

Impact of Nutraceuticals on Dysmenorrhea

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ABSTRACT

A nutraceutical is a compound of the name's nutrition and pharmaceutical. Foods or diet components that play essential roles in ensuring the proper maintenance and regulation of the normal physiological state of an individual are what are called nutraceuticals. There exist a variety of pharmaceutical drugs which can be used to treat dysmenorrhea yet each one of them has severe side effects. Conversely, lifestyle modifications and dietary supplements were found to make a huge difference in the occurrence and treatment of dysmenorrhea. This work is aimed at investigating comprehensive research of nutritional supplements and dieting with reference to dysmenorrhea. This research is focused on the nuances of menstrual pain and an effective nutritional diet that may be applied as treatment to avoid monthly pain. Dysmenorrhea is the most common condition in women of child bearing-age. It is marked by pain-wracking uterine cramps during the menstruating period. Where secondary dysmenorrhea is the pain in the pelvis caused by a pelvic pathology present, in primary dysmenorrhea the pain is not due to any inherent cause. Nutraceuticals or naturally derived substances with medical benefits have proven to be very promising at least in many research papers, yet their potential has yet to be realized in the large-scale clinical application in any condition. Historical relevance of natural goods in drug discovery is depicted by the reality that large numbers of medications available today like the first analgesic aspirin are produced using plant-derived substances.

Keywords: Dysmenorrhea, Pelvic Pain, Nutraceutical, Women, Menstrual Cycle

INTRODUCTION

Dysmenorrhea: What it Is and Why It Matters

Initially dysmenorrhea is a very common gynaecological complication and occurs in 71-90 percent of women across the world; who are in the reproductive age. The hallmark of the condition is painful menstrual cramps unrelated to pelvic pathology, and it significantly affects the fulfilment of daily activities, school performance, and the quality of life. The cost which is economical is quite considerable as nearly half or 40.9 of young women claim to be performing poorly in academics and 20.1

of them state they miss out on school or university due to dysmenorrhea. [1]

What are Nutraceuticals and why are they important?

Combining nutrition and pharmaceutical is how people define nutraceuticals, bioactive substances in food and which goes beyond nutrition. They are attractive as a result of their availability, favourable overall safety efficacies, and application of analgesic, antioxidant, and anti-inflammatory effects to heal the pathophysiology of dysmenorrhea. [2,3]

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.



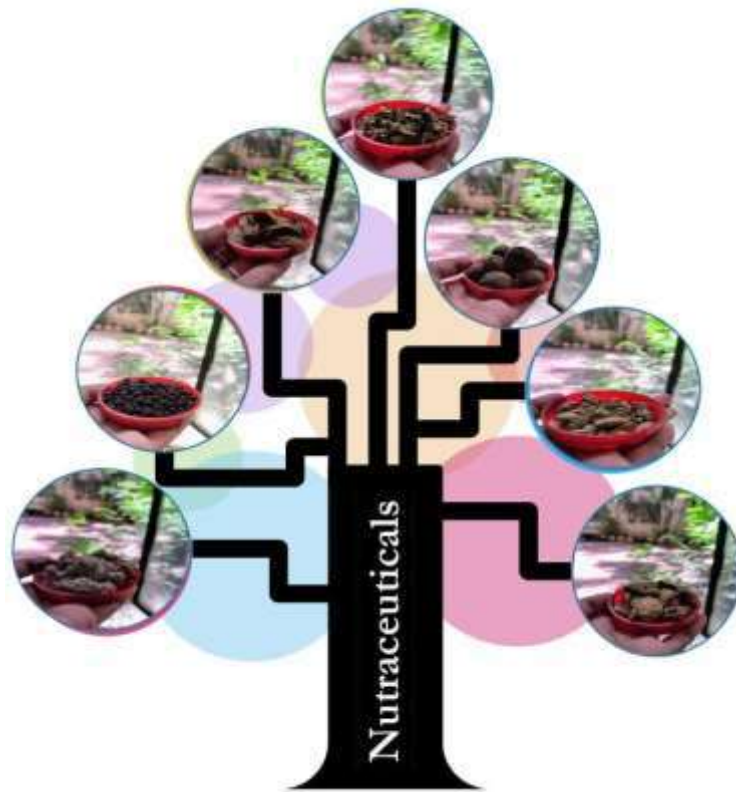


Figure 1: Nutraceuticals

Drawbacks of Traditional Therapy:

The recent used first-line treatments, that is, hormonal contraception and nonsteroidal anti-inflammatory medicines, have a number of disadvantages in this respect, including a 20-25 percent failure rate, incompatibility with patient conditions, and relative side effects, including a high risk of stroke. Other treatment methods have been coming into focus due to such trammels. [2]

