International Journal of Innovative Technologies in Social Science

e-ISSN: 2544-9435

Operating Publisher
SciFormat Publishing Inc.
ISNI: 0000 0005 1449 8214

2734 17 Avenue SW,
Calgary, Alberta, T3E0A7,
Canada
+15878858911
editorial-office@sciformat.ca

ARTICLE TITLE	MEDICAL NUTRITION THERAPY, TARGETED SUPPLEMENTATION, AND MICROBIOTA MODULATION IN ENDOMETRIOSIS: A NARRATIVE REVIEW
DOI	https://doi.org/10.31435/ijitss.3(51).2026.6204
RECEIVED	17 July 2026
ACCEPTED	15 September 2026
PUBLISHED	18 September 2026
LICENSE	The article is licensed under a **Creative Commons Attribution 4.0 International License.**

MEDICAL NUTRITION THERAPY, TARGETED SUPPLEMENTATION, AND MICROBIOTA MODULATION IN ENDOMETRIOSIS: A NARRATIVE REVIEW

Aneta Sobek *(Corresponding Author, Email: anetasobek.50@gmail.com)*
Medical Center in Łańcut Sp. z o.o., Łańcut, Poland
ORCID ID: 0009-0002-6759-5419

Katarzyna Kraska
Medical Center in Łańcut Sp. z o.o., Łańcut, Poland
ORCID ID: 0009-0004-0464-6826

Jan Potoniec
Gabriel Narutowicz Municipal Specialist Hospital in Krakow, Krakow, Poland
ORCID ID: 0009-0000-5282-7833

Weronika Kępa
Independent Researcher, Poland
ORCID ID: 0009-0000-8378-9681

Joanna Kadłuczka
Ludwik Rydygier Specialist Hospital in Cracow, Kraków, Poland
ORCID ID: 0009-0002-9347-0767

Aleksandra Papuga
Independent Public Health Care Facility in Myślenice, Poland
ORCID ID: 0009-0003-6851-7102

Magdalena Grzymek
The University Hospital in Krakow, Kraków, Poland
ORCID ID: 0009-0000-4337-0261

Aleksandra Pawłucka
St. John Grande Hospital of the Brothers Hospitallers of Saint John of God, Kraków, Poland
ORCID ID: 0009-0005-6765-9314

Katarzyna Pawłucka
Jagiellonian University Medical College, Krakow, Poland
ORCID ID: 0009-0001-4273-6599

Justyna Bury
Medical University of Silesia in Katowice, Poland
ORCID ID: 0009-0001-4778-2375

Martyna Więcławek
The University Hospital in Krakow, Kraków, Poland
ORCID ID: 0009-0006-7956-9962

ABSTRACT

Endometriosis is a chronic, estrogen-dependent inflammatory disease for which conventional treatments often prove insufficient. This narrative review comprehensively evaluates the impact of Medical Nutrition Therapy (MNT), targeted supplementation, and the intestinal microbiota on the pathomechanism and clinical course of endometriosis. A structured literature search was conducted across PubMed, Scopus, and Google Scholar databases, analyzing evidence-based studies published primarily between 2016 and 2026. The synthesized findings demonstrate that personalized non-pharmacological interventions exhibit significant therapeutic potential. Specifically, the low-FODMAP diet effectively alleviates overlapping gastrointestinal symptoms, while the Mediterranean diet reduces oxidative stress and modulates estrogen metabolism. Conversely, routine gluten elimination lacks justification without specific medical indications. Targeted supplementation with vitamin D, Omega-3 fatty acids, and antioxidants exhibits immunomodulatory properties, though clinical efficacy often varies due to phenotypic heterogeneity. Furthermore, emerging evidence highlights the gut-uterine axis as a key etiopathogenetic paradigm; dysbiosis and endotoxin translocation actively drive pelvic inflammation, making estrobolome modulation highly promising. Ultimately, nutritional interventions serve as a synergistic complement to conventional medicine, highlighting the urgent need to shift from universal protocols toward multidisciplinary, precision dietary care tailored to the patient's individual metabolic and microbial phenotype.

KEYWORDS

Endometriosis, Mediterranean Diet, Low-FODMAP, Supplementation, Microbiota, Oxidative Stress

CITATION

Sobek, A., Kraska, K., Potoniec, J., Kępa, W., Kadłuczka, J., Papuga, A., Grzymek, M., Pawłucka, A., Pawłucka, K., Bury, J., & Więcławek, M. (2026). Medical nutrition therapy, targeted supplementation, and microbiota modulation in endometriosis: A narrative review. *International Journal of Innovative Technologies in Social Science*, 3(51). https://doi.org/10.31435/ijitss.3(51).2026.6204

Introduction

Endometriosis is one of the most common, yet most enigmatic, chronic gynecological diseases, defined as the presence of tissue resembling the mucous membrane of the uterine cavity (endometrium)—comprising both glandular and stromal cells—outside its natural, intrauterine location. It is estimated that this condition affects approximately 10% to 15% of women of reproductive age worldwide, translating to nearly 190 million patients globally. In the subpopulation of women struggling with infertility and chronic pelvic pain (CPP), the incidence of endometriosis dramatically increases, reaching levels of 30% to even 50% (*Muharam et al., 2025; Wilder et al., 2025*). Despite growing social and medical awareness, endometriosis still remains a disease with a significant degree of underrecognition. This phenomenon, referred to in the literature as diagnostic delay, averages 7 to 10 years from the onset of the first symptoms to the establishment of a final diagnosis *(Wilder et al., 2025)*. This is partly due to the trivialization and normalization of pain symptoms by patients and medical personnel, as well as the fact that the ultimate gold standard for diagnosis for many years remained an invasive surgical intervention—laparoscopy with histopathological examination of collected specimens.

From a clinical perspective, endometriosis is characterized by extraordinary heterogeneity. In modern gynecology, three main phenotypes of the disease are distinguished: superficial peritoneal endometriosis (SUP), ovarian endometriosis in the form of endometrial cysts, colloquially known as "chocolate cysts" (ovarian endometriomas, exOMA), and the most severe form—deep infiltrating endometriosis (DIE), which penetrates tissues to a depth of more than 5 millimeters and often infiltrates adjacent organs, such as the large intestine, rectum, urinary bladder, or ureters. It is precisely this diversity of lesions that translates into a broad and non-specific spectrum of symptoms. These include, apart from the aforementioned chronic pelvic pain, extremely painful menstruation (dysmenorrhea), deep pain during sexual intercourse (dyspareunia), as well as painful defecation (dyschezia) and painful urination (dysuria), especially in the perimenstrual period. The chronic nature of these ailments leads to a cascade of negative psychosocial consequences, including an elevated risk of developing depressive disorders, anxiety states, social isolation, as well as a significant decline

in professional productivity (absenteeism and presenteeism), which generates enormous costs for healthcare systems and the global economy *(Buggio et al., 2017)*.

