15 (2026) 100163

Contents lists available at ScienceDirect

Journal of Endometriosis and Uterine Disorders

journal homepage: www.elsevier.com/locate/jeud

Review

Effectiveness of the natural compounds for the treatment of dysmenorrhea: A narrative overview

Stefania Greco [a,b], Giovanni Delli Carpini [c], Abel Duménigo González [a], Gaia Goteri [d], Andrea Ciavattini [c], Pasquapina Ciarmela [a,*,1]

[a] Department of Experimental and Clinical Medicine, Università Politecnica delle Marche, 60126 Ancona, Italy
[b] Department of Life, Health and Health Profession Sciences, Link Campus University, Rome, Italy
[c] Department of Clinical Sciences, Università Politecnica delle Marche, 60126 Ancona, Italy
[d] Department of Biomedical Sciences and Public Health, Università Politecnica delle Marche, 60126 Ancona, Italy

ARTICLE INFO

Keywords:
Dysmenorrhea
Natural compound
Pelvic pain

ABSTRACT

Dysmenorrhea is a prevalent condition among women of reproductive age, causing significant pelvic pain during menstruation. While conventional treatments such as NSAIDs and hormonal contraceptives are commonly used, they may cause side effects, leading to interest in alternative therapies. This review investigates the potential of natural compounds and complementary treatments in alleviating dysmenorrhea symptoms, comparing their effectiveness and safety to standard pharmacological treatments.

Search was conducted in PubMed, Scopus, Web of Science, and Google Scholar, focusing on human studies involving natural compounds and alternative therapies for dysmenorrhea. Both clinical trials and observational studies were included.

Several natural compounds were identified with potential benefits for managing dysmenorrhea. Herbal remedies such as ginger, fennel, and chamomile demonstrated anti-inflammatory effects and pain reduction. Omega-3 fatty acids and magnesium supplements showed significant efficacy in reducing pain intensity. Complementary therapies, including acupuncture and psychological support, were also highlighted as effective in enhancing pain relief and improving overall well-being.

Natural compounds and complementary therapies offer promising, safer alternatives to conventional treatments for dysmenorrhea. Further research is needed to validate their long-term efficacy and establish clear clinical guidelines. While natural compounds offer a promising alternative for dysmenorrhea management, particularly for patients unresponsive to NSAIDs, the current evidence base is limited by small sample sizes and methodological heterogeneity. Future research must prioritize large-scale, rigorously designed randomized controlled trials to establish standardized dosing, long-term safety profiles, and definitive clinical guidelines. Integrating these approaches, especially when combined with psychological support, could significantly improve the quality of life for women suffering from dysmenorrhea.

Introduction

Dysmenorrhea, defined as pain during the menstrual cycle, is a debilitating condition affecting millions of women worldwide, with a wide range of reported prevalence (17–90%) [1,2]. This disorder can impact women of all ages, but it is particularly prevalent among younger individuals during puberty and early adulthood [1]. Dysmenorrhea is categorized into two primary types, primary and secondary, according to the absence or presence of an underlying organic disease.

Primary dysmenorrhea typically begins in concomitance with the onset of ovulatory cycles. Thus, it may present within the first 6–12 months, or up to two years after menarche [3,4]. The association with ovulatory cycles seems to be related to the breakdown of lysosomes containing prostanoids secondary to the reductions in progesterone levels at the end of luteal phase [2] (Fig. 1).

The pain is typically localized in the pelvic region but may radiate to

* Corresponding author.
E-mail address: p.ciarmela@univpm.it (P. Ciarmela).

[1] Given her role as Associate Editor, Pasquapina Ciarmela had no involvement in the peer-review of this article and has no access to information regarding its peer-review. Full responsibility for the editorial process for this article was delegated to another journal editor.

https://doi.org/10.1016/j.jeud.2026.100163
Received 11 March 2026; Accepted 23 April 2026
Available online 29 April 2026

the lumbosacral area of the back and upper thighs. Women often describe the pain as cramp-like, sharp, or dull in nature. Additional symptoms can include nausea, vomiting, headaches, dizziness, fatigue, and sleep disturbances [2,5,6]. These symptoms can significantly disrupt daily activities and substantially affect quality of life. Importantly, the lack of any identifiable pathological condition causing these symptoms may exacerbate the psychological impact of this phenomenon [7,8].

In contrast, secondary dysmenorrhea refers to menstrual pain associated with organic diseases, such as endometriosis, adenomyosis, congenital uterine abnormalities, uterine fibroids, large cesarean scar niche, endometrial polyps, intrauterine adhesions, or pelvic inflammatory disease [9,10]. Patients affected by this type of dysmenorrhea can also suffer from the consequences of the organic diseases, such as infertility, heavy menstrual bleeding, iron-deficiency, and anemia. Furthermore, dysmenorrhea can affect emotional and social well-being, contributing to issues such as loss of sexual activity and depression. The overall impact of dysmenorrhea is widespread among women. The World Health Organization (WHO) estimates that dysmenorrhea is the leading cause of chronic pelvic pain, highlighting its significance as a health concern. Moreover, the effects of dysmenorrhea can lead to absenteeism from work or school, as well as emotional effects such as mood swings and fatigue. Meanwhile, secondary dysmenorrhea is associated with even greater risks due to the underlying organic diseases, underscoring the importance of recognition and management of this condition in improving the quality of life for those affected [11]. While several high-quality systematic reviews and meta-analyses have previously evaluated individual natural compounds for dysmenorrhea (such as those by Proctor and Murphy on herbal therapies, Smith et al. on acupuncture, and Snipe et al. on omega-3 s), the landscape of alternative therapies is rapidly expanding. The present narrative review aims to bridge a critical gap by providing a comprehensive, clinically oriented synthesis of both well-established and emerging natural compounds. Unlike prior reviews that often focus narrowly on efficacy statistics, this manuscript systematically integrates recent mechanistic insights with practical clinical implications, specifically addressing the multidisciplinary management of patients who are refractory to, or contraindicated for, conventional pharmacological treatments.

Etiology and pathophysiological mechanisms

Numerous studies in the literature have investigated the etiology and pathophysiological mechanisms underlying the onset of dysmenorrhea [12]. Although the pathogenic mechanisms are not yet fully understood, the literature suggests that dysmenorrhea is a complex, multifactorial process. A study by Lundstrom et al. found that dysmenorrhea is associated with elevated prostaglandin levels [13]. Prostaglandins play a key role in regulating ovulation and the physiology of the endometrium, including its proliferation and the changes it undergoes during menstruation [14]. High levels of prostaglandins lead to increased myometrial activity, stronger uterine contractions, and, consequently, pain. Additionally, elevated prostaglandin levels recruit inflammatory mediators, such as leukotrienes, which accumulate in the endometrium following the decline in progesterone levels during the late luteal phase. The concentration of these mediators is believed to be directly proportional to the intensity of menstrual cramps and pain [15,16]. Vasopressin also plays a significant role in the pathophysiology of dysmenorrhea by enhancing uterine contractions, which can lead to ischemic or hypoxic events in the uterus. This, in turn, increases the sensitivity of nerve endings and contributes to the onset of inflammation and pain [17,18].

The literature highlights the role of genetics in the pathophysiology of dysmenorrhea. One of the most significant genetic studies suggests that primary dysmenorrhea tends to run in families, particularly affecting adolescent and young women. Specifically, it has been found that mothers with dysmenorrhea are more likely to transmit the condition to their daughters, suggesting a genetic predisposition. A study comparing pain intensity in monozygotic and dizygotic twins found that pain was more severe in monozygotic twins, who were more frequently affected by dysmenorrhea, further supporting this genetic link [19].

Other genetic studies have identified differences in gene expression between women with and without dysmenorrhea, highlighting the differential modulation of certain genes (either overexpressed or under expressed) in women with the condition. One study identified common variants in the Zinc finger MIZ-type containing 1 (ZMIZ1) gene (locus rs76518691) and the Nerve Growth Factor (NGF) gene (rs7523831) that increase the risk of primary dysmenorrhea. The NGF gene is involved in pain production, while ZMIZ1 is mainly associated with autoimmune

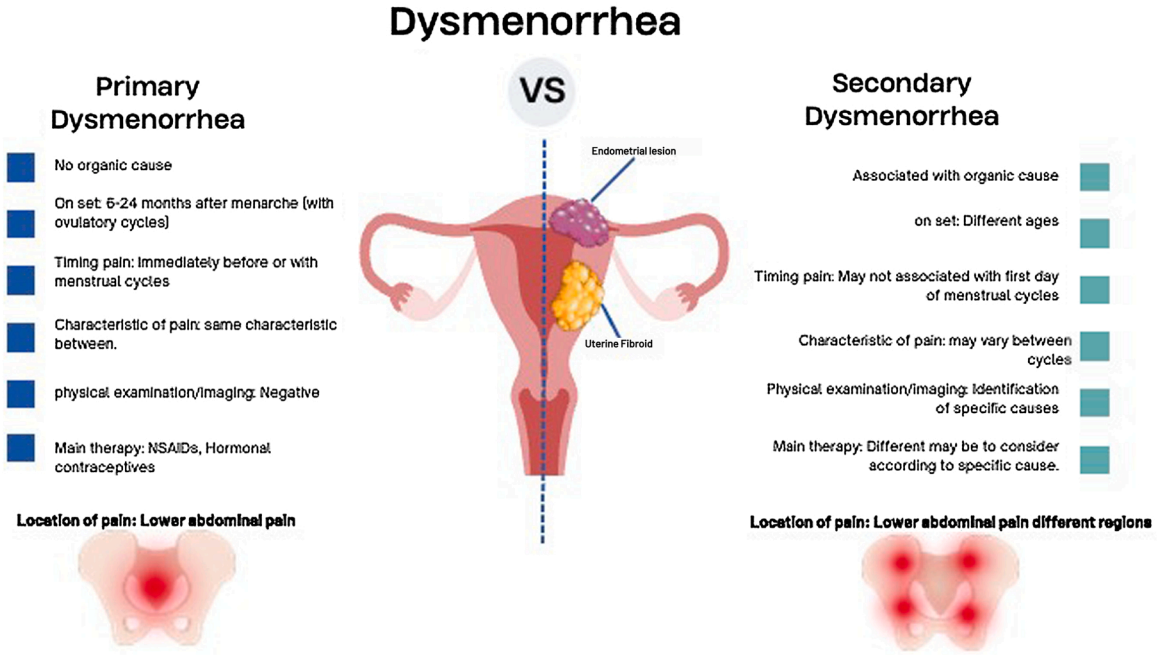

Fig. 1. Representative list of differences between primary and secondary dysmenorrhea.

diseases. Another study on Taiwanese individuals with dysmenorrhea found a correlation with a polymorphism in the Brain-Derived Neurotrophic Factor (BDNF) gene (Val66Met), suggesting that this polymorphism affects pain modulation systems and could regulate pain intensity [20] (Fig. 2).