Disadvantage of Painkillers Used in Dysmenorrhea:

Experiencing painful menstruation (dysmenorrhea) is a symptom that restricts normal functioning, and this condition may need the intervention of painkillers. According to certain data, it may combat between 70 and 90 percent of women [4]. It takes 1-3 days to heal, and is caused by an excess of pro-inflammatory types of prostaglandins (mainly Prostaglandin F_{2a} and Prostaglandin 2) in your pelvic muscles [5]. Menstrual discomfort can be treated with an analgesic and anti-inflammatory agent, e.g., belonging to the nonsteroidal anti-inflammatory group, which, with prolonged application, may also contribute to the impairment of kidney glomerular filtration or lesions

of the gastrointestinal mucosa [6]. There should be efforts to minimise the distribution of such preparations by those women with menstrual pain. Some of the other approaches in the field of medicine used to minimize menstrual pain include oral contraception, danazol, hysterectomy, acupuncture among others. Moreover, painful menstruation is the most frequent reason of temporary nonattendance in the school of young girls, and it absolutely only confirms the size of the problem and necessity of development of the options of medical support in this aspect [7]. The existing standard medication used to treat dysmenorrhea is anti-inflammatory drugs and oral contraceptives pills. Nevertheless, non-steroidal anti-inflammatory has undesirable complications such as peptic ulcers, hepatorenal anomalies, and allergies [8]. Moreover, oral contraceptive pills decrease the number of Prostaglandins but suppresses ovulation, which has the effect of making blood become hypercoagulated, possible breast-related morbidity, pregnancy complications, cultural and religious issues/concerning. It is encouraging that non drug interventions may be effective in managing the symptoms after all, much exercise; the topical usage of a heating pad; intake of ginger, cinnamon, curcumin, fish oil, vitamins and minerals;

acupuncture or even surgery are treatment modalities that may help relieve the symptoms [9,10]. This study indicated that especially women, who had dysmenorrhea and were using Non-steroidal anti-inflammatory treatment options, there were more susceptible to stroke twice as more likely as compared to women who did not use non-steroidal anti-inflammatory tools. This shows that non-steroidal anti-inflammatory might greatly promote the occurrence of stroke in women experiencing dysmenorrhea. [11]

Advantages of Nutraceuticals:

By directly addressing the severe restrictions of Non-steroidal anti-inflammatory and oral contraceptive pills as described in your text, nutraceuticals provide obvious benefits over conventional treatments for dysmenorrhea. Contrary to Non-steroidal anti-inflammatory, which induce glomerular filtration reduction, liver damage, and gastrointestinal damage, nutraceuticals have great safety profiles devoid of renal, hepatic, or gastrointestinal concerns. Ginger acts as an inhibitor on cyclooxygenase and lipoxygenase, resulting in an inhibition of leukotriene and prostaglandin synthesis. Therefore, ginger has been used as an anti-inflammatory acting by inhibition of prostaglandin synthesis. Ginger is therefore worthy of consideration as an analgesic in primary dysmenorrhea. [12] Well-tolerated therapeutic choices" like ginger, curcumin, and omega-3 fatty acids are often quoted as "might be employed as an alternative to non-steroidal anti-inflammatory drugs" without harmful consequences. Studies comparing cinnamon to ibuprofen show similar efficient pain relief but with better safety profiles; bee propolis provides dysmenorrhea relief & "with no negative effects." [13,14] Regarding the cardiovascular and reproductive issues with Oral contraceptive pills, nutraceuticals offer no blood hypercoagulation hazards and in fact help to preserve natural hormonal activity. Although Oral contraceptive pills suppress ovulation and raise thrombotic risks, vitamin D supplementation enhances natural hormone regulation without disrupting reproductive cycles; omega-3 fatty acids improve cardiovascular health while treating dysmenorrhea. Unlike Oral contraceptive pills that cause religious and cultural strife, natural supplements are very well tolerated in many different

backgrounds and do not have pregnancy-related problems, so they are appropriate for women looking to planning families. [15,16]

Pathophysiology and Treatment Targets of Dysmenorrhea:

Prostaglandin Mediated Pain Mechanism:

Due to increased production of prostaglandins, particularly Prostaglandin F₂α and Prostaglandin E₂ that cause myometrial contractions and vasoconstriction, excessive production of prostaglandins is what leads to primary dysmenorrhea. The major therapeutic target is its cyclooxygenase pathway which is critical to synthesizing prostaglandins. [17]

Elements of Oxidative and Inflammatory Stress:

The recent evidence indicates that oxidative stress and inflammation are significant contributors of dysmenorrhea pathophysiology. Increased inflammatory biomarkers and reduced antioxidant effect in women with dysmenorrhea, provides further therapeutic targets which can be used in nutraceutical treatments. [18]

Neurological and hormonal causes:

Nutraceuticals can mediate hormonal fluctuations in many ways and the pathology also includes a complex involvement of the neurological system including the 5-Hydroxytryptamine receptor/Ca²⁺/mitogen activated protein kinase signalling pathway. [19]

Evidence Based Appraisal of Specific Nutraceuticals:

Omega-3 Fatty Acids:

Many methodical reviews have revealed that the use of omega-3 supplements significantly reduces the intensity and the length of dysmenorrhea. A large study enrolling 44 teenagers also showed that fish oil treatment produced an impressive reduction in visual analog scale scores, painkiller intake and school time missed compared with a placebo. [20]

1. Mechanism:

The anti-inflammatory effect of omega-3 oleic acids is because they can alter the formation of prostaglandins, therefore, inhibiting the formation of the inflammation mediator. There have been reduced cases of severe primary dysmenorrhea with a recommended daily dose of 1.1 grams or greater.

Vitamin D:

Based on an in-depth meta-analysis published in eight randomized controlled trials to 695 individuals, consumption of vitamin D supplements considerably reduced the level of pain (Standardized Mean Difference: -1.404, 95% CI: -2.078 to -0.731). In line with the analysis, the best efficacy was recorded in the weekly doses exceeding 50,000 IU. [21]

1. Response Dose Correlation:

Subgroup analysis showed that the pain was decreased both when there was greater than 70 days use of the medication, and less, the therapeutic onset of the medication was shown to be quick regardless of the dose provided, as long as it was properly dosed. [22]

Curcumin:

The recent systematic reviews of 17 studies proved that curcumin plays a significant effect in lessening degree and length of dysmenorrhea by many methods. In clinical research, the reduction of pain and improvement in the quality of life have been observed with the intake of 500 mg of curcumin with 5 mg of piperine in the diet on a daily basis. [23]

1. Mechanisms:

Curcumin has been shown to work by:

Reduced production of prostaglandins and Cyclooxygenase-2 inhibition. The linear reduction in antioxidant activity and oxidative stress. Neurotransmitter regulation (dopamine and serotonin). Enhancing vitamin D Improving levels

Ginger (*Zingiber officinale*):

Many meta-analyses confirm the efficiency of ginger to treat dysmenorrhea. In a systematic review of six trials that compared ginger to placebo, ginger was

only better: the weighted mean difference was 1.55 cm on a 10 cm visual analog scale (95% CI: 0.68-2.43). [24]

1. Active Compounds in Ginger:

These medicinal effects are caused by chemicals zingiberene, shogaol and gingerol. It has been tested that 500 mg taken thrice a day during the first three days of menstruation is effective. [25]

Other Remedies:

1. Cinnamon & Fennel:

As per a comprehensive meta-analysis, not only ginger, but also fennel decreased the level of pain when compared to a placebo, with the most advantageous effect; cinnamon not only conferred such an effect but it also relieved the hours of pain. The investigation used 12 herbal remedies with a high degree of efficacy.

2. Vitamin E:

It is believed to have analgesic effect since it contributes so much to the safeguarding of the cellular membranes against peroxidative breakage. Its analgesic effects may be as a result of repression of the spinal cord of the dorsal horns N-Methyl-D-aspartate. [26]

3. Vitamin C:

It has been proposed that it suppresses blood flow measures of inflammation, most probably due to its antioxidant activity. It is well known that the outflow of inflammatory substances is accompanied by pain sensitivity. Thus, the anti-inflammatory and antioxidant properties of this vitamin can minimize the pain. [26]

Traditional Herbs Remedies:

A study on Dangguijagyag-san and other traditional preparations has been promising and it needs further comprehensive research to establish an optimal dosage and safety aspects. [27]

Allopathic Remedies in Treatment of Dysmenorrhea:

Allopathic (conventional western medicine) treatments for dysmenorrhea primarily involve medications that address pain and inflammation. Here are common examples:

Nonsteroidal Anti-Inflammatory Drugs.

These are considered the first-line treatment for dysmenorrhea. They work by inhibiting prostaglandin synthesis, which is responsible for uterine contractions and pain.