The etiopathogenesis of endometriosis, despite decades of intensive research, has still not been definitively deciphered. Although the theory of retrograde menstruation, proposed by John Sampson in the 1920s, remains the most widely accepted model explaining the transfer of live endometrial cells through the fallopian tubes into the peritoneal cavity, it does not fully explain the phenomenon. The phenomenon of retrograde menstruation affects up to 90% of menstruating women, while endometriosis develops in only 10%. The current scientific consensus indicates that a conducive, dysfunctional micro-climate within the abdominal cavity, based on the coexistence of immunological, endocrinological, as well as genetic and epigenetic disorders, is necessary for the implantation and survival of ectopic endometrial cells (*Jiang et al., 2021; Cuadrado-Torroglosa et al., 2024*).

At the core of the pathophysiology of endometriosis lies a profound dysregulation of the immune system and a chronic, sterile inflammatory state. In a properly functioning organism, immune cells (such as macrophages or Natural Killer - NK cells) effectively eliminate cellular debris entering the peritoneal cavity. In patients with endometriosis, however, an impairment of the phagocytic capabilities of macrophages and a decrease in the cytotoxicity of NK cells are observed. Furthermore, dramatically elevated concentrations of pro-inflammatory cytokines (such as interleukins IL-1β, IL-6, IL-8, tumor necrosis factor TNF-α) and growth factors, including vascular endothelial growth factor (VEGF), are found in the peritoneal fluid of these patients. This creates a highly toxic and inflammatory environment that not only irritates nerve endings (causing pain) but also promotes angiogenesis (the formation of new blood vessels) and neurogenesis around the disease foci, ensuring their survival and invasive growth.

An integral element of this inflammatory microenvironment is systemic and local oxidative stress. Blood entering the peritoneal cavity undergoes hemolysis, releasing iron. Excess iron, through the Fenton reaction, generates enormous amounts of reactive oxygen species (ROS). This phenomenon, coupled with the depletion of the body's natural antioxidant mechanisms, leads to DNA damage, lipid peroxidation, and further exacerbation of the inflammatory cascade. Another pillar of the disease is its estrogen dependence. Endometriotic lesions exhibit an overexpression of aromatase—the enzyme converting androgens into estrogens—which allows them to locally and autonomously produce estradiol, stimulating their own growth (*Pellegrini et al., 2020; Tassinari et al., 2023*). Simultaneously, these tissues are characterized by progesterone resistance, which disrupts natural mechanisms inhibiting proliferation.

Given the complexity of the presented mechanisms, conventional treatment methods are often insufficient. Surgical interventions, although effective in removing visible lesions and improving pelvic anatomy, are associated with a high recurrence rate, reaching up to 40-50% within 5 years of the procedure (*Barrea et al., 2025; Wójtowicz et al., 2025*). Pharmacotherapy, in turn, relying primarily on non-steroidal anti-inflammatory drugs (NSAIDs) and hormonal suppression (combined oral contraceptives, progestins, GnRH analogs), is purely symptomatic. These therapies do not cure the underlying cause of the disease, and upon their discontinuation, symptoms almost always return *(Barrea et al., 2025)*. Moreover, chronic hormonal therapy is burdened with a range of severe side effects, such as hot flashes, mood swings, weight gain, or loss of bone mineral density, and is contraindicated in women trying to conceive.

Faced with growing frustration related to the limitations of conventional medicine, a clear shift towards seeking complementary therapeutic strategies is observed in the scientific and clinical world. Considering that endometriosis is a disease driven by inflammation, oxidative stress, and estrogen dysregulation, modifying environmental and lifestyle factors emerges as a logical and promising target for intervention. In this context, dietary interventions, phytotherapy, and targeted supplementation are gaining significance as safe tools modulating the aforementioned pathophysiological pathways. Research from recent years, extensively documented by the review by *Muharam et al. (2025),* provides increasing evidence that nutrients can directly influence gene expression, inhibit the production of inflammatory mediators, and support estrogen detoxification, offering patients a non-pharmacological chance to regain control over their own health.

The purpose of this review article is a comprehensive, multifaceted analysis and synthesis of the latest literature reports regarding the impact of varied nutritional models, targeted supplementation (including vitamins, minerals, and fatty acids), and plant compounds (polyphenols) on the clinical course of endometriosis. This paper aims to systematize the current state of knowledge, critically evaluate the efficacy of individual non-pharmacological interventions, and indicate promising directions for future clinical trials in the field of holistic management of this chronic disease.

Methodology

This paper constitutes a narrative review; however, the literature retrieval process was based on a structured search methodology. A comprehensive search was conducted across the PubMed/MEDLINE, Scopus, and Google Scholar databases, primarily encompassing publications from 2016 to 2026, to focus on the latest findings within evidence-based medicine (EBM). However, an exception was made for a select few articles published prior to 2016, which were included in the analysis due to their breakthrough nature and fundamental significance for understanding the discussed pathomechanisms.

The search was anchored to the core term "endometriosis," which was cross-referenced using Boolean operators (AND, OR) with three thematic blocks: nutritional models (e.g., *diet, Mediterranean diet, low-FODMAP*), targeted supplementation (e.g., *vitamin D, omega-3, oxidative stress*), and phytotherapy (*polyphenols, curcumin, resveratrol*).

The retrieved records were subjected to a two-stage selection process. The analysis exclusively included full-text, English- or Polish-language articles from peer-reviewed scientific journals—primarily randomized controlled trials (RCTs), observational studies of high evidence value, systematic reviews, and key preclinical studies elucidating the pathomechanisms of the disease at the molecular level. Case reports, letters to the editor, and grey literature were excluded from the analysis.

Following an initial screening of abstracts, the selected full texts underwent a critical substantive evaluation. The gathered material was used to conduct a multifaceted narrative synthesis, structured into thematic blocks illustrating the impact of specific nutritional interventions on the pathophysiology and clinical course of endometriosis.