As a multifactorial condition, the onset of dysmenorrhea is also linked to other factors. For example, smoking or exposure to tobacco smoke may worsen menstrual pain, likely because nicotine induces vasoconstriction, particularly in the myometrium [21]. Other debated risk factors for dysmenorrhea include a low body mass index (BMI), prolonged menstrual bleeding, a history of pregnancy loss, suspected pelvic inflammatory disease, premenstrual syndrome, and psychological symptoms [22]. Modifiable risk factors, such as poor mental health—including depression, anxiety, frequent life changes, limited social relationships, or stress—have also been associated with menstrual pain [23]. Additionally, lower socioeconomic status, low fish consumption, and mood disorders can exacerbate symptoms [23]. Among protective factors, a review suggests that the use of oral contraceptives is associated with a reduction in pain, highlighting the potential influence of hormonal contraception in this condition, primarily by inhibition of ovulation [24].

Literature search strategy

A literature search was conducted using PubMed, Scopus, and Web of Science to identify studies investigating natural compounds and complementary approaches for the management of dysmenorrhea. The search included combinations of the following keywords: dysmenorrhea, menstrual pain, natural compounds, herbal medicine, dietary supplements, omega-3 fatty acids, ginger, curcumin, magnesium, vitamins, and complementary therapies. Only studies conducted in humans and published in English were considered. Priority was given to randomized controlled trials, meta-analyses, and systematic reviews when available. Relevant references cited in the retrieved articles were also screened to identify additional studies (Table. 1).

Diagnosis and treatment

The diagnosis of dysmenorrhea relies on an accurate history conducted on patients reporting lower abdominal pain associated with menstruation. The precise definition of the timing and duration of dysmenorrhea is useful in distinguishing the primary or secondary nature of dysmenorrhea. Indeed, the pain related to primary dysmenorrhea begins right before or in concomitance with bleeding, and lasts up to three days [2,10], while pain associated with secondary dysmenorrhea may be more constant and not necessarily related to the onset of bleeding [25]. Patients affected by primary dysmenorrhea usually report the same pain characteristics at each menstrual cycle, while secondary dysmenorrhea may be associated with different pain patterns and associated symptoms [2]. The age at onset is within two years from menarche for primary dysmenorrhea, with a peak in the late teens to early twenties. Secondary dysmenorrhea could present at different ages, regardless of the onset of ovulatory cycles [9]. The intensity of pain may be easily quantified with a numeric rating scale (NRS), usually by a self-determined reporting of pain intensity from 1 to 10 [26]. The use of patient-reported outcomes (PROs) like symptom diaries may have a potential role in objectifying pain and supporting patients and clinicians in quantifying the impact on quality of life [27]. History should also focus on concomitant symptoms that could suggest organic causes or different aetiologies (deep dyspareunia, dysuria, dyschezia, painful rectal bleeding, haematuria, shoulder tip pain, fatigue, or infertility) or surgical history (cesarean section, intrauterine device placement, uterine curettage). Physical examination is typically negative in primary dysmenorrhea, while it may detect signs of organic causes (e.g., deep endometriosis nodules, adnexal masses, vaginal discharges, or abnormal uterine size). Imaging is helpful in confirming the primary nature of dysmenorrhea or identifying secondary causes, particularly when there is no response to empiric treatment [10]. The first choice is a transvaginal or abdominal ultrasound examination of the pelvis that is accurate for diagnosis of ovarian and deep endometriosis, adenomyosis, uterine fibroids, congenital uterine abnormalities, or pelvic inflammatory disease [2,10,28]. MRI should also be considered, particularly when transvaginal ultrasound cannot be performed. Laparoscopy may be

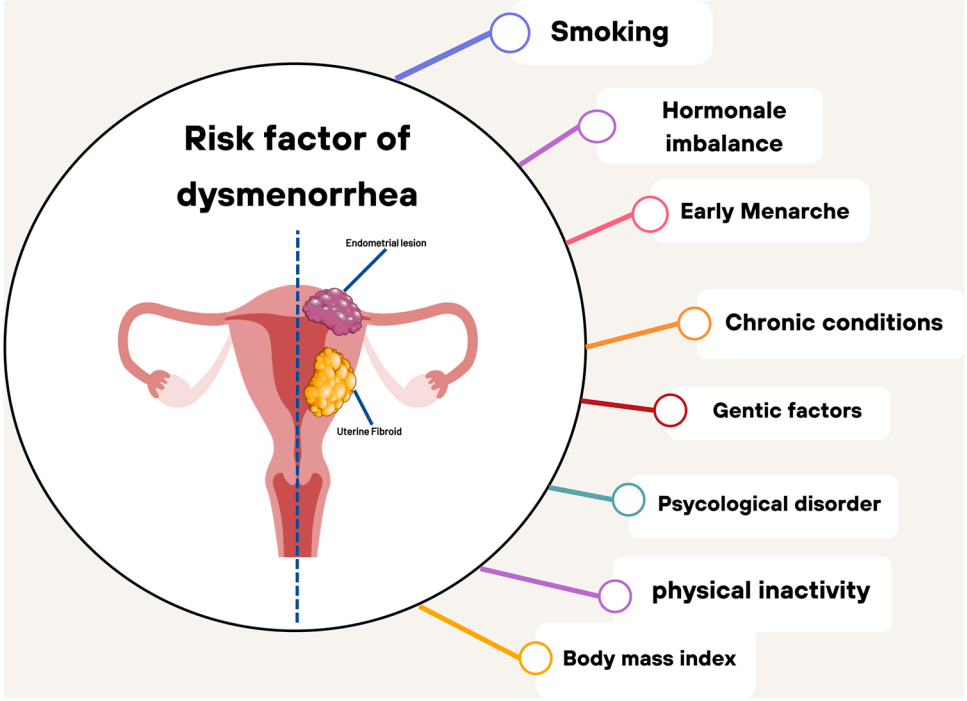

Fig. 2. Representative list of the risk factors causing the dysmenorrhea.

Table 1
Overview of natural compounds for the management of primary dysmenorrhea: proposed mechanisms of action and summary of clinical evidence.

Compound	Proposed mechanism of action	Key clinical evidence & study types	Main clinical findings & limitations
Omega-3 Fatty Acids	Modulates the arachidonic acid pathway, decreasing pro-inflammatory prostaglandins (PGE2, PGF2α).	Meta-analyses and high-quality RCTs.	Strong evidence for reducing pain intensity; well-tolerated. Considered one of the best-evidenced natural therapies.
Ginger	Inhibits COX and LOX pathways, reducing prostaglandin and leukotriene synthesis.	Systematic reviews, Meta-analyses, and RCTs (e.g., n = 150).	Efficacy is comparable to NSAIDs in pain reduction. However, some evidence relies on relatively small cohorts; larger validations are required.
Curcumin / Turmeric	Inhibits COX-2 enzyme; exhibits strong anti-inflammatory and antioxidant properties.	RCTs (e.g., n = 70) and recent Meta-analyses.	Significant reduction in pain intensity. Interpretation remains cautious due to the small sample sizes and single-center nature of the primary trials.
Magnesium	Natural calcium antagonist; promotes smooth muscle relaxation and inhibits prostaglandin release.	RCTs (e.g., 300 mg/day) and Meta-analyses.	Consistent evidence for pain reduction. Efficacy strongly depends on the chemical form (e.g., organic/liposomal) and synergistic use with Vitamin B6.
Chamomile	Antispasmodic and anti-inflammatory effects, primarily attributed to apigenin.	Systematic reviews and RCTs.	Effective in reducing pelvic pain and menstrual distress. Evidence quality across primary studies varies.
Cinnamon	Anti-inflammatory and analgesic properties.	RCTs (e.g., n = 80) and Meta-analysis (9 studies, n = 647).	Significantly reduces pain intensity and shortens pain duration. Further large-scale, multi-center studies are recommended.
Berries	Anti-inflammatory action via anthocyanins (inhibition of pro-inflammatory cytokines).	Extrapolated from general inflammation studies.	Preliminary evidence. There is a critical lack of dysmenorrhea-specific RCTs, making clinical efficacy speculative at this stage.
Peppermint	Menthol modulates calcium and TRP channels, exerting an antispasmodic effect on smooth muscle.	Small RCTs (e.g., n = 127) and aromatherapy systematic reviews.	Potential symptomatic relief, but specific clinical efficacy is difficult to isolate due to confounding concomitant treatments (e.g., ibuprofen, massage).
Vitex	Dopaminergic activity; modulation of prolactin secretion.	Extrapolated predominantly from Premenstrual Syndrome (PMS) trials.	Highly speculative for primary dysmenorrhea. Lacks targeted, rigorously designed clinical validation for menstrual cramps.
Adlay	Anti-inflammatory and muscle relaxant properties.	Predominantly *in vitro* and animal models; single clinical trial.	Encouraging mechanistic rationale, but human clinical evidence is currently insufficient to consider it a definitive treatment.
Saffron	Antispasmodic, anti-inflammatory, and mood-regulating properties.	Meta-analyses and RCTs.	Effective in reducing both menstrual pain intensity and associated premenstrual mood symptoms.
Vitamin E & Zinc	Antioxidant action; inhibits arachidonic acid release (Vit E) and modulates COX-2 (Zinc).	RCTs and double-blind trials.	Both compounds independently show clinically relevant reductions in pain severity and duration.

employed as a last diagnostic tool, allowing histopathological confirmation and immediate treatment of secondary causes [28]. It is important to highlight how patients affected by primary dysmenorrhea need to be re-evaluated over time in order to identify the potential onset of organic causes of dysmenorrhea, which may have had a subtle clinical presentation in the years immediately following menarche, also considering that patients affected by primary dysmenorrhea are at higher risk of developing chronic pain syndromes. [10,29].

