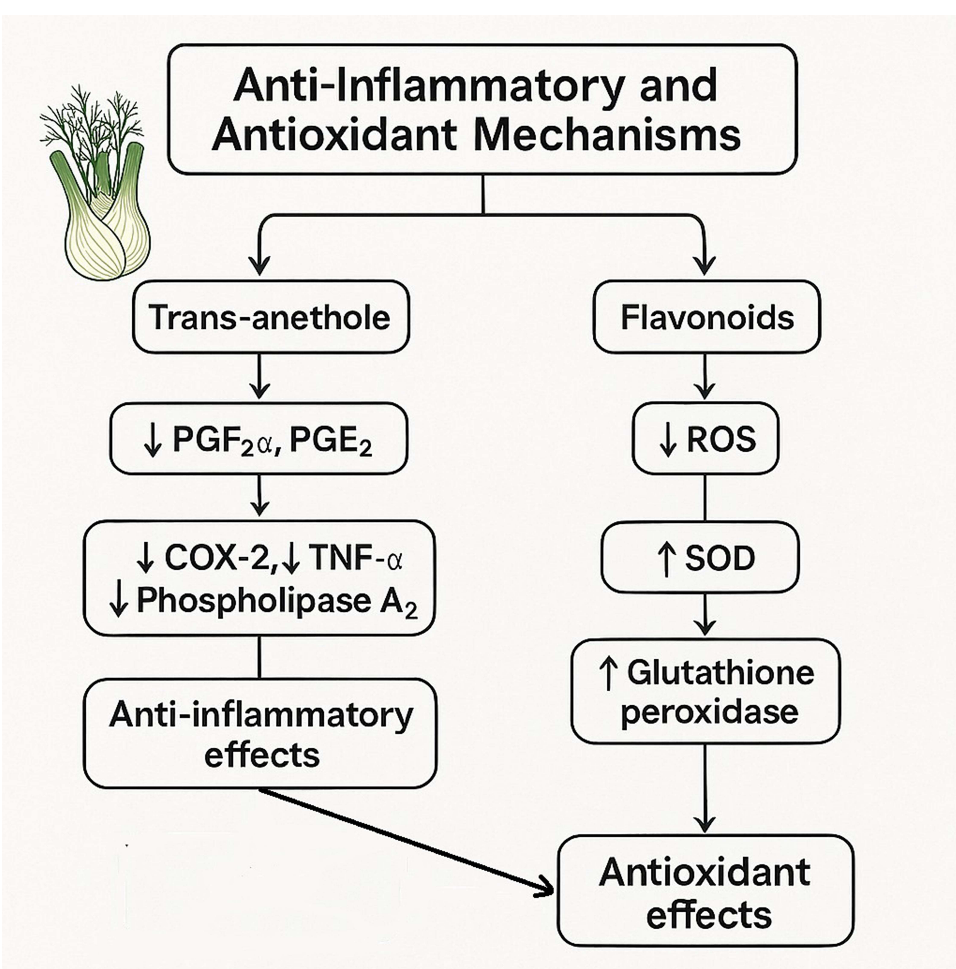


Figure 1 Mechanistic Pathways of Fennel's Anti-Inflammatory and Antioxidant Effects in Dysmenorrhea.

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comparable to papaverine.[12] The mechanism involves blockade of voltage-dependent calcium channels, reducing intracellular Ca^{2+} influx and thereby decreasing myometrial contractility.[11,12]

This action directly counteracts the prostaglandin-mediated hypercontractility characteristic of primary dysmenorrhea. Additionally, fennel's mild phytoestrogenic activity mediated by anethole and flavonoids may modulate endometrial prostaglandin synthesis by influencing estrogen receptor signaling, although this pathway requires further validation in human endometrial tissue.[8,35] Akhavan Amjadi et al (2010) observed that fennel not only reduced pain but also increased menstrual flow, interpreted as relief from spastic obstruction a finding consistent with smooth muscle relaxation.[26]

Estrogenic Activity

Foeniculum vulgare has been utilized for centuries in traditional medicine as a phytoestrogenic agent. Its estrogen-like effects underlie several therapeutic applications, including the stimulation of lactation, alleviation of menstrual pain, facilitation of labor, and enhancement of libido. The primary bioactive constituent responsible for these actions is anethole, a phenylpropene compound abundant in fennel essential oil. Notably, research indicates that dianethole and photoanethole bioactive derivatives formed as polymeric forms of anethole contribute significantly to its estrogenic potency.[36]