Results

1. The Impact of Nutritional Models on the Clinical Course of Endometriosis

1.1. Reduction of Gastrointestinal Symptoms: From the Low-FODMAP Diet to Long-Term Hybrid Strategies

One of the most common, yet most burdensome clinical problems in patients with endometriosis is the coexistence of severe gastrointestinal symptoms. It is estimated that a significant percentage of women diagnosed gynecologically experience a syndrome of overlapping symptoms strikingly similar to Irritable Bowel Syndrome (IBS) *(Brouns et al., 2023).* These complaints, colloquially referred to as "endo-belly," encompass chronic bloating, painful abdominal cramps, excessive gas production, and disturbed bowel habits. The mechanism of this phenomenon is multifactorial; it results from the presence of inflammatory foci adjacent to the intestines, the release of pro-inflammatory prostaglandins, and the phenomenon of pelvic organ cross-sensitization, as a result of which the enteric nervous system becomes overly reactive *(Wilder et al., 2025).* Given the limited efficacy of standard pharmacotherapy, scientific literature is paying increasing attention to self-management strategies, among which nutritional modifications based on the restriction of fermentable carbohydrates play a leading role *(Buggio et al., 2017; Habib et al., 2022).*

Particular hopes are associated with a diet low in fermentable oligo-, di-, and monosaccharides and polyols (low-FODMAP). These compounds are short-chain carbohydrates characterized by poor absorption in the small intestine. After reaching the large intestine, they undergo rapid fermentation by the microbiota, leading to a drastic increase in gas production and mechanical distension of the intestinal walls, exacerbating pain in patients with a lowered visceral pain threshold. Highly significant evidence for the clinical efficacy of this model is provided by the rigorous EndoFOD clinical trial conducted by *Varney et al. (2025).* In this randomized, controlled cross-over study, it was demonstrated that a 28-day strict low-FODMAP diet yielded a positive clinical response in 60% of patients (compared to 26% in the control group). Restricting the intake of these carbohydrates not only reduced non-specific symptoms (abdominal pain, bloating) but also led to a significant improvement in standardized quality of life questionnaires. Importantly, this intervention did not affect psychological indices (stress or anxiety levels), proving that the observed relief resulted directly from the physiological offloading of the digestive tract. These conclusions are strongly supported by the review by *Habib et al. (2022),* who confirm the clinical validity of applying the low-FODMAP diet for the effective reduction of symptoms in patients with coexisting endometriosis and irritable bowel syndrome (IBS). The authors further point out that reducing pro-inflammatory factors in the diet acts synergistically with the supply of antioxidants and Omega-3 fatty acids, directly influencing prostaglandin synthesis pathways.

While the short-term efficacy of a rigorous protocol has been well documented, its application in the course of chronic diseases remains a challenge. Valuable data from a long-term perspective is provided by the prospective pilot study by *van Haaps et al. (2023),* which evaluated the impact of the low-FODMAP diet and an empirical "endometriosis diet" over 6 months. To maximize adherence, randomization was abandoned in favor of the voluntary choice of a model with close support from a dietitian. The results proved that structured, long-term nutritional support constitutes a highly effective non-pharmacological tool—patients noted a significant reduction in pelvic pain and a decreased frequency of bloating after half a year.

However, it must be remembered that maintaining a classic low-FODMAP diet over the long term carries the risk of nutritional deficiencies and the development of dysbiosis, which could paradoxically exacerbate inflammation. For this reason, as noted in their review by *O'Brien et al. (2024),* a FODMAP-gentle approach has emerged, relying on the selective restriction of only the most problematic carbohydrates, which reduces psychological pressure on patients. The most breakthrough direction, however, is the integration of the fermentation-restricting protocol with models of proven anti-inflammatory action, which has resulted in the concept of a FODMAP-modified Mediterranean-style diet.

1.2. The Mediterranean Diet and the Quenching of Inflammatory and Estrogen Pathways

As aptly highlighted by the team of *Wilder et al. (2025)*, endometriosis is a disease strictly dependent on estrogens and driven by systemic inflammation. While reducing FODMAP intake acts primarily symptomatically (mechanically), implementing the principles of the Mediterranean diet (MD) targets the very molecular foundation of the disease. Modern lifestyle medicine utilizes objective tools, such as the Dietary Inflammatory Index (DII).

Fundamental evidence for the existence of a direct relationship between a pro-inflammatory diet profile and the pathogenesis of the condition is provided by a cross-sectional study by Liu et al. (2023). Analysis of data from the NHANES database (3410 participants) revealed that women whose dietary habits placed them in the highest tertile of DII scores (a pro-inflammatory diet) had a staggering 57% higher risk of being diagnosed with endometriosis (OR: 1.57). This correlation persisted independently of BMI or the use of contraception, which indisputably proves that pro-inflammatory dietary stimuli act as an independent catalyst for pathophysiological processes.

The response to this clinical need is Medical Nutrition Therapy (MNT), the foundation of which—as indicated by *Barrea et al. (2025)* - should be the Mediterranean diet. A high intake of dietary fiber optimizes the microbiome, regulating the activity of the beta-glucuronidase enzyme, which facilitates the binding and excretion of excess estrogens in feces, preventing their reabsorption into the bloodstream. In turn, Omega-3 fatty acids, polyphenols, and antioxidant vitamins contained in the diet competitively inhibit pro-inflammatory prostaglandin production pathways (the COX-2 pathway) and reduce local oxidative stress.

1.3. The Role of the Gluten-Free Diet: Immunological Pathways and a Critical Evaluation of Efficacy

A third key model in self-management strategies is the gluten-free diet (GFD). Its popularity stems from the understanding of the phenomenon of increased intestinal barrier permeability. As analyzed by *Cuadrado-Torroglosa et al. (2024)*, gluten metabolism disorders and intestinal inflammation exhibit the ability to modify the uterine microenvironment, impairing the decidualization process and the response to progesterone.

The potential benefits of eliminating gliadin are confirmed by a systematic review conducted by *Sverrisdóttir et al. (2022).* It consistently demonstrated the positive impact of a gluten-free diet on pain perception, including significant alleviation of dysmenorrhea and pelvic pain. Nevertheless, evaluating the efficacy of the GFD requires a critical perspective, as called for by the narrative review of *Brouns' team (2023).* These authors point to the strong overlap of symptoms between endometriosis and, for example, irritable bowel syndrome, which means that the reported relief may largely result from a strong psychological mechanism (the placebo/nocebo effect). Additionally, after adjusting the results for confounding factors (such as body weight changes), the positive effects of the intervention often disappeared.

Furthermore, Brouns' team warns against the iatrogenic risk of unjustified gluten elimination. Long-term adherence to a GFD without a dietitian's supervision leads to a decrease in dietary fiber intake and the development of deficiencies. According to the current consensus, structured gluten elimination should be recommended primarily in cases of endometriosis coexisting with celiac disease or objectively documented non-celiac gluten sensitivity (NCGS).