Currently, treatment options for dysmenorrhea range from pain management using medications, such as nonsteroidal anti-inflammatory drugs (NSAIDs), analgesics, and hormonal therapies, to non-pharmacological strategies. These alternative methods include the use of natural remedies, relaxation techniques, physical exercise, and lifestyle modifications, which may involve psychological therapies. In fact, some studies have demonstrated improvements in the pathophysiology of dysmenorrhea following psychological interventions, such as cognitive-behavioral therapy (CBT) and biofeedback. These approaches aim to reduce the anxiety and emotional distress associated with dysmenorrhea, while also providing patients with strategies to manage pain more effectively.

Pharmacological treatment

Effective pain management is essential for improving the quality of life in individuals affected by dysmenorrhea. There are various treatment strategies available to alleviate the pain associated with this condition, including pharmacological therapy.

One of the most used pharmacological methods for relieving dysmenorrhea-related pain is the use of nonsteroidal anti-inflammatory drugs (NSAIDs). NSAIDs act as cyclooxygenase (COX) inhibitors, blocking the enzyme responsible for the synthesis of prostaglandins [21,30,31]. As previously mentioned, prostaglandins are a key factor in uterine contractions, and their reduction leads to a decrease in the intensity of pain associated with dysmenorrhea [21]. Each NSAID has its own spectrum of action; for example, ibuprofen, naproxen, and acetaminophen alleviate pain by targeting the inflammation associated with dysmenorrhea. Fenamates, such as mefenamic acid, have a dual action by both inhibiting prostaglandin production and blocking their activity [21,30–32].

Despite differences in the types of NSAIDs and their specific actions, a study by Marjoribanks et al. showed that when comparing NSAIDs to a placebo in the treatment of dysmenorrhea, NSAID therapy was effective

regardless of the specific drug used. Generally, NSAID therapy follows a scheduled regimen, as sporadic or "as-needed" use has been shown to reduce their overall effectiveness [31]. Treatment typically should begin one to two days before the onset of symptoms [21,30–32].

While NSAIDs provide significant benefits in managing dysmenorrhea, they can also cause side effects. Being weak acids, NSAIDs can lead to gastric mucosal damage, ulcers, and gastrointestinal bleeding. Studies have also shown that patients may experience side effects such as nausea, headaches, dizziness, drowsiness, or dry mouth while using NSAIDs [21,30–32]. Additionally, NSAIDs can negatively affect the kidneys, liver, and circulatory system, increasing the risk of thromboembolic complications. However, these adverse effects typically occur with prolonged use of NSAIDs, while dysmenorrhea usually lasts only 2–3 days, reducing the risk of serious side effects [33].

Another strategy for reducing dysmenorrhea symptoms is the use of hormonal contraceptives. Hormonal contraceptives are highly effective in treating dysmenorrhea as they reduce the production of prostaglandins and leukotrienes, by inhibiting ovulation, subsequent progesterone production by the corpus luteum and endometrial proliferation [10]. Hormonal contraceptives can be classified into short-acting options, such as combined oral contraceptives, progestins-only pills, vaginal rings, and transdermal patches, or long-acting methods, such as progestin intrauterine devices (IUDs), subcutaneous etonogestrel implants, which last around three years, and medroxyprogesterone acetate injections [34].

Several studies have shown that scheduled treatment with these combined hormonal contraceptives is effective in 70%–80% of cases [35]. However, prolonged use of hormonal contraceptives may increase the risk of cardiovascular events [36]. Indeed, the choice of treatment is based on the patient's medical history [37,38]. Four categories of medical eligibility criteria for contraceptive use are usually defined, ranging from conditions for which there is no restriction for the use of a contraceptive method to conditions that represents an unacceptable health risk if the contraceptive method is used [39].

The presence of secondary causes guides the management plan. Indeed, therapeutic choices may also include different medical therapies (e.g., antibiotics for pelvic inflammatory disease or GnRH agonists/antagonists for endometriosis or uterine fibroids), as well as surgery for selected cases of uterine fibroids or endometriosis [40].

Non-pharmacological treatment

Non-pharmacological approaches offer a complementary or alternative way to manage dysmenorrhea, especially for those who are unable or unwilling to rely on medications for long periods due to potential side effects.

Thermotherapy involves the application of heat to the lower abdomen or pelvic area using heating pads, hot water bottles, or adhesive heat wraps. This technique has been widely studied and is well-documented as an effective method for relieving menstrual pain by increasing blood flow and relaxing uterine muscles. The heat can block pain signals and soothe the muscle contractions caused by prostaglandins, the primary drivers of uterine cramping during menstruation. Two independent studies have shown that heat therapy works comparably to NSAIDs in reducing pain intensity, without the gastrointestinal side effects commonly associated with long-term NSAID use [41,42].

Regular physical activity has been found to decrease menstrual pain by increasing endorphin levels, which act as natural painkillers. Endorphins, released during physical exertion, enhance mood and reduce the perception of pain. Research has indicated that women who engage in aerobic activities such as light jogging, yoga, and swimming experience a notable reduction in dysmenorrhea-related symptoms. Yoga has been identified as an effective method due to its combination of stretching, muscle relaxation, and breathing techniques, which help regulate the autonomic nervous system and reduce uterine spasms. Multiple clinical studies suggest that engaging in regular exercise can reduce the severity and duration of menstrual cramps over time [43].

Relaxation methods such as Progressive Muscle Relaxation (PMR), meditation, and deep breathing exercises offer a mental and physical approach to alleviating menstrual pain. These techniques reduce muscle tension and anxiety, both of which can exacerbate pain perception. PMR involves tensing and then relaxing different muscle groups to promote body-wide relaxation, which can help lessen the discomfort associated with uterine contractions. Deep breathing exercises and meditation encourage a focus on controlled breathing and mindfulness, reducing stress and helping to modulate pain pathways. Also that relaxation exercises can improve overall quality of life and reduce the need for pharmacological intervention in some women [44].

Acupuncture and acupressure are traditional Chinese medicine techniques that have gained traction as alternative treatments for dysmenorrhea. These therapies involve stimulating specific pressure points on the body to alleviate pain and promote relaxation. Acupuncture uses fine needles inserted into the skin at specific points, whereas acupressure applies physical pressure to the same points. Clinical studies have demonstrated that acupuncture, when performed regularly, can significantly reduce menstrual pain and improve other associated symptoms such as fatigue and nausea [45]. Furthermore, a comprehensive Cochrane review by Smith et al. reached cautiously positive conclusions regarding the efficacy of acupuncture, noting that while it may provide pain relief and improve menstrual symptoms, the current evidence is limited by the methodological quality and risk of bias of the available studies [46].

CBT and psychological counselling are vital for women whose dysmenorrhea is exacerbated by stress, anxiety, or mood disorders. Dysmenorrhea is often associated with heightened emotional distress, which can intensify pain perception. CBT works by addressing negative thought patterns and teaching coping mechanisms for pain management. By reframing perceptions of pain and reducing anxiety, CBT helps in minimizing both the psychological and physical symptoms of dysmenorrhea. Several studies have indicated that CBT and similar psychological interventions can improve pain outcomes, particularly for women who suffer from chronic dysmenorrhea or comorbid conditions such as depression or anxiety [47].

Overall non-pharmacological treatments for dysmenorrhea provide diverse options for individuals seeking alternative or complementary strategies to alleviate menstrual pain [48]. These methods including thermotherapy, physical exercise, relaxation techniques, acupuncture, and psychological counselling offer effective, low-risk interventions that address both the physical and emotional aspects of dysmenorrhea. Although these treatments may not fully replace pharmacological methods in severe cases, they provide valuable tools for improving pain management and overall quality of life [42].

Dietary supplements and natural compounds

In recent years, there has been a growing interest in the use of natural compounds and dietary interventions as alternative or complementary therapies for managing dysmenorrhea. These approaches are particularly appealing for individuals seeking to minimize the side effects of long-term pharmacological treatments, such as NSAIDs or hormonal therapies. A variety of natural supplements have been studied for their ability to alleviate menstrual pain, with promising results emerging from clinical trials and observational studies [35,49].

Beyond dysmenorrhea, natural compounds and dietary strategies have shown significant potential in addressing a broad spectrum of gynecological conditions, including polycystic ovary syndrome (PCOS), endometriosis, and uterine fibroids. In the context of uterine fibroids, recent studies have highlighted the potential role of strawberries as a dietary intervention. Rich in bioactive compounds such as ellagic acid, flavonoids, and vitamin C, strawberries exhibit strong antioxidant and anti-inflammatory properties. These bioactive components may contribute to the modulation of pathways involved in fibroid growth by

reducing oxidative stress, suppressing chronic inflammation, and potentially inhibiting the estrogen-driven proliferation of fibroid tissue. Recent studies suggest that regular consumption of strawberries or their extracts could help mitigate fibroid-related symptoms and slow disease progression [50,51].