- Ibuprofen (Advil, Motrin)
- Naproxen (Aleve, Naprosyn)
- Mefenamic acid (Ponstel, Meftal)
- Diclofenac
- Ketoprofen
- Aspirin

The symptoms and pain compromise the quality of life of the women and their capacity to accomplish normal day tasks [28]. Nonsteroidal anti-inflammatory drugs are the first choice of treatment in the primary dysmenorrhea today. The adverse effects of NSAIDs include gastrointestinal toxicities, risk of cardiovascular, renal harms and liver harms. The second-line drug is hormone adjustment with oral contraceptives or intrauterine, as well as IUD devices. Combined oral contraception pills have proven to be beneficial in lowering the severity of dysmenorrhea [29]. The reactions of adverse nature to estrogen contraceptives arise in the form of nausea, vomiting, headaches, tenderness of the breast, and alterations in body weight. Moreover, using progesterone oral contraceptive pills, a patient may have acne, gain weight, become hairy, and even experience depression [30]. Another therapy is that of the osteopathic manipulative medicine. Osteopathic manipulative treatment is a non-supportive care approach that is intended to enhance joint functioning, muscular tension and viscerosomatic reflection [31]. Dysmenorrhea is noticed to have viscerosomatic reflexes in the T10-L2 area which can in theory be effectively treated by use of Osteopathic manipulative treatment [32].

Clinical Applications and Dosing Recommendations:

Dosing Protocols:

1. Magnesium:

Dosing: Studies typically use 150–300mg daily. Both doses appear similarly effective at reducing pain. [33]

2. Vitamin D:

Dosing: Randomized trials used either a single large dose (300,000IU given 5 days before menstruation under physician supervision. High doses should be monitored by a healthcare professional. [34]

3. Vitamin B1:

Dosing: 100MG per day for 90 days. Not recommended for women without known or probable deficiency. [35]

4. Curcumin:

Dosing: 1g/day, started at onset of pain or prior to menses. [36]

5. Calcium:

Dosing: Standard dietary intake or supplements up to 1,200mg/day, depending in individual requirement and dietary habits. [37]

Combination Therapy Approaches:

Combination therapy approaches using nutraceuticals for dysmenorrhea have been explored in several clinical studies, with evidence suggesting synergistic effects in reducing menstrual pain when certain nutrients and supplements are used together.

Vitamin E and Omega-3 Fatty Acids:

A double-blind, randomized clinical trial investigated the effects of vitamin E (200 IU) and omega-3 fatty acids (300 mg; 180 mg eicosahexanoic acid and 120 mg Docosahexaenoic acid), both separately and in combination, on women with primary dysmenorrhea. All supplement groups reported significant pain relief compared to placebo; notably, the combination of vitamin E and omega-3 was superior to either supplement alone ($p < .05$), indicating additive or synergistic benefit. The study emphasizes the safety and efficacy of these nutraceuticals as alternatives or adjuncts to non-steroidal and anti-inflammatory

drugs, which may have higher complication risks. [38]

Herbal Combination Therapies:

Multi-herb formulations (including chamomile, ginger, cinnamon, fennel, rosemary, valerian, zataria, and vitex agnus-castus) are frequently used in traditional medicine. Clinical studies report that combination herbal preparations may alleviate menstrual pain more effectively than single-herb interventions, likely due to varied mechanisms

antispasmodic, anti-inflammatory, analgesic and hormonal modulation. Dosing varies by formulation but typically aligns with standardized extracts used in published trials. [39]

Spice Blends (Ginger, Dill, Cumin):

Some research has tested combinations of spices for dysmenorrhea management, with findings that blended use can provide cumulative relief of pain and associated symptoms beyond single spices. [40]

Table-1: Effect of nutraceuticals on dysmenorrhea with dosage and safety profile & advantages over non-steroidal anti-inflammatory drugs