2. The Impact of Targeted Supplementation and Phytotherapy

2.1. Vitamin D and Omega-3 Fatty Acids: Biochemical Efficacy Versus the Placebo Effect Phenomenon

In the context of endometriosis treatment, immense hopes are attached to substances with immunomodulatory potential, among which vitamin D (calciferol) comes to the forefront (*Wójtowicz et al., 2025).* Vitamin D (calcitriol) acts not only as a "vitamin" but as a powerful steroid hormone binding to the VDR (Vitamin D Receptor), which is present in the cell nucleus of the endometrium. The combination of calcitriol with VDR creates a complex that heterodimerizes with the RXR (Retinoid X Receptor) and binds to vitamin D response elements (VDRE) in gene promoters. Since vitamin D receptors (VDR) are expressed both in normal endometrium and in ectopic disease foci, it is postulated that normalizing its serum concentration can inhibit cell proliferation and silence local inflammatory responses *(Mehdizadehkashi et al., 2021).* Additionally, vitamin D induces the differentiation of regulatory T cells (Tregs), which exhibit the ability to suppress an excessive immune response in the lesser pelvis, creating an environment less "hospitable" to endometrial cell invasion *(Muharam et al., 2025)*.

Strong evidence confirming the biochemical efficacy of calciferol is provided by a double-blind, randomized clinical trial conducted by *Mehdizadehkashi et al. (2021)*. In a group of patients taking high, therapeutic doses of vitamin D (50,000 IU every two weeks for 12 weeks), not only a statistically significant decrease in pelvic pain complaints was noted, but above all, measurable metabolic benefits were observed. This intervention led to a drastic reduction in high-sensitivity C-reactive protein (hs-CRP) levels—a key marker of systemic inflammation—and a significant increase in total antioxidant capacity (TAC). These results constitute hard evidence that vitamin D actively modulates the patient's immunological microenvironment, mitigating oxidative stress at the cellular level.

Nevertheless, a rigorous analysis of the literature dictates caution in treating vitamin D and other supplements as universal analgesics. The clinical picture becomes significantly more nuanced when we analyze the study by *Almassinokiani et al. (2016)*. In this trial, patients diagnosed and treated surgically (laparoscopically) were administered 50,000 IU of vitamin D weekly. After 24 weeks of observation, the researchers found no statistically significant differences in the intensity of pelvic pain and dysmenorrhea between the study group and the control group. This suggests that in the case of advanced lesions that have already been removed via surgical ablation, supplementation alone may not yield additional benefits in terms of pain perception.

Even deeper light is shed on the complexity of pain management by the breakthrough DYNAMIC study by *Nodler et al. (2020),* conducted on a difficult-to-treat population of adolescents and young women. In a multi-arm cross-over study, the efficacy of vitamin D (2000 IU/day) and Omega-3 polyunsaturated fatty acids (1000 mg of fish oil/day) was evaluated compared to a placebo. The results proved surprising: although a significant improvement in visual analog scale (VAS) pain scores was noted in the vitamin D arm, almost identical improvement was observed in the group receiving the placebo. In turn, Omega-3 fatty acids, widely considered a strong anti-inflammatory factor, brought only marginal, statistically insignificant relief in this comparison, reducing pain half as effectively as the placebo alone.

The juxtaposition of these three studies leads to crucial clinical conclusions. Firstly, chronic pain in endometriosis—especially in young patients—is a phenomenon with a powerful neuropsychological component, susceptible to a strong placebo effect associated with the mere provision of therapeutic care to the patient. Secondly, discrepancies in the results prove that targeted supplementation should not be treated as a primary analgesic. Instead, based on hard biochemical data *(Mehdizadehkashi, 2021)*, vitamin D (like Omega-3 fatty acids) should be viewed as an element of long-term metabolic therapy. Its main goal is to correct deficiencies, reduce systemic oxidative stress (increase TAC), and stabilize the lipid profile, which in a long-term perspective inhibits disease progression, even if the short-term analgesic effect varies.

Alongside vitamin D, one of the most frequently analyzed components of Medical Nutrition Therapy (MNT) in endometriosis are polyunsaturated fatty acids from the Omega-3 family (n-3 PUFAs), primarily eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) *(Muharam et al., 2025).* The fundamental therapeutic mechanism of EPA (eicosapentaenoic acid) and DHA (docosahexaenoic acid) in endometriosis relies on their competitive nature relative to arachidonic acid (AA). Under physiological conditions, AA is a substrate for cyclooxygenases (COX-1 and COX-2) in the synthesis of series 2 prostaglandins (PGE2) and thromboxanes, which exhibit strong pro-inflammatory and nociceptive properties within the lesser pelvis. EPA, exhibiting a higher affinity for COX enzymes, displaces arachidonic acid from the synthesis pathway,

redirecting the process toward series 3 prostaglandins (PGE3) and resolvins (RvE1, RvD1), which are mediators that "quench" inflammation (pro-resolving mediators) *(Sienko et al., 2023).* This mechanism is critical for patients with endometriosis, as chronically elevated levels of PGE2 are found locally in the peritoneal fluid, which induces nerve ending hypersensitivity (allodynia) and stimulates angiogenesis via the inductive expression of VEGF (Vascular Endothelial Growth Factor) *(Wilder et al., 2025).* Inhibiting the COX-2 pathway by n-3 PUFAs directly reduces VEGF concentration in endometrial tissue, which can inhibit the growth of ectopic foci and their vascularization *(Barrea et al., 2025; Sienko et al., 2023).*

A recent systematic review conducted by *Sienko et al. (2023)* confirms that EPA exhibits strong anti-inflammatory properties, and its serum level could potentially serve as a marker of disease severity. The authors emphasize that n-3 PUFAs possess a unique ability to modulate the microenvironment of endometriotic lesions, which in basic and preclinical studies correlates with the inhibition of angiogenesis and the stimulation of endometrial cell apoptosis. This mechanism is extremely promising, as it directly targets the "fuel" of endometriosis: inflammation and the uncontrolled proliferation of ectopic tissues.

Despite such strong theoretical premises, transitioning to the clinical phase and proving the efficacy of Omega-3 in alleviating pain in women with endometriosis encounters significant methodological barriers. The pilot study PurFECT1, published by *Abokhrais et al. (2020),* serves as the prime example of this. Although the authors confirmed that an intervention using n-3 PUFAs is fully acceptable to patients and safe (no adverse events), the pilot nature of the study did not allow for unambiguous confirmation of analgesic efficacy. Paired with previously mentioned results from studies such as *Nodler et al. (2020),* where fish oil supplementation yielded much weaker effects than a placebo, the conclusion emerges that Omega-3 intake alone may be insufficient as a standalone analgesic therapy in a disease as complex as endometriosis.

Where do these discrepancies between promising biochemistry and inconclusive clinical results originate? Clinicians point out that endometriosis is a disease of immense phenotypic heterogeneity. There is a probability that the efficacy of Omega-3 fatty acid supplementation depends on the baseline n-3 to n-6 ratio in the patient's diet, her individual metabolic status, and the degree of disease advancement.