Clinical and preclinical studies have demonstrated that fennel essential oil is well tolerated in the management of primary dysmenorrhea, with a favorable safety profile compared to conventional pharmacotherapies. Experimental models reveal that fennel extract, in a dose-dependent manner, markedly suppresses uterine contractions triggered by oxytocin and prostaglandins.[12] Furthermore, animal studies have shown that moderate doses of fennel extract enhance mammary gland development, while higher doses induce hypertrophy of reproductive tissues, including the oviduct, endometrium, myometrium, and cervix—consistent with estrogenic stimulation.[37]

Traditionally, fennel has also been employed to address female infertility. Supporting this use, experimental evidence shows that fennel extract modulates reproductive endocrinology by elevating serum levels of follicle-stimulating hormone (FSH) while reducing circulating concentrations of yolk precursor proteins and testosterone.[38] In a complementary study, Devi et al examined the effects of an acetone extract of fennel fruits on the mammary glands and oviducts of experimental animals; their findings corroborated the extract's estrogenic activity, demonstrating histological and functional changes comparable to those induced by endogenous estrogens.[39]

Clinical Application in the Treatment of Primary Dysmenorrhea

Clinical trials consistently support fennel's efficacy in reducing pain intensity, duration, and associated symptoms in primary dysmenorrhea. Multiple RCTs report that 30 mg of fennel extract three times daily initiated 2–3 days before menstruation significantly reduces pain scores on visual analog scales (VAS) within 1–2 hours, with effects sustained over 2–3 cycles.[4,24,29] Fennel's efficacy is non-inferior to NSAIDs: Manochehri Tarshizi et al (2005) found fennel as effective as ibuprofen, while Namavar Jahromi et al (2003) and Modaress Nejad & Asadipour (2006) reported comparable outcomes to mefenamic acid.[9,10,16]

Importantly, fennel exhibits a superior safety profile, with minimal gastrointestinal or systemic side effects.[24,29] Combination regimens such as fennel with vitamin E or mefenamic acid show additive or synergistic benefits, enabling lower NSAID doses and faster pain relief.[17,28] These findings position fennel as a first-line phytotherapeutic alternative, particularly for adolescents and women with NSAID intolerance.

Comparative Efficacy Against Standard Pharmacotherapies

Modaress Nejad and Asadipour (2006) reported that fennel extract demonstrated non-inferiority to mefenamic acid (500 mg TDS) in improving participants' ability to attend academic or work obligations during menses.[9] Namavar Jahromi et al (2003) further corroborated these findings, noting that both fennel and mefenamic acid significantly reduced the need for supplementary painkillers, with fennel exhibiting a more favorable gastrointestinal tolerability profile.[10]

Symptom-Specific and Systemic Benefits

Beyond pain alleviation, fennel demonstrated broader symptom-modifying effects. Ghodsi and Asltoghiri (2014) documented significant reductions in nausea, fatigue, and headache severity common systemic manifestations of primary dysmenorrhea in the fennel group compared to baseline, suggesting a systemic modulatory effect on prostaglandin-mediated symptoms.[4]

Delaram and Foroozandeh (2011) additionally reported improved menstrual regularity and reduced incidence of premenstrual tension following two cycles of fennel supplementation.[23] These findings imply that fennel may influence not only uterine contractility but also hypothalamic pituitary ovarian axis regulation or inflammatory cascades linked to cyclical symptomatology.

Onset and Duration of Therapeutic Action

The temporal dynamics of fennel's effect provide further clinical relevance. Omidvar et al (2012) noted that pain relief in the fennel group began within 2 hours of the first dose a timeframe comparable to fast-acting NSAIDs and was sustained throughout the menstrual episode.[25] Bokaie et al (2013), using a liquid drop formulation (2% fennel oil), observed a progressive decline in pain intensity scores from cycle 1 to cycle 2, suggesting a cumulative or adaptive therapeutic benefit with repeated use.[29]

Safety and Tolerability Profile

Adverse events across trials were consistently mild and infrequent. Moslemi et al 2012[24] and Nasehi et al 2013[17] reported no serious adverse effects in fennel-treated groups; minor complaints such as mild dizziness or transient epigastric discomfort occurred at rates comparable to placebo. In contrast, NSAID control groups frequently reported gastrointestinal upset (heartburn, epigastric pain), highlighting fennel's improved safety margin for long-term or repeated-cycle use.