In addition to strawberries, other natural compounds, including curcumin, resveratrol, quercetin, omega-3 fatty acids, adlay and saffron have been studied for their ability to suppress inflammation and angiogenesis, processes that are critical in the pathophysiology of fibroids and endometriosis [52–54]. These interventions often work synergistically by addressing hormonal imbalances, improving metabolic health, and enhancing immune responses.

Adlay, a grain commonly used in traditional medicine, has shown potential in improving hormonal balance and reducing inflammation, making it a valuable addition to dietary strategies for managing gynecological disorders [55]. Saffron, known for its mood-enhancing properties, also exhibits anti-inflammatory and antioxidant effects, which may play a role in alleviating the pain and inflammation associated with these conditions [56,57].

These interventions often work synergistically by addressing hormonal imbalances, improving metabolic health, and enhancing immune responses. By addressing the underlying mechanisms driving these conditions, natural compounds and dietary strategies provide a holistic, integrative approach to gynecological health. They not only offer symptom relief but may also improve reproductive outcomes and reduce the risk of complications, enhancing the overall quality of life for affected individuals. The growing body of evidence underscores the potential of these interventions as both preventive and therapeutic tools in managing complex gynecological disorders.

Omega-3 fatty acids

One of the most extensively researched natural supplements for dysmenorrhea is omega-3 fatty acids, primarily found in fatty fish (such as salmon and sardines), flaxseeds, chia seeds, and walnuts. Omega-3 fatty acids, especially eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), have potent anti-inflammatory properties. They are precursors to anti-inflammatory prostaglandins (PG3), which counteract the pro-inflammatory prostaglandins (such as PGF2α) responsible for inducing strong uterine contractions during menstruation [58].

Several clinical studies have shown that omega-3 supplementation can significantly reduce the intensity and duration of menstrual cramps. For instance, a randomized controlled trial involving 120 female students with primary dysmenorrhea found that those who received omega-3 supplements experienced a marked reduction in menstrual pain compared to the placebo group [58]. Another study present in the literature demonstrated that women who consumed omega-3 supplements reported less severe pain and required fewer painkillers during menstruation [59].

The beneficial effects of omega-3 fatty acids in dysmenorrhea are attributed to their ability to modulate the production of prostaglandins, reducing the synthesis of prostaglandin F2α (PGF2α), a potent stimulator of uterine contractions. By competing with arachidonic acid, the omega-6 fatty acid precursor of pro-inflammatory prostaglandins, omega-3 s shift the balance towards the production of less inflammatory eicosanoids, thereby alleviating uterine cramping [60]. Additionally, omega-3 s have been shown to inhibit the activity of (NF-KB), a key regulator of inflammation, further reducing the inflammatory response during menstruation [61].

Ginger (Zingiber officinale)

Ginger has a long history of use in traditional medicine for its anti-inflammatory and analgesic properties, and recent research supports its efficacy in managing dysmenorrhea. The active components in ginger, particularly gingerol and shogaol, are known to inhibit the production of prostaglandins and leukotrienes, two classes of inflammatory mediators that play a crucial role in menstrual pain [62]. Ginger's effectiveness in dysmenorrhea has been compared to that of NSAIDs in several studies.

In a clinical trial involving 150 women with primary dysmenorrhea, those who consumed 250 mg of ginger capsules four times a day during the first three days of menstruation reported a significant reduction in pain intensity compared to a placebo group [63]. The reduction in pain was comparable to that seen in women taking NSAIDs, suggesting that ginger may serve as a natural alternative for pain relief. Another randomized study found that ginger, when taken at the onset of menstruation, effectively reduced both the duration and severity of menstrual pain [62]. However, although these results are promising, it must be noted that this trial involved a relatively small cohort of 150 women, and further large-scale, methodologically rigorous studies are required to confirm these findings and definitively rule out publication bias.

Ginger's anti-inflammatory effects are primarily mediated through the inhibition of COX and lipoxygenase (LOX) enzymes, which are involved in the biosynthesis of prostaglandins and leukotrienes, respectively. By suppressing these enzymes, ginger reduces the production of PGF2α, thereby alleviating uterine contractions and inflammation [64]. Moreover, ginger's antioxidant properties help neutralize reactive oxygen species (ROS), which are elevated during the inflammatory response, further contributing to its pain-relieving effects.

Turmeric (Curcuma longa)

Turmeric is another natural remedy widely used for its anti-inflammatory and analgesic effects, particularly in traditional Ayurvedic and Chinese medicine. The primary bioactive compound in turmeric, curcumin, has been extensively studied for its role in modulating inflammatory pathways. Like ginger, curcumin inhibits the COX and LOX pathways, reducing the production of inflammatory mediators such as prostaglandins and cytokines.

Clinical studies have demonstrated turmeric's efficacy in alleviating dysmenorrhea symptoms. In a study involving 70 women with primary dysmenorrhea, curcumin supplementation for three consecutive menstrual cycles resulted in a significant reduction in pain intensity compared to a placebo group [65]. Another study compared the effects of curcumin to those of mefenamic acid, a commonly prescribed NSAID for dysmenorrhea, and found that both treatments were similarly effective in reducing menstrual pain [66]. While significant, the interpretation of these results must remain cautious due to the small sample size ($n = 70$) and the inherent limitations of small-scale single-center trials.

Curcumin's anti-inflammatory properties are primarily due to its ability to inhibit the NF-KB signaling pathway, which plays a central role in the regulation of inflammatory responses. By downregulating NF-KB and other pro-inflammatory cytokines such as tumor necrosis factor-alpha (TNF-α) and interleukin-6 (IL-6), curcumin helps reduce inflammation and pain associated with dysmenorrhea [65]. Additionally, curcumin enhances the body's endogenous antioxidant defense systems, such as glutathione peroxidase, further mitigating oxidative stress and inflammation.

Magnesium

Magnesium (Mg) is a vital mineral that serves as a natural calcium antagonist, playing a fundamental role in regulating neuromuscular activity and uterine contractility. At the cellular level, magnesium competes with calcium for entry into myometrial cells via voltage-gated channels, inhibiting the influx of calcium ions into smooth muscle cells. By reducing intracellular calcium concentrations, magnesium promotes smooth muscle relaxation, reduces the frequency and intensity of uterine contractions, and alleviates the vasospasm of uterine vessels, which is considered a primary driver of ischemic menstrual pain [67].

Furthermore, magnesium's efficacy is linked to its ability to modulate the arachidonic acid cascade, thereby inhibiting the overproduction and release of prostaglandins (PGF2α and PGE2), the key mediators of uterine hyper-contractility and pain [68]. While early clinical interest was anchored by foundational trials in the 1990s, notably a randomized controlled trial (RCT) demonstrating that 250 mg of magnesium daily significantly reduced the intensity and duration of symptoms [69], the clinical landscape has since been substantially updated with high-quality evidence. A 2020 randomized, double-blind, placebo-controlled trial confirmed these early findings, demonstrating that a 300 mg daily dose of magnesium significantly reduced pain intensity and associated symptoms, such as backache and headache, in university students [70]. Advancements in nutritional science have further refined the clinical application of magnesium, focusing on improved delivery systems and bioavailability. Recent systematic reviews and meta-analyses [71] confirm that magnesium is one of the few minerals with consistent evidence supporting its use for primary dysmenorrhea. However, current research emphasizes that efficacy is highly dependent on the chemical form; organic salts (e.g., magnesium citrate, bisglycinate) show superior absorption compared to inorganic preparations [71]. Moreover, newly developed liposomal magnesium formulations significantly enhance gastrointestinal tolerance and cellular uptake by encapsulating the mineral in phospholipid vesicles, thereby maximizing its anti-spasmodic potential [72]. Additionally, current clinical insights highlight the synergistic combination of magnesium and Vitamin B6 (pyridoxine), as B6 acts as a chaperone to increase magnesium's intracellular concentration.

Chamomile (Matricaria chamomilla)

Several studies have investigated the potential effects of chamomile on dysmenorrhea, largely due to its anti-inflammatory, antispasmodic, and mild sedative properties.

A clinical study involving 90 participants compared chamomile capsules, ibuprofen, and no treatment, showing that both active interventions were associated with a significant reduction in menstrual pain compared to the control group [73].

Similarly, another study by the same authors reported that chamomile supplementation was associated with reductions in both pain intensity and menstrual duration in a cohort of 90 participants. Additional studies conducted in young women have reported comparable findings, suggesting a potential beneficial effect of chamomile in the management of dysmenorrhea. However, these results should be interpreted with caution, as the available evidence is limited by relatively small sample sizes, heterogeneity in study design, and, in some cases, the absence of placebo-controlled groups. Therefore, although chamomile appears to be a promising complementary option, further well-designed randomized controlled trials are required to confirm its efficacy and establish standardized treatment protocols.

Cinnamon (Cinnamomum zeylanicum)

Cinnamon has also shown promise in the management of menstrual pain due to its anti-inflammatory and analgesic properties. Jahangirifar et al. examined the effects of cinnamon on primary dysmenorrhea in 80 patients. The participants were divided into two groups: one treated with cinnamon capsules and the other with a placebo. The results indicated that the group treated with cinnamon experienced a significant reduction in menstrual pain compared to the placebo group [74]. To address the limitations of relying on isolated, small-scale trials, recent higher-level evidence has further substantiated its clinical efficacy. A comprehensive systematic review and meta-analysis evaluating herbal medicines across nine studies and 647 patients confirmed that cinnamon provides substantial relief for primary dysmenorrhea. Specifically, the pooled data demonstrated that cinnamon interventions not only significantly reduced pain intensity compared to placebo but were also uniquely effective in significantly shortening the overall duration of menstrual pain [75]. While this meta-analytic evidence strengthens the clinical rationale for cinnamon, further large-scale, rigorously designed studies are still recommended to establish standardized dosages and definitively confirm these findings.