Modern science thus indicates that Omega-3s should not be viewed as a temporary analgesic agent. Their role in MNT is much broader: they are intended to systematically "quench" the body's inflammatory background, creating an environment less conducive to disease progression. As suggested by *Sienko's team (2023),* future research must move beyond simple "supplement vs. placebo" comparisons and focus on evaluating fatty acids as part of a broader, anti-inflammatory dietary model, in which Omega-3s act synergistically with other components, such as polyphenols or antioxidant vitamins.

2.2. N-acetylcysteine and Polyphenols: Targeted Intervention in Antioxidant and Angiogenic Processes

In the search for non-pharmacological strategies inhibiting the progression of endometriosis, N-acetylcysteine (NAC) and selected plant polyphenols, such as resveratrol and curcumin, are gaining increasing clinical attention. These substances, owing to their multidirectional action, demonstrate potential in moderating so-called mitochondrial quality control (MQC), which in the case of endometriosis is crucial for reducing chronic oxidative stress and inhibiting the invasive potential of ectopic foci *(Pellegrini et al., 2020).*

Efficacy of N-acetylcysteine (NAC)

NAC, a glutathione precursor, exhibits strong antioxidant and anti-inflammatory properties. Prospective studies, including works by *Porpora et al. (2013)* and newer reports indicate its unique efficacy in reducing the size of ovarian endometrial cysts (endometriomas). In patient groups receiving NAC, not only a statistically significant reduction in lesion diameter was observed, but also a meaningful improvement in dysmenorrhea, dyspareunia, and chronic pelvic pain (CPP). Importantly, this therapy is associated with improved fertility parameters—in patients with a so-called "reproductive desire," higher pregnancy rates were noted following short-term supplementation. The mechanism of action of NAC exhibits a unique ability to inhibit the nuclear translocation of the NF-κB (Nuclear Factor kappa-light-chain-enhancer of activated B cells) factor. NF-κB is the "master switch" of inflammation, responsible for the overexpression of genes encoding the cytokines IL-1β, IL-6, and TNF-α. By blocking NF-κB activation, NAC prevents a self-perpetuating inflammatory loop, which explains the clinically observed reduction in the size of endometrial cysts (endometriomas) in prospective studies.

The Potential of Polyphenols: Resveratrol and Curcumin

In the field of phytotherapy, resveratrol and curcumin are the subjects of intense research due to their ability to modulate key disease signaling pathways, including angiogenesis (VEGF inhibition), cell proliferation, and apoptosis induction within endometriotic lesions. Systematic studies indicate that these polyphenols—acting synergistically—can regulate metabolic homeostasis, inhibit tissue invasiveness, and quiet local immune responses. These compounds regulate mitochondrial dynamics, restoring functionality to damaged organelles and reducing the production of reactive oxygen species (ROS) *(Pellegrini et al., 2020)*. This action constitutes a vital element in inhibiting the invasive potential of ectopic foci, making phytotherapy a promising direction in complementary metabolic therapy. As noted by *Tassinari et al. (2023),* while conventional methods, such as the chronic use of non-steroidal anti-inflammatory drugs (NSAIDs), carry the risk of significant side effects, polyphenols offer a safer alternative due to a dual mechanism of action: phytoestrogenic properties and direct inhibition of inflammatory cascades. Curcumin additionally modulates the PI3K/Akt/mTOR pathway, which is often overexpressed in endometrial lesions, leading to their excessive proliferation. Although preclinical evidence and animal models demonstrate extremely promising efficacy in "quenching" endometriosis, the scientific community unanimously emphasizes that further, rigorously designed randomized clinical trials involving humans are necessary to fully translate these discoveries into clinical care standards.

2.3. Innovative Supplementation Directions: PEA, EGCG, and Melatonin

Alongside commonly used Omega-3 fatty acids and classic antioxidants, contemporary medical literature points to three exceptionally promising substances with unique molecular mechanisms: palmitoylethanolamide (PEA), epigallocatechin gallate (EGCG), and melatonin *(Stochino Loi et al., 2020; Wójtowicz et al., 2025).*

PEA is an endogenous fatty acid amide that exhibits potent properties alleviating neuropathic pain through the modulation of mast cell activity and the inhibition of neuroinflammation within the lesser pelvis. As *Indraccolo and Indraccolo (2017)* demonstrated in their study, supplementation with micronized PEA combined with polydatin (a highly bioavailable resveratrol derivative) led to a statistically significant reduction in chronic pelvic pain (CPP) and dysmenorrhea in patients for whom standard first-line therapy proved ineffective.

An equally significant direction is the application of epigallocatechin gallate (EGCG)—the primary polyphenol present in green tea. As concluded by the critical analysis by *Wójtowicz et al. (2025)*, EGCG possesses documented anti-angiogenic properties and, in preclinical studies and initial human trials, results in a measurable decrease in the size of endometriotic lesions. By quenching vascular growth factors, EGCG cuts off ectopic structures from their blood supply, which limits their invasiveness.

In turn, in the context of systemic oxidative stress, melatonin deserves special attention. A systematic review conducted by the *team of Stochino Loi (2020)* unambiguously indicates that melatonin acts not only as a chronobiotic improving sleep quality, but primarily as a remarkably potent antioxidant and immunomodulator. Studies included in this review prove that melatonin induces apoptosis in ectopic endometrial cells and significantly reduces pelvic pain complaints, lowering the need for classic analgesic pharmacotherapy. The capacity to simultaneously decrease central nervous system sensitization and quench free radicals makes melatonin a valuable adjunct to the multidisciplinary treatment of endometriosis.

3. Microbiota and Endometriosis: The Gut-Uterine Axis and the Estrobolome as Therapeutic Targets

3.1. The Concept of the Gut-Uterine Axis and the Bacterial Contamination Theory

Contemporary pathophysiology of endometriosis shifts the interpretative weight from the isolated theory of retrograde menstruation to a multifactorial immunological model in which the microbiota plays a key role. According to the Bacterial Contamination Theory, proposed and developed by *Jiang et al. (2021)*, the physiological barrier of the reproductive organs and the digestive tract constitutes the first point of contact with pathogens. Dysbiosis—defined as an imbalance of the microbial community—leads to the translocation of bacterial endotoxins, particularly lipopolysaccharides (LPS), into the bloodstream and directly into the peritoneal fluid.

LPS, being components of Gram-negative bacterial cell walls, activate Toll-like receptors (TLR4) on the surface of peritoneal macrophages. This activation initiates a signaling cascade dependent on the nuclear

transcription factor NF-κB, which leads to the massive production of pro-inflammatory cytokines (IL-6, TNF-α, IL-1β). The inflammatory environment created in this way not only promotes the adhesion of endometrial cells to the peritoneum but also stimulates local angiogenesis via the overexpression of VEGF, establishing a "niche" conducive to the survival and proliferation of ectopic tissues *(Jiang et al., 2021; Xholli et al., 2023)*.