Combination Therapy and Synergistic Potential

Emerging evidence supports fennel's role in combination regimens. Nasehi et al (2013) found that co-administration of fennel extract with vitamin E not only matched ibuprofen's efficacy but also enhanced participant-reported satisfaction and reduced analgesic dependency.[17] Similarly, Nesa et al (2019) demonstrated that combining fennel with mefenamic acid achieved faster pain resolution (within 1 hour) compared to mefenamic acid alone, suggesting a pharmacokinetic or pharmacodynamic synergy that warrants further investigation.[28]

Physiological and Hormonal Correlates

Although most trials focused on symptomatic outcomes, Akhavan Amjadi et al (2010) uniquely assessed menstrual blood volume, reporting a paradoxical increase in flow alongside pain reduction interpreted not as a pathological effect but as relief from excessive uterine spasm causing obstructed outflow.[26]

Collectively, these findings position fennel not merely as an analgesic alternative but as a multi-target therapeutic agent addressing pain, systemic symptoms, functional impairment, and uterine hypercontractility in primary dysmenorrhea with a safety profile conducive to repeated use in adolescent and young adult populations.

Discussion

Interpretation of Core Findings

Although narrative reviews do not provide the same level of reproducibility as systematic reviews, they remain valuable when the available evidence is methodologically diverse and requires contextual interpretation rather than quantitative aggregation.[21]

This narrative review was conceived to address a critical gap in integrative gynecology: the lack of a consolidated, mechanism-to-clinic synthesis of fennel (*Foeniculum vulgare*) as a therapeutic agent for primary dysmenorrhea. Our analysis demonstrates that fennel is not merely a folk remedy but a phytochemically sophisticated intervention whose efficacy stems from a triad of actions anti-inflammatory modulation via prostaglandin suppression, direct antispasmodic effects on uterine smooth muscle, and systemic symptom relief supported by consistent clinical evidence. Crucially, fennel achieves therapeutic outcomes comparable to NSAIDs while offering a markedly superior safety profile, particularly regarding gastrointestinal tolerability. These findings position fennel as a viable, culturally resonant, and patient-preferred first-line option for millions of adolescents and women burdened by menstrual pain.

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A growing body of evidence supports the therapeutic potential of *Foeniculum vulgare* (fennel) in alleviating primary dysmenorrhea, a common gynecological condition characterized by painful menstrual cramps without underlying pelvic pathology. A recent meta-analysis by Shahrahmani et al (2021) demonstrated that fennel significantly reduced the intensity of dysmenorrheic pain compared to placebo (SMD = −0.632; 95% CI: −0.827 to −0.436; $p < 0.001$), with no statistical heterogeneity ($I^2 = 0\%$, p = 0.807), supporting the robustness of the effect across seven randomized trials. However, when directly compared to mefenamic acid a commonly prescribed nonsteroidal anti-inflammatory drug fennel showed no statistically significant difference in pain reduction (SMD = −0.214; 95% CI: −0.446 to 0.017; p = 0.07), suggesting comparable efficacy between herbal and conventional pharmacological interventions.[6,40]

Despite these promising findings, conflicting data exist. Another meta-analysis reported a significant overall benefit of fennel in reducing dysmenorrhea (fixed-effect OR = 0.573, 95% CI: 0.414–0.793; p = 0.001), but also highlighted substantial heterogeneity ($I^2 = 95.96\%$), likely stemming from variations in fennel preparations, dosing regimens, and study populations.[41] This heterogeneity underscores the current inability to determine an optimal dosage or formulation, thereby calling for standardized, multicenter clinical trials to clarify fennel's therapeutic profile.

The analgesic and antispasmodic effects of fennel appear to be mediated through multiple biological pathways. Preclinical studies have identified that fennel essential oil exhibits significant antinociceptive activity in murine models, with methanolic and ethyl acetate extracts showing the most potent effects in acetic acid–induced writhing tests.[42] Moreover, fennel oil demonstrates concentration-dependent inhibition of prostaglandin E_2–induced uterine contractions, a key mechanism in dysmenorrhea pathophysiology.[12] In vitro, both alcoholic extracts and essential oils of fennel suppress smooth muscle spasms by antagonizing acetylcholine and histamine receptors in guinea pig ileum, and by inhibiting oxytocin- and prostaglandin-mediated uterine activity.[43]

Phytochemically, fennel's efficacy is attributed to its rich composition of volatile oils (notably anethole), flavonoids, and phenolic compounds, which collectively confer antioxidant, anti-inflammatory, and antispasmodic properties.[11,32] Additionally, fennel exhibits mild estrogenic activity, which may contribute to menstrual cycle regulation and symptom relief in dysmenorrhea.[36]

In summary, current evidence spanning clinical meta-analyses, in vivo pharmacological models, and in vitro mechanistic studies supports fennel as a safe and effective herbal alternative for managing primary dysmenorrhea. However, variability in extract composition and a lack of standardized protocols necessitate further high-quality trials to establish evidence-based clinical guidelines.

