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The Role of Dietary Supplements and Bioactive Compounds in Endometriosis: Current Knowledge

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Abstract

Endometriosis is a chronic gynecological disorder affecting 6–10% of women of reproductive age, with increasing rates of diagnosis highlighting its emerging clinical relevance. The pathogenesis of endometriosis is multifactorial, involving chronic inflammation, oxidative stress, enhanced angiogenesis and immune dysregulation. Conventional hormonal and surgical therapies often fail to provide sustained relief, prompting interest in adjuvant strategies, including dietary supplementation and bioactive compounds. Evidence from clinical and experimental studies suggests that vitamins C and E, polyphenols, omega-3 fatty acids, vitamin D, N-acetylcysteine, bromelain, inositols, and probiotics may modulate oxidative stress, inflammatory responses, and endometrial cell proliferation. Despite promising findings, standardized trials evaluating the efficacy and safety of these interventions are lacking, underscoring the need for further well-designed clinical studies.

Keywords: endometriosis, dietary supplements, bioactive compounds, inflammation.

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Introduction

Endometriosis is a chronic gynecological disease affecting approximately 6–10% of women of reproductive age and represents a significant clinical problem due to chronic pelvic pain, menstrual cycle disturbances, dyspareunia, and infertility [1–3]. The increasing rate of diagnosis highlights the need to identify effective and safe therapeutic strategies.

The pathogenesis of endometriosis is multifactorial and involves chronic inflammation, increased oxidative stress, enhanced angiogenesis, and immune dysregulation [2,4]. Standard treatment approaches, including hormonal pharmacotherapy and surgical interventions, do not always result in sustained clinical improvement, and their effectiveness is often limited by adverse effects and disease recurrence.

Consequently, there is growing interest in adjunctive strategies for the management of endometriosis, including dietary interventions, dietary supplementation, and the use of bioactive compounds that may modulate inflammatory processes, oxidative stress, and endometrial cell proliferation [1,5–7].

The aim of this study is to review current scientific evidence regarding the efficacy and potential application of dietary supplements and bioactive compounds in endometriosis.

Methods

A narrative review of the literature was conducted, including scientific publications from 2013 to 2025 addressing the role of dietary supplements, bioactive compounds, and nutritional interventions in endometriosis. The analysis encompassed randomized and non-randomized clinical studies, observational studies, experimental research (in vitro and in vivo), systematic reviews, meta-analyses, and narrative reviews.

Publications were identified through searches of the PubMed, Scopus, and Web of Science databases. The review included studies involving women diagnosed with endometriosis or experimental models of the disease that examined the effects of dietary supplements or specific bioactive compounds on clinical symptoms, inflammatory markers, oxidative stress, or pathophysiological mechanisms of endometriosis. Only publications in the English language were considered.

The analysis incorporated evidence of varying scientific strength, which was explicitly indicated in the presentation of the results. No formal methodological quality assessment of the included studies was performed, which constitutes a limitation of the present review.

Results

The analysis of the literature indicated that the greatest research interest in the context of supplementation in endometriosis concerns substances with antioxidant and anti-inflammatory properties, including vitamins, polyphenols, omega-3 fatty acids, N-acetylcysteine, probiotics, and selected compounds modulating the immune response.

A summary of the most frequently analyzed dietary supplements and bioactive compounds, their mechanisms of action, the characteristics of the available studies, and their potential clinical applications is presented in Table 1.

Table 1. Dietary supplements and bioactive compounds in endometriosis – mechanisms of action and characteristics of available studies

Substance/group	Main mechanisms of action described in the literature	Type of studies included in the review	Main observed effects
Vitamins C and E	Reduction of oxidative stress; inhibition of lipid peroxidation	Randomized clinical trials; meta-analyses	Reduction of pain; decreased oxidative stress markers
Vitamin D	Modulation of inflammatory and immune responses	Randomized clinical trials	Good tolerability; no clear superiority over placebo in pain reduction
Omega-3 fatty acids	Inhibition of pro-inflammatory eicosanoid synthesis; modulation of cytokines (TNF-α, IL-6)	Clinical studies	Reduction in pain severity; improvement of symptoms
Polyphenols (curcumin, resveratrol, quercetin)	Inhibition of NF-κB activation, angiogenesis, and endometrial cell proliferation	In vitro and in vivo studies; narrative and systematic reviews	Attenuation of inflammatory and proliferative processes