3.2. The Estrobolome: Microbiological Regulator of Estrogen Dominance

One of the most intriguing aspects of the link between the microbiota and endometriosis is the so-called estrobolome—a pool of intestinal bacteria possessing the ability to metabolize estrogens *(Jiang et al., 2021).* In a healthy organism, estrogens are secreted into bile conjugated with glucuronic acid, which prevents their reabsorption in the intestine. The estrobolome bacteria, through the production of beta-glucuronidase enzymes, deconjugate these compounds, restoring them to a biologically active form *(Xholli et al., 2023).*

In the course of endometriosis, dysbiosis characterized by an increased abundance of beta-glucuronidase-producing strains is frequently observed. This leads to increased enterohepatic circulation of free estradiol. This condition exacerbates systemic estrogen dominance, which is the primary growth factor for endometriosis lesions. Studies by *Barrea et al. (2025)* indicate that modifying the diet by increasing dietary fiber intake and utilizing appropriate probiotic therapy can inhibit the activity of this enzyme, promoting the excretion of estrogens in feces, which constitutes vital support for classic hormonal therapy.

3.3. Characterization of the Microbiome in Endometriosis: The Decline in Lactobacillus Dominance

Microbiome analysis of patients with endometriosis consistently demonstrates significant differences relative to a control group. The most replicable observation is a drastic decline in the dominance of bacteria from the *Lactobacillus* genus in the reproductive tract and in the intestinal lumen. *Lactobacillus* spp. act as guardians of homeostasis, maintaining a low pH and inhibiting pathogen colonization through the production of bacteriocins and hydrogen peroxide.

Research indicates that in endometriosis, the niche physiologically occupied by *Lactobacillus* is often taken over by bacteria associated with bacterial vaginosis (BV), such as *Gardnerella*, *Prevotella*, or *Atopobium*. As emphasized by *Xholli et al. (2023),* this shift in the microbiological profile is linked not only to chronic inflammation but also to an alteration in the peritoneal metabolome. Substances secreted by pathogens—short-chain fatty acids (SCFAs) in abnormal concentrations, toxic metabolites—can directly influence the epigenetics of endometrial cells, promoting a phenotype that is more invasive and resistant to apoptosis.

3.4. Probiotic Therapy as the Future of Disease Management

The prospect of using probiotics in treating endometriosis is based on restoring the "core" microbiota (i.e., eubiosis). *Wójtowicz et al. (2025) and Jiang (2021)* highlight that the clinical efficacy of probiotics depends on the selection of specific strains that, in preclinical studies, have shown the capacity to seal the intestinal barrier (by increasing the expression of tight junction proteins, such as occludin and zonulin).

Nevertheless, microbiome science is in a transitional phase. Although evidence for the action of probiotics in animal models is unequivocally positive (reduction in lesion size, pain reduction), clinical trials involving humans are heterogeneous. Some studies point to an improvement in pain parameters following probiotic use, while others show no significant differences. This stems from the fact that every patient possesses a unique "microbial signature" *(Jiang et al., 2021).* Therefore, the latest trends indicate the necessity of applying molecular diagnostics of the microbiota before implementing interventions, so that probiotic therapy can be targeted (so-called precision probiotics) rather than empirical *(Xholli et al., 2023).* The microbiota, in light of current knowledge, is thus not merely a passive observer of the disease, but an active participant in its pathogenesis, making it one of the most crucial targets for future, non-invasive methods of endometriosis treatment.

4. Integration of Medical Nutrition Therapy in a Multidimensional Model of Endometriosis Treatment

4.1. Synthesis: Diet and Supplementation as Modulators of Inflammation

The results of the conducted analysis indicate that Medical Nutrition Therapy (MNT) in endometriosis is not merely an "add-on" to gynecological care, but constitutes a potential pillar of self-management strategy. The pivotal mechanism underpinning most positive outcomes *(Varney et al., 2025; Liu et al., 2023)* is the reduction of systemic inflammation. Both the low-FODMAP and Mediterranean diets, by altering the cytokine secretion profile (IL-6, TNF-α) and regulating COX-2/NF-κB pathways, create an environment less favorable to the progression of ectopic lesions.

However, as the review by *Wójtowicz et al. (2025)* demonstrates, there is a clear discrepancy between promising molecular mechanisms and hard clinical evidence (RCTs). This suggests that supplements (Omega-3, vitamin D) act most effectively not as acute "painkillers," but as long-term metabolic modulators that must be utilized based on precise diagnostics of deficiencies and the patient's phenotype.

4.2. Endometriosis Phenotypes and Causes of Result Heterogeneity

Why do studies such as PurFECT1 *(Abokhrais et al., 2020*) or *Nodler's trial (2020)* show limited efficacy of supplementation, while observational studies point to a significant improvement in QoL? The answer lies in the immense phenotypic heterogeneity of endometriosis. This disease is not a homogenous entity; one patient is dominated by peritoneal inflammation, another by a bowel component (IBS-like), and yet another by deep infiltrating endometriosis (DIE) with a neurological component.

The findings of *van Haaps et al. (2023)* clearly suggest that personalizing the diet—that is, tailoring it to the predominant symptoms—is more effective than applying rigid protocols. The ambiguity of evidence regarding the gluten-free diet *(Brouns et al., 2023)* confirms that blindly eliminating entire product groups can lead to iatrogenic deficiencies, which in themselves can worsen inflammation rather than extinguish it.

4.3. The Gut-Uterine Axis: A New Frontier in Pathophysiology

A breakthrough point in the discussion is the role of the microbiota. The concept of the "bacterial contamination theory" *(Jiang et al., 2021)* and the function of the estrobolome in regulating the enterohepatic circulation of estradiol alter our understanding of endometriosis as a purely hormonal disease. Results signify that dysbiosis is not merely a side effect of the illness, but its active promoter. Probiotic therapy, though in the phase of early research, seems to be the most promising pathway in "sealing" the intestinal barrier and reducing LPS translocation. It should be noted, however, that without standardizing strains and implementing microbiome diagnostics (so-called precision nutrition), probiotics will remain only "empirical support" instead of a targeted therapy.

4.4. Psychological Impact and the Placebo Effect

The fact that research on MNT in endometriosis is encumbered by a strong placebo component cannot be overlooked. As noted by *Buggio et al. (2017),* for patients with chronic pain, engaging in the process of active dietary change is a form of regaining agency over their own bodies. This "psychological effect of agency" significantly impacts the subjective perception of pain, which explains why such large improvements are often observed in control groups *(Nodler et al., 2020)*. In future studies, it is essential to separate the physiological effect of the intervention from the effect of improved psychological well-being resulting from engagement in diet therapy.