Nutraceutical	Effect on Dysmenorrhea	Advantages Over non-steroidal anti-inflammatory drugs	Source of Nutraceutical	Dosage	Safety Profile
Omega-3 Fatty Acid	May reduce pain severity, especially with vitamin B1	No GI/renal toxicity, cardiovascular benefits	Fish oil, flaxseed, chia seeds	≥ 1.1 g/day	Excellent, minimal side effects
Ginger	May reduce pain intensity	Equal efficacy without side effects	Ginger root, ginger supplements	500mg Ter in day $\times$ 3 days	Generally safe, rare mild GI upset
Vitamin D	May help ameliorate symptoms	No organ toxicity, enhances natural function	Sunlight, fortified foods, supplements	300,000 IU (50,000 IU/week)	Well-tolerated, no serious AEs
Curcumin	Not specifically addressed	Multi-target action, no hepatic damage	Turmeric root, turmeric supplements	1g/day	Minimal side effects
Cinnamon & Fennel	No consistent evidence of effectiveness	Anti-inflammatory, analgesic, Antispasmodic, anti-inflammatory	Cinnamon bark, fennel seeds	420mg TID, Extract capsules (fennel)	Safe, no serious adverse events, well-tolerated, no contraindications
Vitamin E	No evidence of effectiveness	Antioxidant, membrane stabilization	Nuts, seeds, vegetable oils	400 IU daily	Safe in recommended doses
Vitamin C	Pain is reduced by the anti-inflammatory and antioxidant characteristics.	antioxidant & anti-inflammatory properties	Citrus fruits, berries, vegetables	1000mg daily (2 $\times$ 500mg tablets)	No significant side effects, water-soluble vitamin
Vitamin B1	May reduce pain intensity	Nervous system support	Whole grains, legumes, supplements	100mg per day for 90 days	Safe, water-soluble vitamin
Calcium	Mentioned as potentially beneficial for menstrual pain	Natural muscle relaxation, Bone health benefits	Dairy products, leafy greens, almonds	1,200mg/day	No effect on serum calcium levels

FUTURE RESEARCH DIRECTIONS:

Clinical Trial Priorities:

1.High-Quality Randomized Clinical Trials:

Ginger is "highly helpful in the alleviation of primary dysmenorrhea," according to their research. Additional patient studies are needed to ascertain the effectiveness and safety of various ginger dosages. [41] A wide range of interventions for primary dysmenorrhea, from vitamin D supplementation, herbal formulations, heat therapy, manual treatment, and acupuncture-related therapies, have been evaluated by high-quality randomized controlled trials (RCTs). Due to heterogeneity and bias risk, the quality of evidence from randomized clinical trials is only fair to middling, but meta-analysis of these trials shows that vitamin D supplementation is helpful in lowering the severity of pain in women with primary dysmenorrhea, especially at dosages higher than baseline. Overall, although several interventions are found effective in relieving primary dysmenorrhea, the necessity of well-designed, large-scale, high-quality RCTs still exists to establish efficacy, maximize dosing, and ascertain safety. [42]

2. Comparative Effectiveness Studies:

The best treatment plans can only be developed by head-to-head comparisons of several nutraceuticals with combination treatments. Comparative efficiency There aren't many studies on nutraceuticals for dysmenorrhea, and most of them concentrate on individual supplements rather than direct comparisons or combination therapies. Even though 27 randomized controlled trials looked at a variety of supplements, both herbal and non-herbal, very few of them directly compared different nutraceuticals to one another, and most comparisons were based on single studies with small sample sizes, according to a significant systematic review. [42]

CONCLUSION:

There is growing clinical data supporting the use of nutraceuticals such omega-3 fatty acids, vitamin D, curcumin, and ginger in the management of dysmenorrhea. These therapies provide possible options or complement to conventional therapies

since they have generally favourable safety profiles and multiple mechanisms of action that address the complex pathophysiology of dysmenorrhea. [44][45] Omega-3 fatty acids ($\geq 1.1\text{g/day}$) Because of the significant impact of omega-3 fatty acids on the experience of menstrual pain, which limits patients' daily functioning and causes girls to miss school, people often take pain relievers on a regular basis, which has a long list of negative side effects. [44] Vitamin D- Vit. D deficiency and primary dysmenorrhea in women were treated with vit. D supplements, which lessened the intensity of dysmenorrhea-related discomfort. Vit. D supplementation raised serum 25(OH)D levels, reduced painkiller usage, and revealed a significant negative correlation between serum 25(OH)D levels and pain severity. [46] Curcumin- (500mg daily) Through a variety of mechanisms, curcumin drastically and efficiently alleviates pain and alleviates the symptoms of Pre-menstrual syndrome (behavioural, emotional, and physical ailments).[47] Ginger-(1,500mg daily) According to reports, ginger was more effective for pain alleviation, and there was no discernible difference between ginger and non-steroidal anti-inflammatory drugs. Significant research gaps still exist, though, including need for better combination therapy regimens, consistent preparations, long-term safety data, and more high-quality clinical trials. Medical practitioners should consider nutraceuticals as evidence-based therapy options for dysmenorrhea, especially for patients who are unable to use conventional treatments. Future dysmenorrhea treatment will probably entail customized, multimodal strategies that combine conventional therapies with evidence-based nutraceutical interventions.

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HOW TO CITE: Khushi Gupta*, Saloni Borse, Anjali Gavit, Impact of Nutraceuticals on Dysmenorrhea, *Int. J. Sci. R. Tech.*, 2025, 2 (10), 341-350. <https://doi.org/10.5281/zenodo.17373886>