Berries

Berries, particularly those rich in antioxidants, such as blueberries, raspberries, and cranberries, have been suggested as potential natural treatments for dysmenorrhea. Although scientific evidence on their specific efficacy in alleviating menstrual pain remains limited, the anti-inflammatory properties of berries may offer some relief from dysmenorrhea symptoms. Berries contain high levels of flavonoids, such as anthocyanins, which can help reduce inflammation associated with menstrual cramps [76,77].

Blueberries are rich in flavonoids, particularly anthocyanins, which possess anti-inflammatory properties. These compounds may help reduce the inflammation linked to dysmenorrhea by inhibiting pro-inflammatory cytokines [78,79].

Raspberries are also known for their high antioxidant content, which may contribute to reducing menstrual pain. Incorporating raspberries into smoothies, yogurts, or cereals can provide beneficial nutrients that may support overall health and reduce inflammation [78].

Cranberries are well-known for their anti-inflammatory and antibacterial properties, commonly used in managing urinary tract infections. Consuming cranberry juice may also have potential benefits in reducing inflammation associated with dysmenorrhea, though further research is needed to confirm this effect [78].

Blackcurrants are another source of antioxidants, including vitamin C and anthocyanins, which may help alleviate inflammation and menstrual pain [80].

It must be strongly emphasized that the current evidence supporting berries for dysmenorrhea is largely preliminary and extrapolated. While the anti-inflammatory mechanisms of these fruits are well-documented in general contexts, there is currently a critical lack of robust, dysmenorrhea-specific randomized controlled trials to confidently support their clinical efficacy. One study presents in the literature investigated the effects of blueberry juice on inflammation, suggesting that it may reduce inflammatory markers in the blood. However, the study did not specifically focus on dysmenorrhea [80,81].

Peppermint (Mentha piperita)

Peppermint (*Mentha piperita*) has traditionally been used for its antispasmodic and analgesic properties, which may be relevant in the management of dysmenorrhea. Its main bioactive component, menthol, is known to modulate calcium channels and exert a relaxing effect on smooth muscle, potentially contributing to the reduction of uterine contractions and associated pain. In addition, peppermint may influence visceral pain perception through interactions with transient receptor potential (TRP) channels.

However, clinical evidence regarding peppermint in dysmenorrhea remains limited and heterogeneous. A study involving 127 women reported that the combination of peppermint and ibuprofen resulted in a greater reduction in pain compared to ibuprofen alone [82]. Nevertheless, this study design does not allow for a clear attribution of the observed pain relief to peppermint as a standalone intervention. Additional data derive from studies evaluating peppermint within aromatherapy-based approaches. A systematic review by Najaf Najafi et al. [83] suggested that aromatherapy interventions, including peppermint, may be associated with pain reduction. Yet, these approaches are often combined with massage therapy or other essential oils, making it difficult to isolate the specific therapeutic contribution of peppermint.

Overall, the current evidence supporting peppermint in primary

dysmenorrhea is indirect and limited by methodological heterogeneity, a lack of standardized interventions, and a scarcity of high-quality randomized controlled trials. Therefore, while peppermint may represent a promising complementary approach, further well-designed, isolated studies are required to clarify its specific efficacy and optimal mode of administration.

Vitex (Vitex agnus-castus)

Vitex, also known as chasteberry, is an herbal remedy traditionally used to manage various menstrual disorders, including dysmenorrhea. It is believed to balance female hormones, particularly by regulating the levels of progesterone and estrogen, potentially leading to improvements in menstrual symptoms. Vitex has been widely studied for its role in treating PMS, but its specific effects on dysmenorrhea remain underresearched. Gerhard et al. examined the efficacy of Vitex in treating PMS and found significant improvements in symptoms among participants [84]. Although this study focused on PMS, the potential benefits of Vitex for hormone regulation suggest that it may also be useful for treating dysmenorrhea. Vitex is thought to work by modulating the hypothalamic-pituitary-gonadal axis, increasing the production of luteinizing hormone (LH) and thereby enhancing progesterone levels. This hormone-balancing effect could help reduce menstrual cramping and other dysmenorrhea symptoms [85].

While Vitex has a long history of use in herbal medicine for menstrual disorders, given that current evidence is predominantly extrapolated from PMS research rather than dysmenorrhea-specific cohorts, the clinical efficacy of Vitex for menstrual pain remains highly speculative and requires rigorous validation through targeted clinical trials. As with any herbal remedy, it is important to consult with a healthcare professional before using Vitex, especially if taking other medications or managing existing health conditions.

Adlay (Coix lacryma-jobi)

Adlay, scientifically known as *Coix lacryma-jobi*, is a cereal grain traditionally used in East Asia for its therapeutic properties. Rich in bioactive compounds, including saponins, flavonoids, and polyphenols, Adlay has garnered attention for its potential health benefits, particularly its anti-inflammatory, analgesic, and hormonal-regulating effects. These attributes suggest that Adlay may offer a promising treatment option for alleviating dysmenorrhea.

The therapeutic mechanisms of Adlay in managing dysmenorrhea can be primarily attributed to its anti-inflammatory and analgesic properties. Adlay's bioactive compounds, such as saponins and flavonoids, have been shown to inhibit the activity of pro-inflammatory cytokines, including tumor necrosis factor-alpha (TNF-α) and interleukin-1 beta (IL-1β), as well as cyclooxygenase-2 (COX-2) [55]. COX-2 is the enzyme responsible for the production of prostaglandins, and by reducing its activity, Adlay helps decrease the levels of these pain-inducing substances. This mechanism not only reduces inflammation but also mitigates the intensity of menstrual cramps, providing relief to those suffering from dysmenorrhea [55].

In addition to its anti-inflammatory effects, Adlay has been suggested to play a role in hormonal modulation, which is another key factor in the pathophysiology of dysmenorrhea [86]. In a study of Hsia et al., suggests that Adlay may help regulate estrogen and progesterone levels. In a rat model, the administration of Adlay extract resulted in the modulation of these hormones, potentially reducing uterine hypercontractility and providing pain relief [87]. By restoring hormonal balance, Adlay may help reduce the intensity and frequency of menstrual cramps, offering a promising natural alternative for managing dysmenorrhea.

Furthermore, Adlay has been shown to have diuretic effects, which can alleviate common symptoms associated with menstruation, such as bloating and fluid retention. Many individuals with dysmenorrhea also experience these symptoms due to hormonal fluctuations during their menstrual cycle. Adlay's diuretic properties promote the elimination of excess fluids from the body, thereby reducing bloating and discomfort. In addition to its diuretic effects, Adlay has been demonstrated to improve blood circulation. Poor circulation to the uterine tissues is a common issue in individuals with dysmenorrhea and can exacerbate menstrual pain. By promoting better blood flow, Adlay may help alleviate discomfort caused by inadequate oxygen and nutrient supply to the uterus, further reducing the severity of menstrual pain and promoting overall uterine health [55].

While clinical evidence supporting the use of Adlay for dysmenorrhea remains limited, preliminary studies have shown promising results. For instance, a study by Chiang et al. examined the effects of Adlay extract on women with primary dysmenorrhea and found that it significantly reduced pain severity and improved menstrual regularity. The results suggest that Adlay may offer an effective alternative or complementary treatment to conventional therapies for dysmenorrhea. However, larger-scale randomized controlled trials (RCTs) are needed to confirm these findings and determine the most effective dosages and treatment regimens for clinical use [55].

In conclusion, while further research is necessary to fully understand its clinical efficacy, Adlay holds considerable potential as a natural treatment for dysmenorrhea. Its anti-inflammatory, analgesic, hormonal-regulating, diuretic, and circulatory benefits make it a multifaceted remedy that may address both the physical and hormonal mechanisms involved in menstrual pain. Continued exploration of Adlay's therapeutic properties could pave the way for its use as an adjunct or alternative to conventional treatments for dysmenorrhea. Although these mechanistic insights are promising, it is crucial to note that they are predominantly derived from in vitro and animal models. The single clinical trial by Chiang et al. [55], while encouraging, cannot be considered definitive; further robust clinical validation in larger human cohorts is imperative before drawing firm conclusions regarding its efficacy for dysmenorrhea.

Saffron (Crocus sativus)

Saffron (Crocus sativus), derived from the stigmas of the crocus flower, has been highly regarded for centuries as a spice with therapeutic potential. Its use in traditional medicine is attributed to its rich composition of bioactive compounds, such as crocins, crosetin, and safranal, which are responsible for its antioxidant, anti-inflammatory, and mood-enhancing properties. These attributes make saffron a promising candidate for alleviating the physical and emotional symptoms associated with dysmenorrhea.

The mechanisms through which saffron exerts its beneficial effects in managing dysmenorrhea are multifaceted. A key mechanism is its anti-inflammatory activity, which is critical in alleviating the pain and discomfort associated with menstrual cramps. Prostaglandins, which are produced during menstruation, play a pivotal role in the pathogenesis of dysmenorrhea by causing uterine contractions and inducing pain. The bioactive compounds found in saffron, particularly crocins, crosetin, and safranal, have been shown to inhibit the activity of pro-inflammatory enzymes, including COX-2 and LOX [88]. COX-2 is a critical enzyme involved in the synthesis of prostaglandins, and by inhibiting its activity, saffron helps reduce the production of these pain-inducing substances. This action alleviates both the inflammatory response and the associated uterine contractions that lead to dysmenorrhea, thus providing relief from menstrual cramps [88,89].