Limitations of Current Evidence

Despite promising results, several limitations persist across the literature. First, nearly all clinical trials originate from Iran or South Asia,[17,24,29] limiting generalizability to other populations with different dietary, hormonal, or genetic backgrounds. Second, methodological heterogeneity exists in fennel preparations capsules, drops, or oils with variable standardization of active constituents (trans-anethole content), making dose-response relationships difficult to establish. Third, most trials are short-term (1–3 cycles), offering no data on long-term safety or efficacy. Fourth, none measure objective biomarkers such as serum prostaglandin levels to correlate symptom reduction with biochemical change. Finally, several studies[23,27] lack full methodological transparency (randomization concealment, blinding procedures), reducing confidence in effect size estimates.

Scientific, Clinical, and Policy Implications

Scientifically, fennel exemplifies how traditional medicinal knowledge can be validated through modern pharmacological inquiry. The convergence of ex vivo (Ostad et al, 2001),[12] phytochemical,[11] and clinical evidence[4,29] creates a robust mechanism-to-bedside narrative.

Clinically, fennel offers gynecologists a safe, effective, and culturally acceptable alternative for adolescents and women who cannot tolerate NSAIDs or prefer non-hormonal options. Given the high prevalence of dysmenorrhea[7] affecting up to 95% of young women integrating fennel into first-line management could reduce analgesic overuse and school/work absenteeism.

At the policy level, fennel aligns with WHO's traditional medicine strategy, which encourages evidence-based integration of herbal medicines into primary care. Standardized fennel extracts could be included in national essential medicine lists, particularly in low-resource settings where access to pharmaceuticals is limited. Future efforts should focus on:

- Developing pharmacopeial standards for fennel preparations,
- Conducting large, multicenter RCTs with objective endpoints,
- Exploring fennel's potential in secondary dysmenorrhea (endometriosis), where inflammation also plays a central role.

In conclusion, fennel is not merely a folk remedy but a scientifically grounded therapeutic agent whose integration into modern gynecological practice could significantly improve menstrual health equity and quality of life for millions of women worldwide.

Adverse Effects and Contraindications of Foeniculum vulgare in Adults and Adolescents

While *Foeniculum vulgare* (fennel) is widely regarded as safe for short-term use in adults and adolescents, emerging clinical and toxicological evidence indicates that its consumption is not without risk, particularly with prolonged or high-dose administration. The herb's favorable tolerability in clinical trials for primary dysmenorrhea characterized by minimal gastrointestinal upset, dizziness, or epigastric discomfort at standard doses (30 mg TDS of standardized extract) must be weighed against potential endocrine, allergic, and toxicological concerns.[17,24,29]

A primary safety consideration stems from fennel's phytoestrogenic activity, mediated predominantly by *trans*-anethole and flavonoid constituents. Although this property underlies its therapeutic efficacy in menstrual pain and lactation support, it also poses significant risks in individuals with hormone-sensitive conditions. Preclinical data demonstrate that chronic administration of fennel extract (200 mg/kg/day for 8 weeks) in female rats induces endometrial hyperplasia, disrupts estrous cyclicity, and elevates serum estradiol levels raising concerns about potential stimulation of estrogen receptor–positive tissues in humans.[44] Consequently, fennel is contraindicated in patients with a history of estrogen-dependent malignancies, including breast, ovarian, or endometrial cancer, or in those with unexplained uterine bleeding until further clinical safety data are available.