Conclusions

1. Verification of Non-Pharmacological Efficacy in Light of EBM

Based on the conducted analysis of the gathered literature, it must be stated that non-pharmacological interventions in treating endometriosis are in a transitional phase from empirical "self-management" strategies to evidence-based medicine (EBM). Although the assembled data unequivocally demonstrate that dietary modification and targeted supplementation offer patients substantial support, their clinical efficacy remains highly individualized. We conclude that a universal dietary protocol for endometriosis does not exist; rather, one must speak of "metabolic profiling of the patient". RCT trials to date, often burdened with methodological error resulting from the phenotypic heterogeneity of the studied groups, do not allow for the formulation of definitive guidelines; however, they do not preclude the therapeutic potential of these methods. A key conclusion is the necessity to change the research paradigm: from evaluating "diet as a drug" to evaluating "diet as an environmental modifier" that optimizes the response to hormonal and surgical treatment.

2. The Gut-Uterine Axis as a Novel Etiopathogenetic Paradigm

A fundamental conclusion drawn from analyzing the relationship between the microbiota and the course of endometriosis is the recognition of the gut-uterine axis as a pivotal regulator of endocrine homeostasis. The bacterial contamination theory, integrating dysbiosis with the NLRP3 inflammasome cascade, shifts the perception of endometriosis from a disease of an isolated organ to a systemic disorder, wherein the intestines act as an inflammatory "bioreactor". We deduce that future therapeutic strategies must focus on stabilizing the intestinal barrier. The implementation of targeted probiotic therapy, based on strains with proven capability to seal tight junctions, may become a breakthrough in halting the progression of ectopic lesions. It is essential, however, to move away from using broad-spectrum probiotics toward precision microbiome diagnostics, which will allow for individualized estrobolome modulation and a reduction in the enterohepatic circulation of free estrogens.

3. The RCT Paradox in Nutrition Research – A Lesson for the Future

The analysis of discrepancies between results from animal model studies and clinical trials (RCTs) leads to the conclusion that current standards for designing clinical trials are poorly adapted to the specificity of dietary interventions. In RCT-type studies, the patient receives a supplement as a "monotherapy," which contradicts the nature of nutrition, which exerts a pleiotropic effect. We conclude that future research should utilize an N-of-1 trial design or integrated models where supplementation serves as an adjunct to standard medical care, rather than a substitute. It is also necessary to extend observation periods—the metabolic effects of a diet (e.g., changes in cell membrane fatty acid profiles or microbiome stabilization) only become apparent after 6–12 months, which disqualifies most short-term, 8-week pilot trials.

4. The role of the Clinical Dietitian in a multidisciplinary model

The compiled data unequivocally point to the need to include a clinical dietitian as an integral member of the therapeutic team (a multidisciplinary endometriosis care team). Patients with endometriosis frequently adopt risky, exclusionary dietary models (e.g., GFD without indications, extreme FODMAP restrictions), which leads to iatrogenic deficiencies in micronutrients such as iron, B vitamins, or calcium. We infer that the safe implementation of MNT requires the supervision of a professional who will conduct a differential diagnosis between non-specific bowel symptoms and genuine food sensitivities. Such care not only reduces the risk of complications but significantly elevates the patient's quality of life via "nutritional education" that mitigates food-related anxiety—a component often overlooked yet crucial for visceral pain perception. As appropriately summarized by *Habib et al. (2022)*, managing endometriosis requires an uncompromisingly holistic approach, centered on the global reduction of inflammation, supporting detoxification pathways, and alleviating bothersome symptoms. These authors emphasize that integrating a qualified dietitian into a multidisciplinary therapeutic team yields immense benefits, particularly in younger patients and during the early stages of the disease, allowing inflammatory progression to be halted before advanced tissue alterations occur.

5. Future Directions

In light of the above synthesis, we propose the following priorities for future scientific research:

Metabolic phenotyping: Studies should divide patients into groups (e.g., obese with insulin resistance vs. lean with dysbiosis) prior to initiating supplementation.

Standardization of markers: Integrating inflammatory markers other than hs-CRP into studies (e.g., IL-1β, TNF-α cytokine levels, zonulin levels as an intestinal permeability marker).

Long-term studies: Funding observational projects lasting a minimum of 12-24 months that will assess the impact of diet on the recurrence rate of lesions after surgical procedures.

Supplement analysis in the context of synergy: Instead of testing single substances, combinations should be evaluated (e.g., EPA+DHA + polyphenols + probiotics) to achieve a synergistic anti-inflammatory effect.

6. Final Conclusion

Endometriosis remains a condition for which complete cure via non-pharmacological means is currently impossible; nevertheless, implementing personalized Medical Nutrition Therapy represents one of the most promising avenues supporting modern medicine. We conclude that the gynecologist should not view dietary recommendations as an "alternative to hormonal therapy," but as a tool optimizing the response to treatment and significantly improving the patient's daily functioning. The key to future success is a holistic approach that integrates advanced microbiological diagnostics, precise supplementation, and nutritional education, which ultimately will translate into the reduction of systemic inflammation—the primary engine of progression for this debilitating disease.

Declarations Conflicts of Interest: No conflicts of interest to declare.

Funding: This research received no external funding.