In addition to its anti-inflammatory properties, saffron's potent antioxidant activity plays an important role in mitigating the severity of dysmenorrhea. Oxidative stress is believed to contribute to increased uterine sensitivity and pain during menstruation. Studies have shown that oxidative damage to uterine tissues exacerbates the discomfort and inflammation commonly seen in dysmenorrhea. Saffron, with its high levels of antioxidant compounds such as crocin and safranal, helps neutralize free radicals and reduce oxidative stress in the body. By

protecting the uterine tissues from oxidative damage, saffron not only reduces pain intensity but also promotes overall uterine health. This antioxidant effect enhances the ability of saffron to alleviate menstrual cramps and improve the well-being of individuals suffering from dysmenorrhea [90].

Moreover, saffron's mood-enhancing properties contribute to its effectiveness in managing the emotional distress that often accompanies dysmenorrhea. Many individuals with dysmenorrhea experience anxiety, depression, irritability, and other mood disturbances, which can exacerbate the perception of pain. Saffron has been shown to have antidepressant-like effects, primarily through its influence on serotonin and dopamine levels in the brain. The active compound safranal, in particular, has demonstrated neuroprotective properties and has been shown to reduce anxiety and depressive symptoms [91]. A study by Marx et al. found that saffron supplementation significantly reduced anxiety and depressive symptoms in women with primary dysmenorrhea, which, in turn, improved their overall quality of life during menstruation [92]. By addressing both the physical and emotional symptoms of dysmenorrhea, saffron offers a holistic approach to managing the condition.

Vitamin E

Vitamin E is a potent antioxidant that has been studied for its ability to reduce menstrual pain. By neutralizing free radicals, vitamin E can help mitigate oxidative stress, which is often elevated during menstruation and contributes to inflammation and pain. In a study involving 100 women with primary dysmenorrhea, those who took 400 IU of vitamin E daily for two months reported a significant reduction in pain intensity compared to a control group [93].

Vitamin E's primary mode of action in dysmenorrhea involves its antioxidant properties, which help reduce the oxidative damage that exacerbates inflammation during menstruation. By decreasing the levels of lipid peroxidation and stabilizing cell membranes, vitamin E reduces the sensitivity of nociceptors (pain receptors) to prostaglandins, thereby alleviating pain [93,94].

Zinc

Zinc is another essential micronutrient that has shown promise in reducing menstrual pain. Zinc's anti-inflammatory and antioxidant properties make it a potential candidate for managing dysmenorrhea. A clinical trial involving adolescent girls found that zinc supplementation (30 mg/day) during the luteal phase of the menstrual cycle significantly reduced the severity of dysmenorrhea [95].

Zinc is believed to reduce the production of prostaglandins by inhibiting the enzyme phospholipase A2, which is involved in the release of arachidonic acid, a precursor to prostaglandins. By lowering prostaglandin levels, zinc reduces uterine contractions and pain. Additionally, zinc acts as an antioxidant, protecting cells from oxidative stress, which is heightened during menstruation [96].

Clinical implications and future perspectives

Natural compounds may have a potential role as a complementary treatment in the 20–30% of patients who may not have a complete response to pharmacological treatment and in those patients with relative (category 3) or absolute (category 4) contraindications to oral contraceptives [37]. The reported prevalence of patients with relative or absolute contraindications varies widely between 2.4% and 31.3% according to different settings and populations [97–99]. However, before widespread integration in the clinical practice of natural compounds, their effectiveness should be verified in properly designed clinical trials. Indeed, the safety profile, the adequate dosage, the timing and duration of administration, the potential side effects, and the pharmacological interactions with other medications should be adequately confirmed. Since the effectiveness of natural compounds could be reduced or augmented in the presence of concomitant organic disease, their potential application should also be studied in relation to the primary or secondary nature of dysmenorrhea. Therefore, patients reporting dysmenorrhea should be clinically evaluated before choosing a natural compound. In addition, the management of those patients should be multidisciplinary, with the involvement of both gynecologists and dieticians, to adhere to the correct indications, define the treatment modality, and avoid self-management. Correct information, both between operators and patients, should be the cornerstone of the introduction of natural compounds. Information should encompass the expected benefits, the security profile, the maximum dosage, the knowledge of symptoms that may need further medical evaluation, and critical and timely re-evaluations. Finally, the economic aspects of the clinical introduction of natural compounds should not be overlooked. Populations at low socio-economic index may have difficulties affording long-term therapies with natural compounds; therefore, their introduction should not create barriers to access to care. Future pre-clinical and clinical research is undoubtedly needed to address different aspects of the potential role of natural compounds in the management of dysmenorrhea.

Strengths and limitations

This narrative review has several limitations that must be acknowledged. First, as a narrative synthesis rather than a systematic review, the study selection process is inherently susceptible to selection bias. We did not employ a quantitative assessment of the risk of bias for the included trials. Furthermore, many of the clinical trials cited suffer from methodological limitations, including small sample sizes, short follow-up periods, and a lack of standardized dosing regimens. Consequently, while the mechanistic rationales provided are robust, the clinical efficacy of several emerging compounds (such as berries and Vitex) remains speculative and relies heavily on indirect evidence.

Conclusions

In conclusion, this review highlights the diverse therapeutic potential of natural compounds and complementary strategies in managing dysmenorrhea. While robust clinical evidence supports the use of omega-3 fatty acids, ginger, and magnesium, anchored by coherent mechanistic data, other emerging interventions, such as berries and Vitex, require further rigorous, dysmenorrhea-specific investigation. The integration of these alternative therapies is particularly clinically relevant for the subset of patients experiencing refractory pain or those with contraindications to conventional hormonal and NSAID treatments. Ultimately, a multidisciplinary approach that tailors non-pharmacological interventions to individual patient profiles, while acknowledging current evidentiary limitations, is essential for optimizing outcomes and improving the quality of life in affected women.

CRediT authorship contribution statement

SG, AC and PC proposed the idea for the review. S.G., G.D.C., A.D.G. and P.C. performed the literature search. S.G., G.D.C., A.D.G., G.G., A.C. and P.C. Wrote the article. All authors have read and agreed to the published version of the manuscript.

Ethical approval

This article is a review. It does not involve human or animal subjects and therefore does not require ethical approval.

Institutional review board statement

Not applicable.

Informed consent statement

Not applicable.

Consent to participate

Not applicable.

Consent for publication

All authors fulflled all conditions required for authorship and approved the submission of the manuscript.

Code availability

Not applicable.

Declaration of Generative AI and AI-assisted technologies in the writing process

Not applicable.

Funding

This research received no external funding.

Data availability

Not applicable.

Declaration of competing interest

The authors have no competing interests to declare.