N-acetylcysteine (NAC)	Antioxidant and anti-proliferative effects	Observational studies; in vitro and in vivo models	Reduction in the volume of endometriotic lesions
Bromelain + alpha-lipoic acid	Synergistic anti-inflammatory activity	In vitro and in vivo studies	Suppression of inflammatory responses
Inositols (D-chiro-inositol)	Hormonal regulation; modulation of cellular metabolism	Animal models	Inhibition of endometriotic lesion development
Probiotics (*Lactobacillus* spp.)	Modulation of gut microbiota; reduction of NLRP3 inflammasome expression	Clinical studies	Partial attenuation of inflammatory response

Vitamins C and E, as potent antioxidants, play a key role in neutralizing free radicals and inhibiting lipid peroxidation. Clinical studies have demonstrated that combined supplementation with vitamins C and E may lead to a reduction in pain and oxidative stress biomarkers in patients with endometriosis. These effects have been confirmed mainly in randomized clinical trials and meta-analyses involving relatively small patient cohorts, while data from long-term studies remain limited [14,16,17,26]. Similarly, other naturally derived antioxidants, such as epigallocatechin-3-gallate (EGCG), have been shown to reduce oxidative stress and inflammatory markers in endometriotic cells, which may play a significant role in alleviating disease-related symptoms [15].

Vitamin D supplementation may influence the course of endometriosis through modulation of inflammation, oxidative stress, and immune function [27]. However, its analgesic effect remains inconclusive. In a clinical study in which patients with endometriosis received vitamin D or placebo, pain reduction was observed in all groups, with no significant advantage of supplementation over placebo [18].

Omega-3 fatty acids are among the most extensively studied supportive substances in patients with endometriosis. Their mechanism of action includes inhibition of pro-inflammatory eicosanoid

synthesis and modulation of cytokines such as TNF-α and IL-6 [5,18]. Clinical studies indicate that omega-3 fatty acid supplementation may lead to pain reduction and improvement of endometriosis-related symptoms in young women [18].

A significant group of bioactive compounds includes polyphenols such as curcumin, resveratrol, and quercetin. Scientific reviews indicate that polyphenols can inhibit inflammatory pathways, including suppression of NF-κB activation, which contributes to their therapeutic potential in endometriosis management [22]. Curcumin exhibits NF-κB-modulating activity and inhibits endometrial cell proliferation [13]. Resveratrol affects angiogenesis and VEGF expression, which may limit the progression of endometriotic lesions [13,22]. Quercetin demonstrates immunomodulatory effects in laboratory studies on endometrial cells, suggesting a potential impact on inflammatory processes in endometriosis [23]. It should be emphasized that most data regarding polyphenols originate from in vitro studies and animal models, and the number of clinical studies evaluating their efficacy in women with endometriosis remains limited [13,22,23].

Experimental and clinical studies indicate that N-acetylcysteine (NAC) exhibits antioxidant and anti-proliferative effects, leading to a reduction in the volume of endometriotic cysts and inhibition of endometrial cell proliferation, suggesting its potential effectiveness as an adjunctive therapy in endometriosis management [24,25]. Bromelain, in combination with NAC and alpha-lipoic acid, has demonstrated strong anti-inflammatory properties in in vivo and in vitro models, suggesting that such combinations may represent an effective supportive therapeutic approach in endometriosis [21]. It should be noted that the observed reductions in endometriotic cyst volume are derived primarily from observational and experimental studies, while randomized clinical trials remain limited [24,25].