Additionally, fennel contains furocoumarins (psoralen) and phenylpropenes (notably estragole), which have been implicated in phototoxic and photoallergic reactions, particularly upon dermal exposure to concentrated essential oils.[45]

While the levels present in therapeutic oral doses (30–46 mg/day of extract) are unlikely to pose significant risk over 2–3 menstrual cycles as used in clinical trials the long-term safety of daily or year-round consumption remains unestablished. Regulatory bodies such as the European Medicines Agency (EMA) recommend limiting estragole intake and favoring sweet fennel cultivars with low estragole content for medicinal use.[11]

Notably, no evidence of dependence, withdrawal, or abuse potential has been reported with fennel use, and it is not associated with sedation or cognitive impairment. However, due to its modulatory effects on cytochrome P450 enzymes (particularly CYP1A2 and CYP3A4) and potential interactions with hormonal or anticoagulant medications, fennel should be used cautiously in patients on concurrent pharmacotherapy, especially oral contraceptives, tamoxifen, or.[3]

In summary, while fennel offers a well-tolerated, non-hormonal alternative for managing primary dysmenorrhea in adolescents and adults, its use requires individualized risk assessment. Contraindications include known hypersensitivity to *Apiaceae* plants, history of hormone-sensitive cancers, and concurrent use of medications with narrow therapeutic indices. Future research should prioritize long-term safety monitoring and establish maximum safe durations of use in reproductive-aged women.

Primary dysmenorrhea, remains a common and often debilitating condition, motivating interest in complementary options such as *Foeniculum vulgare*. Clinical findings suggest that fennel may reduce pain intensity and improve associated symptoms, with effects comparable to NSAIDs in some trials. Proposed mechanisms including modulation of COX-2 activity, attenuation of prostaglandin synthesis, and calcium-channel interactions provide a plausible biological basis, although most mechanistic evidence is derived from preclinical studies and only limited human biomarker data are available.

To reduce the inherent limitations of narrative reviews, we aimed to improve the transparency and structure of the manuscript by clearly presenting the review objective, literature identification process, eligibility considerations, and interpretive framework, in line with recommended quality principles for narrative review articles.[46]

Short-term use appears well tolerated, but long-term safety remains uncertain, particularly regarding cumulative exposure to estragole, who Despite these promising findings, several limitations of the current evidence base should be acknowledged. First, a considerable proportion of clinical trials evaluating *Foeniculum vulgare* for primary dysmenorrhea have been conducted in Iran and neighboring regions, which may limit the generalizability of the findings to populations with different genetic, dietary, and cultural backgrounds.[9,29] Second, notable heterogeneity exists in the formulations and dosages of fennel used across studies, including capsules, essential oils, and oral drops, often without clear phytochemical standardization of active constituents such as trans-anethole, which complicates cross-study comparisons and dose–response interpretation.[9,12] Third, the duration of follow-up in most trials has been relatively short, typically limited to one to three menstrual cycles, restricting conclusions regarding sustained efficacy and long-term safety.[9,29] Finally, some studies provide limited methodological detail regarding allocation concealment or blinding procedures, which may increase the potential risk of bias. These considerations highlight the need for well-designed, multicenter randomized controlled trials using standardized fennel preparations and longer follow-up periods to further clarify the clinical role of *Foeniculum vulgare* in the management of primary It affects many women.se clinical relevance has yet to be fully defined.

Future multicenter randomized controlled trials using standardized *Foeniculum vulgare* preparations, harmonized dosing protocols, and validated outcomes are needed to confirm efficacy and establish external validity.

Conclusion

Taken together, the available evidence suggests that *Foeniculum vulgare* may offer a culturally acceptable, low cost, and generally well tolerated option for the management of primary dysmenorrhea, particularly in settings where traditional herbal remedies are already embedded in menstrual care. However, the current data are largely derived from regional trials with variable methodological quality, short follow up durations, and heterogeneous formulations, and the proposed mechanisms of action remain only partially validated by human biomarker studies. Moreover, although short term safety profiles are encouraging, important uncertainties persist regarding long term use, high dose preparations, and estragole related toxicological risks. Therefore, these findings should be interpreted cautiously, and larger multicenter trials in diverse populations are warranted.

Therefore, stronger evidence from standardized, adequately powered, multicenter randomized controlled trials incorporating rigorous methodological safeguards, mechanistic biomarker endpoints, and comprehensive long term safety monitoring is needed before fennel can be confidently recommended for broad integration into global clinical guidelines for primary dysmenorrhea.

Ethics Statement

This article is based exclusively on the analysis of scientific literature indexed and retrieved from authoritative databases. This article dose not involve human subjects, animal experiments,or clinical interventions. Consequently, this study is exempt from ethical approval and no approval from an ethics committee was required or requested.

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This article has not been presented at any national or international conference, and no abstract nor preliminary report of this study has been previously published. However, we would like to thank all the authors whose articles and reaserch contributed to the compilation and presentation of our article.

Author Contributions

Saboura Sahebi: Conceptualization, methodology, writing – original draft, writing – review & editing, project administration. 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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