References

[1] Vlachou E, Owens DA, Lavdaniti M, Kalemikerakis J, Evagelou E, Margari N, et al. Prevalence, wellbeing, and symptoms of dysmenorrhea among university nursing students in Greece. Diseases 2019;7(1).
[2] Ferries-Rowe E, Corey E, Archer JS. Primary dysmenorrhea: diagnosis and therapy. Obstet Gynecol 2020;136(5):1047–58.
[3] Kho KA, Shields JK. Diagnosis and management of primary dysmenorrhea. JAMA 2020;323(3):268–9.
[4] Khalesi ZB, Beiranvand SP, Bokaie M. Efficacy of chamomile in the treatment of premenstrual syndrome: a systematic review. J Pharmacopuncture 2019;22(4):204–9.
[5] Femi-Agboola DM, Sekoni OO, Goodman OO. Dysmenorrhea and its effects on school absenteeism and school activities among adolescents in selected secondary schools in Ibadan, Nigeria. Niger Med J 2017;58(4):143–8.
[6] Eryilmaz G, Ozdemir F, Pasinlioglu T. Dysmenorrhea prevalence among adolescents in eastern Turkey: its effects on school performance and relationships with family and friends. J Pediatr Adolesc Gynecol 2010;23(5):267–72.
[7] Burnett M, Lemyre M. No. 345-primary dysmenorrhea consensus guideline. J Obstet Gynaecol Can 2017;39(7):585–95.
[8] Iacovides S, Avidon I, Baker FC. What we know about primary dysmenorrhea today: a critical review. Hum Reprod Update 2015;21(6):762–78.
[9] Nagy H, Carlson K, Khan MAB. Dysmenorrhea. Treasure Island (FL): StatPearls; 2025.
[10] Bernardi M, Lazzeri L, Perelli F, Reis FM, Petraglia F. Dysmenorrhea and related disorders. F1000Res 2017;6:1645.
[11] Latthe P, Latthe M, Say L, Gulmezoglu M, Khan KS. WHO systematic review of prevalence of chronic pelvic pain: a neglected reproductive health morbidity. BMC Public Health 2006;6:177.
[12] Dawood MY. Primary dysmenorrhea: advances in pathogenesis and management. Obstet Gynecol 2006;108(2):428–41.
[13] Lundstrom V, Green K, Svanborg K. Endogenous prostaglandins in dysmenorrhea and the effect of prostaglandin synthetase inhibitors (PGSI) on uterine contractility. Acta Obstet Gynecol Scand Suppl 1979;87:51–6.
[14] Maia Jr H, Haddad C, Coelho G, Casoy J. Role of inflammation and aromatase expression in the eutopic endometrium and its relationship with the development of endometriosis. Womens Health (Lond) 2012;8(6):647–58.
[15] Jabbour HN, Sales KJ, Smith OP, Battersby S, Boddy SC. Prostaglandin receptors are mediators of vascular function in endometrial pathologies. Mol Cell Endocrinol 2006;252(1-2):191–200.
[16] Balbi C, Musone R, Menditto A, Di Prisco L, Cassese E, D'Ajello M, et al. Influence of menstrual factors and dietary habits on menstrual pain in adolescence age. Eur J Obstet Gynecol Reprod Biol 2000;91(2):143–8.
[17] Lundstrom V, Green K. Endogenous levels of prostaglandin F2alpha and its main metabolites in plasma and endometrium of normal and dysmenorrheic women. Am J Obstet Gynecol 1978;130(6):640–6.
[18] Chia CF, Lai JH, Cheung PK, Kwong LT, Lau FP, Leung KH, et al. Dysmenorrhoea among Hong Kong university students: prevalence, impact, and management. Hong Kong Med J 2013;19(3):222–8.
[19] Aouad P, Bui M, Sarraf S, Donnelly T, Chen Y, Jaaniste T, et al. Primary dysmenorrhoea in adolescents and young women: a twin family study of maternal transmission, genetic influence and associations. Aust N Z J Obstet Gynaecol 2022;62(5):725–31.
[20] Wei SY, Chao HT, Tu CH, Lin MW, Li WC, Low I, et al. The BDNF Val66Met polymorphism is associated with the functional connectivity dynamics of pain modulatory systems in primary dysmenorrhea. Sci Rep 2016;6:23639.
[21] Harel Z. Dysmenorrhea in adolescents and young adults: an update on pharmacological treatments and management strategies. Expert Opin Pharmacother 2012;13(15):2157–70.
[22] Grandi G, Ferrari S, Xholli A, Cannoletta M, Palma F, Romani C, et al. Prevalence of menstrual pain in young women: what is dysmenorrhea? J Pain Res 2012;5:169–74.
[23] Wang L, Wang X, Wang W, Chen C, Ronnennberg AG, Guang W, et al. Stress and dysmenorrhoea: a population based prospective study. Occup Environ Med 2004;61(12):1021–6.
[24] Wong CL, Farquhar C, Roberts H, Proctor M. Oral contraceptive pill for primary dysmenorrhoea. Cochrane Database Syst Rev 2009;2009(4):Cd002120.
[25] Kirsch E, Rahman S, Kerolus K, Hasan R, Kowalska DB, Desai A, et al. Dysmenorrhea, a narrative review of therapeutic options. J Pain Res 2024;17:2657–66.
[26] Mizuta R, Maeda N, Tashiro T, Suzuki Y, Oda S, Komiya M, et al. Quality of life by dysmenorrhea severity in young and adult Japanese females: a web-based cross-sectional study. PLoS One 2023;18(3):e0283130.
[27] Piontek K, Gabes M, Kann G, Fechtner M, Apfelbacher C. Quality of patient-reported outcome measures for primary dysmenorrhea: a systematic review. Qual Life Res 2024;33(1):31–43.
[28] Becker CM, Bokor A, Heikinheimo O, Horne A, Jansen F, Kiesel L, et al. ESHRE guideline: endometriosis. Hum Reprod Open 2022;2022(2). hoac009.
[29] Gagnon MM, Elgendy R. Comorbid pain experiences in young women with dysmenorrhea. Women Health 2020;60(8):946–57.
[30] Oladosu FA, Tu FF, Hellman KM. Nonsteroidal antiinflammatory drug resistance in dysmenorrhea: epidemiology, causes, and treatment. Am J Obstet Gynecol 2018;218(4):390–400.
[31] Marjoribanks J, Proctor ML, Farquhar C. Nonsteroidal anti-inflammatory drugs for primary dysmenorrhoea. Cochrane Database Syst Rev 2003;(4):CD001751.
[32] Ryan SA. The treatment of dysmenorrhea. Pediatr Clin North Am 2017;64(2):331–42.
[33] Zhang WY, Li Wan Po A. Efficacy of minor analgesics in primary dysmenorrhoea: a systematic review. Br J Obstet Gynaecol 1998;105(7):780–9.
[34] Davis AR, Westhoff CL. Primary dysmenorrhea in adolescent girls and treatment with oral contraceptives. J Pediatr Adolesc Gynecol 2001;14(1):3–8.
[35] Itani R, Soubra L, Karout S, Rahme D, Karout L, Khojah HMJ. Primary dysmenorrhea: pathophysiology, diagnosis, and treatment updates. Korean J Fam Med 2022;43(2):101–8.
[36] Fabunmi OA, Dludla PV, Nkambule BB. Investigating cardiovascular risk in premenopausal women on oral contraceptives: systematic review with meta-analysis. Front Cardiovasc Med 2023;10:1127104.
[37] Dmitrovic R, Kunselman AR, Legro RS. Continuous compared with cyclic oral contraceptives for the treatment of primary dysmenorrhea: a randomized controlled trial. Obstet Gynecol 2012;119(6):1143–50.
[38] van Vlijmen EF, Wiewel-Verschueren S, Monster TB, Meijer K. Combined oral contraceptives, thrombophilia and the risk of venous thromboembolism: a systematic review and meta-analysis. J Thromb Haemost 2016;14(7):1393–403.
[39] Nguyen AT, Curtis KM, Tepper NK, Kortsmit K, Brittain AW, Snyder EM, et al. U.S. Medical eligibility criteria for contraceptive use, 2024. MMWR Recomm Rep 2024;73(4):1–126.
[40] Khan KS, Champaneria R, Latthe PM. How effective are non-drug, non-surgical treatments for primary dysmenorrhoea? BMJ 2012;344:e3011.
[41] Machado AFP, Perracini MR, Rampazo EP, Driusso P, Liebano RE. Effects of thermotherapy and transcutaneous electrical nerve stimulation on patients with primary dysmenorrhea: a randomized, placebo-controlled, double-blind clinical trial. Complement Ther Med 2019;47:102188.
[42] French L. Dysmenorrhea. Am Fam Physician 2005;71(2):285–91.
[43] Daley AJ. Exercise and primary dysmenorrhoea: a comprehensive and critical review of the literature. Sports Med 2008;38(8):659–70.
[44] Proctor ML, Murphy PA, Pattison HM, Suckling J, Farquhar CM. Behavioural interventions for primary and secondary dysmenorrhoea. Cochrane Database Syst Rev 2007;2007(3):CD002248.
[45] Shetty GB, Shetty B, Mooventhan A. Efficacy of acupuncture in the management of primary dysmenorrhea: a randomized controlled trial. J Acupunct Meridian Stud 2018;11(4):153–8.
[46] Smith CA, Armour M, Zhu X, Li X, Lu ZY, Song J. Acupuncture for dysmenorrhoea. Cochrane Database Syst Rev 2016;4(4):CD007854.
[47] Kwekkeboom KL, Gretarsdottir E. Systematic review of relaxation interventions for pain. J Nurs Scholarsh 2006;38(3):269–77.