Despite growing interest in inositol supplementation in endometriosis, there are currently no randomized controlled trials evaluating the efficacy of these compounds in patients. However, preclinical studies indicate that D-chiro-inositol may inhibit the development of endometriotic lesions in murine models, suggesting a potential influence on hormonal regulation and disease progression [20].

Probiotics may influence intestinal inflammation and modulate immune responses. Alterations in gut microbiota have been associated with increased severity of endometriosis symptoms, and supplementation with *Lactobacillus* species has been shown to reduce NLRP3 inflammasome expression, indicating partial attenuation of inflammatory responses [19].

Systematic reviews and meta-analyses emphasize the importance of an anti-inflammatory diet low in saturated fats and rich in antioxidants, omega-3 fatty acids, fiber, and polyphenols [2,3,6,7,9,12]. Nutritional interventions may contribute to reductions in inflammatory markers, pain severity, and improvements in fertility outcomes [3,7].

Discussion

The collected data indicate that dietary supplementation and bioactive compounds may represent a valuable adjunct to standard endometriosis treatment; however, their effectiveness depends on the type of substance, dosage, duration of use, and the strength of the available scientific evidence. The strongest clinical evidence concerns vitamins C and E as well as omega-3 fatty acids, for which reductions in pain and inflammatory markers have been demonstrated in studies involving patients with endometriosis [14,16,18,26].

In the case of polyphenols, N-acetylcysteine (NAC), bromelain, and inositols, most of the available evidence originates from preclinical studies, which limits the direct translation of these findings into clinical practice. Promising mechanisms of action, such as inhibition of NF-κB activation, angiogenesis, and endometrial cell proliferation, require confirmation in randomized clinical trials [13,21–25].

An important issue remains the safety of long-term supplementation and its potential use as part of adjunctive therapy. Available data on the safety of supplementation in endometriosis are limited and heterogeneous. Clinical studies involving vitamins C and E did not report significant adverse effects; however, the authors emphasized that the administered doses and duration of supplementation were limited [14,16,17,26]. Long-term use of high doses of antioxidants may potentially affect redox homeostasis, indicating the need for further investigation.

With respect to vitamin D, supplementation was well tolerated; however, no clear clinical superiority over placebo in pain reduction was demonstrated, highlighting the need for cautious interpretation of its therapeutic efficacy [18,27]. Omega-3 fatty acids are generally considered safe, although their anti-inflammatory and analgesic effects depend on dosage, duration of supplementation, and the baseline inflammatory status of patients [5,18].

Data regarding N-acetylcysteine, bromelain, and alpha-lipoic acid suggest a favorable safety profile in short-term studies; however, large clinical trials assessing long-term use and potential interactions with hormonal therapy are lacking [21,24,25]. With regard to polyphenols, probiotics, and inositols, review articles emphasize the lack of standardized dosing regimens and the limited number of clinical studies, which currently precludes the formulation of clear therapeutic recommendations [13,19,20,22].

Conclusions

Available evidence suggests that supplementation with compounds exhibiting antioxidant, anti-inflammatory, and immunomodulatory properties may support the management of endometriosis by reducing oxidative stress, modulating inflammatory responses, and limiting endometrial cell proliferation [14,15,24,25]. Particularly promising appear to be combinations of substances such as N-acetylcysteine, bromelain, and alpha-lipoic acid, which have demonstrated synergistic anti-inflammatory effects in preclinical studies [21]. Polyphenols, vitamins C and E, omega-3 fatty acids, and vitamin D may further enhance antioxidant mechanisms and modulate inflammatory processes [13,14,18,22,27], while probiotics represent a potential tool for restoring gut microbiota balance [19].

Despite the growing number of experimental and clinical studies, significant knowledge gaps remain regarding the efficacy of several promising supplements, including inositols and vitamin D. It should be emphasized that standardized clinical dosing has not yet been established for most supplements used in women with endometriosis, which limits the development of precise therapeutic recommendations. This highlights the need for further well-designed studies involving diverse patient populations and standardized supplement dosages to more accurately assess their safety, efficacy, and potential synergistic effects in endometriosis management [13,18,20,27].

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