[48] Li X, Hao X, Liu JH, Huang JP. Efficacy of non-pharmacological interventions for primary dysmenorrhoea: a systematic review and Bayesian network meta-analysis. BMJ Evid Based Med 2024;29(3):162–70.
[49] Ciarmela P, Greco S. Impact of nutrition on female reproductive disorders. Nutrients 2023;15(21).
[50] Giampieri F, Islam MS, Greco S, Gasparrini M, Forbes Hernandez TY, Delli Carpini G, et al. Romina: a powerful strawberry with in vitro efficacy against uterine leiomyoma cells. J Cell Physiol 2019;234(5):7622–33.
[51] Islam MS, Giampieri F, Janjusevic M, Gasparrini M, Forbes-Hernandez TY, Mazzoni L, et al. An anthocyanin rich strawberry extract induces apoptosis and ROS while decreases glycolysis and fibrosis in human uterine leiomyoma cells. Oncotarget 2017;8(14):23575–87.
[52] Islam MS, Greco S, Delli Carpini G, Giannubilo SR, Segars J, Ciavattini A, et al. Hop and artichoke extracts inhibit expression of extracellular matrix components in uterine leiomyoma cells. F S Sci 2021;2(4):407–18.
[53] Greco S, Islam MS, Zannotti A, Delli Carpini G, Giannubilo SR, Ciavattini A, et al. Quercetin and indole-3-carbinol inhibit extracellular matrix expression in human primary uterine leiomyoma cells. Reprod Biomed Online 2020;40(4):593–602.
[54] Islam MS, Castellucci C, Fiorini R, Greco S, Gagliardi R, Zannotti A, et al. Omega-3 fatty acids modulate the lipid profile, membrane architecture, and gene expression of leiomyoma cells. J Cell Physiol 2018;233(9):7143–56.
[55] Chiang Y-F, Huang K-C, Ali M, Hsia S-M. Impact of adlay-based formula on pain and discomfort in women with dysmenorrhea: a randomized controlled trial. Nutrients 2024;16(23):4026.
[56] Rajabi F, Rahimi M, Sharbafchizadeh MR, Tarrahi MJ. Saffron for the management of premenstrual dysphoric disorder: a randomized controlled trial. Adv Biomed Res 2020;9:60.
[57] Pourbagher-Shahri AM, Forouzanfar F. Saffron (*Crocus sativus*) and its constituents for pain management: a review of current evidence. Phytother Res 2023;37(11):5041–57.
[58] Oppedisano F, Macrì R, Gliozzi M, Musolino V, Carresi C, Maiuolo J, et al. The anti-inflammatory and antioxidant properties of n-3 PUFAs: their role in cardiovascular protection. Biomedicines 2020;8(9).
[59] Rahbar N, Asgharzadeh N, Ghorbani R. Effect of omega-3 fatty acids on intensity of primary dysmenorrhea. Int J Gynaecol Obstet 2012;117(1):45–7.
[60] Calder PC. Omega-3 fatty acids and inflammatory processes. Nutrients 2010;2(3):355–74.
[61] Snipe RMJ, Brelis B, Kappas C, Young JK, Eishold L, Chui JM, et al. Omega-3 long chain polyunsaturated fatty acids as a potential treatment for reducing dysmenorrhoea pain: systematic literature review and meta-analysis. Nutr Diet 2024;81(1):94–106.
[62] Rahnama P, Montazeri A, Huseini HF, Kianbakht S, Naseri M. Effect of *Zingiber officinale* R. Rhizomes (ginger) on pain relief in primary dysmenorrhea: a placebo randomized trial. BMC Complement Altern Med 2012;12:92.
[63] Rondanelli M, Fossari F, Vecchio V, Gasparri C, Peroni G, Spadaccini D, et al. Clinical trials on pain lowering effect of ginger: a narrative review. Phytother Res 2020;34(11):2843–56.
[64] Ozgoli G, Goli M, Moattar F. Comparison of effects of ginger, mefenamic acid, and ibuprofen on pain in women with primary dysmenorrhea. J Altern Complement Med 2009;15(2):129–32.
[65] Sharifipour F, Siahkal SF, Qaderi K, Mohaghegh Z, Zahedian M, Azizi F. Effect of curcumin on dysmenorrhea and symptoms of premenstrual syndrome: a systematic review and meta-analysis. Korean J Fam Med 2024;45(2):96–104.
[66] Agarwal D, Chaudhary P. Effect of turmeric-Boswellia-sesame formulation in menstrual cramp pain associated with primary dysmenorrhea-a double-blind, randomized, placebo-controlled study. J Clin Med 2023;12(12).
[67] Parazzini F, Di Martino M, Pellegrino P. Magnesium in the gynecological practice: a literature review. Magnes Res 2017;30(1):1–7.
[68] Proctor ML, Murphy PA. Herbal and dietary therapies for primary and secondary dysmenorrhoea. Cochrane Database Syst Rev 2001;(3):CD002124.
[69] Fontana-Klaiber H, Hogg B. [Therapeutic effects of magnesium in dysmenorrhea]. Schweiz Rundsch Med Prax 1990;79(16):491–4.
[70] Yaralizadeh M, Nezamivand-Chegini S, Najar S, Namjoyan F, Abedi P. Effectiveness of magnesium on menstrual symptoms among dysmenorrheal college students: a randomized controlled trial. Int J Womens Health Reprod Sci 2020;12:70–6.
[71] Koc B, Hosgorler F, Kandis S, Acikgoz B, Kizildag S, Guner O, et al. Chronic organic magnesium supplementation enhances tissue-specific bioavailability and functional capacity in rats: a focus on brain, muscle, and vascular health. Biol Trace Elem Res 2026;204(1):253–67.
[72] Tinsley GM, Harty PS, Stratton MT, Siedler MR, Rodriguez C. Liposomal mineral absorption: a randomized crossover trial. Nutrients 2022;14(16).
[73] Niazi A, Moradi M. The effect of chamomile on pain and menstrual bleeding in primary dysmenorrhea: a systematic review. Int J Community Based Nurs Midwifery 2021;9(3):174–86.
[74] Jahangirifar M, Taebi M, Dolatian M. The effect of Cinnamon on primary dysmenorrhea: a randomized, double-blind clinical trial. Complement Ther Clin Pract 2018;33:56–60.
[75] Xu Y, Yang Q, Wang X. Efficacy of herbal medicine (cinnamon/fennel/ginger) for primary dysmenorrhea: a systematic review and meta-analysis of randomized controlled trials. J Int Med Res 2020;48(6):300060520936179.
[76] Amanak K. Effects of dry figs on primary dysmenorrhea symptoms, perceived stress levels and the quality of life. P R Health Sci J 2020;39(4):319–26.
[77] Onieva-Zafra MD, Fernandez-Martinez E, Abreu-Sanchez A, Iglesias-Lopez MT, Garcia-Padilla FM, Pedregal-Gonzalez M, et al. Relationship between diet, menstrual pain and other menstrual characteristics among Spanish students. Nutrients 2020;12(6).
[78] Lopez-Corona AV, Valencia-Espinosa I, Gonzalez-Sanchez FA, Sanchez-Lopez AL, Garcia-Amezquita LE, Garcia-Varela R. antioxidant, anti-inflammatory and cytotoxic activity of phenolic compound family extracted from raspberries (*Rubus idaeus*): a general review. Antioxidants (Basel). 2022;11(6).
[79] Majdan M, Bobrowska-Korczak B. Active compounds in fruits and inflammation in the body. Nutrients 2022;14(12).
[80] Felgus-Lavefve L, Howard L, Adams SH, Baum JI. The effects of blueberry phytochemicals on cell models of inflammation and oxidative stress. Adv Nutr 2022;13(4):1279–309.
[81] Gopalan A, Reuben SC, Ahmed S, Darvesh AS, Hohmann J, Bishayee A. The health benefits of blackcurrants. Food Funct 2012;3(8):795–809.
[82] Masoumi SZ, Asl HR, Poorolajal J, Panah MH, Oliaei SR. Evaluation of mint efficacy regarding dysmenorrhea in comparison with mefenamic acid: a double blinded randomized crossover study. Iran J Nurs Midwifery Res 2016;21(4):363–7.
[83] Najaf Najafi M, Najaf Najafi N, Rashidi Fakari F, Moeindarbary S, Abdi F, Sadat Hoseini Z, et al. The effect of aromatherapy alone or in combination with massage on dysmenorrhea: a systematic review and meta-analysis. Rev Bras Ginecol Obstet 2021;43(12):968–79.
[84] Holler M, Steindl H, Abramov-Sommariva D, Kleemann J, Loleit A, Abels C, et al. Use of *Vitex agnus-castus* in patients with menstrual cycle disorders: a single-center retrospective longitudinal cohort study. Arch Gynecol Obstet 2024;309(5):2089–98.
[85] Webster DE, He Y, Chen SN, Pauli GF, Farnsworth NR, Wang ZJ. Opioidergic mechanisms underlying the actions of *Vitex agnus-castus* L. Biochem Pharmacol 2011;81(1):170–7.
[86] Sui Y, Xu D. Isolation and identification of anti-inflammatory and analgesic polysaccharides from Coix seed (*Coix lacryma-jobi* L. var. *Ma-yuen* (Roman.) Stapf). Nat Prod Res 2024;38(13):2165–74.
[87] Hsia SM, Yeh CL, Kuo YH, Wang PS, Chiang W. Effects of adlay (*Coix lachryma-jobi* L. var. *Ma-yuen* Stapf.) hull extracts on the secretion of progesterone and estradiol in vivo and in vitro. Exp Biol Med (Maywood) 2007;232(9):1181–94.
[88] Goyal A, Raza FA, Sulaiman SA, Shahzad A, Aaqil SI, Iqbal M, et al. Saffron extract as an emerging novel therapeutic option in reproduction and sexual health: recent advances and future prospectives. Ann Med Surg (Lond) 2024;86(5):2856–65.
[89] Dante G, Facchinetti F. Herbal treatments for alleviating premenstrual symptoms: a systematic review. J Psychosom Obstet Gynaecol 2011;32(1):42–51.
[90] Moshfegh F, Balanejad SZ, Shahrokhabady K, Attaranzadeh A. *Crocus sativus* (saffron) petals extract and its active ingredient, anthocyanin improves ovarian dysfunction, regulation of inflammatory genes and antioxidant factors in testosterone-induced PCOS mice. J Ethnopharmacol 2022;282:114594.
[91] Fukui H, Toyoshima K, Komaki R. Psychological and neuroendocrinological effects of odor of saffron (*Crocus sativus*). Phytomedicine 2011;18(8–9):726–30.
[92] Marx W, Lane M, Rocks T, Ruusunen A, Loughman A, Lopresti A, et al. Effect of saffron supplementation on symptoms of depression and anxiety: a systematic review and meta-analysis. Nutr Rev 2019;77(8):557–71.
[93] Ziaei S, Zakeri M, Kazemnejad A. A randomised controlled trial of vitamin E in the treatment of primary dysmenorrhoea. BJOG 2005;112(4):466–9.
[94] Alikamali M, Mohammad-Alizadeh-Charandabi S, Maghalian M, Mirghafourvand M. The effects of vitamin E on the intensity of primary dysmenorrhea: a systematic review and meta-analysis. Clin Nutr ESPEN 2022;52:50–9.
[95] Obiagwu HI, Eleje GU, Obiechina NJA, Nwosu BO, Udigwe GO, Ikechebelu JI, et al. Efficacy of zinc supplementation for the treatment of dysmenorrhoea: a double-blind randomised controlled trial. J Int Med Res 2023;51(5):3000605231171489.
[96] Teimoori B, Ghasemi M, Hoseini ZS, Razavi M. The efficacy of zinc administration in the treatment of primary dysmenorrhea. Oman Med J 2016;31(2):107–11.
[97] Assiri GA, Bannan DF, Alshehri GH, Alshyhani M, Almatri W, Mahmoud MA. The contraindications to combined oral contraceptives among reproductive-aged women in an obstetrics and gynaecology clinic: a single-centre cross-sectional study. Int J Environ Res Public Health 2022;19(3).
[98] Dutton C, Kim R, Janiak E. Prevalence of contraindications to progestin-only contraceptive pills in a multi-institution patient database. Contraception 2021;103(5):367–70.
[99] Xu Z, Li Y, Tang S, Huang X, Chen T. Current use of oral contraceptives and the risk of first-ever ischemic stroke: a meta-analysis of observational studies. Thromb Res 2015;136(1):52–60.

Dr. Ciarmela is an Associate Professor of Human Anatomy at Università Politecnica delle Marche, Italy. She focused her research investigation in uterine physiology and pathophysiology and explored the role of growth factors. The studies conducted are aimed at understanding the pathogenesis of female diseases and at developing potential therapeutic agents.