REFERENCES

1. Abokhrais, I. M., Denison, F. C., Whitaker, L. H. R., Saunders, P. T. K., Doust, A., Williams, L. J., & Horne, A. W. (2020). A two-arm parallel double-blind randomised controlled pilot trial of the efficacy of omega-3 polyunsaturated fatty acids for the treatment of women with endometriosis-associated pain (PurFECT1). *PLoS One, 15*(2), e0230055. https://doi.org/10.1371/journal.pone.0230055
2. Almassinokiani, F., Khodaverdi, S., Solaymani-Dodaran, M., Akbari, P., & Pazouki, A. (2016). Effects of vitamin D on endometriosis-related pain: A double-blind clinical trial. *Medical Science Monitor, 22*, 5110–5115. https://doi.org/10.12659/msm.901838
3. Barrea, L., Verde, L., Annunziata, G., Chedraui, P., Petraglia, F., Cucalón, G., ... & Muscogiuri, G. (2025). Effectiveness of medical nutrition therapy in the management of patients with obesity and endometriosis: From the Mediterranean diet to the ketogenic diet, through supplementation. The role of the nutritionist in clinical management. *Current Obesity Reports, 14*(1), 1–15. https://doi.org/10.1007/s13679-025-00662-8
4. Brouns, F., Van Haaps, A., Keszthelyi, D., Venema, K., Bongers, M., Maas, J., & Mijatovic, V. (2023). Diet associations in endometriosis: A critical narrative assessment with special reference to gluten. *Frontiers in Nutrition, 10*, 1166929. https://doi.org/10.3389/fnut.2023.1166929
5. Buggio, L., Barbara, G., Facchin, F., Frattaruolo, M. P., Aimi, G., & Berlanda, N. (2017). Self-management and psychological-sexological interventions in patients with endometriosis: Strategies, outcomes, and integration into clinical care. *International Journal of Women's Health, 9*, 327–340. https://doi.org/10.2147/IJWH.S119724
6. Cuadrado-Torroglosa, I., García-Velasco, J. A., & Alecsandru, D. (2024). The impacts of inflammatory and autoimmune conditions on the endometrium and reproductive outcomes. *Journal of Clinical Medicine, 13*(13), 3724. https://doi.org/10.3390/jcm13133724
7. Habib, N., Buzzaccarini, G., Centini, G., Moawad, G. N., Ceccaldi, P. F., Gitas, G., Alkatout, I., Gullo, G., Terzic, S., & Sleiman, Z. (2022). Impact of lifestyle and diet on endometriosis: A fresh look to a busy corner. *Menopause Review, 21*(2), 124–132. https://doi.org/10.5114/pm.2022.116437
8. Indraccolo, U., & Indraccolo, S. R. (2017). Effect of palmitoylethanolamide-polydatin combination on chronic pelvic pain associated with endometriosis: A retrospective observation. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 213*, 135–138. https://doi.org/10.1016/j.ejogrb.2017.04.011
9. Jiang, I., Yong, P. J., Allaire, C., & Bedaiwy, M. A. (2021). Intricate connections between the microbiota and endometriosis. *International Journal of Molecular Sciences, 22*(11), 5644. https://doi.org/10.3390/ijms22115644

10. Liu, P., Maharjan, R., Wang, Y., Zhang, Y., Zhang, Y., Xu, C., ... & Miao, J. (2023). Association between dietary inflammatory index and risk of endometriosis: A population-based analysis. *Frontiers in Nutrition, 10*, 1077915. https://doi.org/10.3389/fnut.2023.1077915
11. Mehdizadehkashi, A., Rokhgireh, S., Tahermanesh, K., Eslahi, N., Minaeian, S., & Samimi, M. (2021). The effect of vitamin D supplementation on clinical symptoms and metabolic profiles in patients with endometriosis. *Journal of Obstetrics and Gynaecology, 41*(7), 1146–1151. https://doi.org/10.1080/09513590.2021.1878138
12. Muharam, R., Yo, E. C., Irzanti, A. N., Mutia, K., Sumapraja, K., Harzif, A. K., ... & Hestiantoro, A. (2025). The role of nutrition in endometriosis prevention and management: A comprehensive review. *International Journal of Fertility and Sterility, 19*(2), 79–89. https://doi.org/10.22074/ijfs.2025.2029021.1683
13. Nodler, J. L., DiVasta, A. D., Vitonis, A. F., Karevicius, S., Malsch, M., Sarda, V., ... & Missmer, S. A. (2020). Supplementation with vitamin D or ω-3 fatty acids in adolescent girls and young women with endometriosis (DYNAMIC): A double-blind, randomized, placebo-controlled trial. *The American Journal of Clinical Nutrition, 112*(1), 187–195. https://doi.org/10.1093/ajcn/nqaa096
14. O'Brien, L., Kasti, A., Halmos, E. P., Tuck, C., & Varney, J. (2024). Evolution, adaptation, and new applications of the FODMAP diet. *Journal of Gastroenterology and Hepatology, 39*(7), 1332–1341. https://doi.org/10.1002/jgh3.13066
15. Pellegrini, C., Maggio, R., & Blandini, F. (2020). Resveratrol in endometriosis: A review of the molecular mechanisms. *International Journal of Molecular Sciences, 21*(21), 8089. https://doi.org/10.3390/ijms21218089
16. Porpora, M. G., Brunelli, R., Costa, G., Imperiale, L., Krasnowska, E. K., Lundeberg, T., Nofroni, I., Piccioni, M. G., Pittaluga, E., Ticconi, C., & Parasassi, T. (2013). A promise in the treatment of endometriosis: An observational cohort study on ovarian endometrioma reduction by N-acetylcysteine. *Evidence-Based Complementary and Alternative Medicine, 2013*, 240702. https://doi.org/10.1155/2013/240702
17. Sienko, A., Cichosz, A., Urban, A., Smolarczyk, R., Czajkowski, K., & Sienko, J. (2023). The effect of two anti-inflammatory dietary components, omega-3 and resveratrol, on endometriosis. *Ginekologia Polska, 94*(10), 820–826. https://doi.org/10.5603/gpl.97573
18. Stochino Loi, E., Pontis, A., Cofelice, V., Pirarba, S., Fida, M., Daniilidis, A., ... & Angioni, S. (2020). Effect of melatonin in endometriosis: A systematic review. *International Journal of Molecular Sciences, 21*(5), 1772. https://doi.org/10.3390/ijms21051772
19. Sverrisdóttir, U. Á., Hansen, S., & Rudnicki, M. (2022). Impact of diet on pain perception in women with endometriosis: A systematic review. *European Journal of Obstetrics & Gynecology and Reproductive Biology, 271*, 1–7. https://doi.org/10.1016/j.ejogrb.2022.02.028
20. Tassinari, V., Smeriglio, A., Stillittano, V., Trombetta, D., Zilli, R., Tassinari, R., ... & Marcoccia, D. (2023). Endometriosis treatment: Role of natural polyphenols as anti-inflammatory agents. *International Journal of Molecular Sciences, 24*(14), 11467. https://doi.org/10.3390/ijms241411467
21. van Haaps, A. P., Wijbers, J. V., Schreurs, A. M. F., Vlek, S., Tuynman, J., De Bie, B., ... & Mijatovic, V. (2023). The effect of dietary interventions on pain and quality of life in women diagnosed with endometriosis: A prospective study with control group. *Human Reproduction, 38*(11), 2216–2227. https://doi.org/10.1093/humrep/dead214
22. Varney, J. E., So, D., Gibson, P. R., Rhys-Jones, D., Lee, Y. S. J., Fisher, J., ... & Muir, J. G. (2025). Effect of a 28-day low FODMAP diet on gastrointestinal symptoms associated with endometriosis (EndoFOD)—A randomised, controlled crossover feeding study. *Alimentary Pharmacology & Therapeutics, 61*(4), 450–462. https://doi.org/10.1111/apt.70161
23. Wilder, L. H., Cabre, H. E., Dickey, M. S., & Redman, L. M. (2025). Endometriosis: Pathophysiology and the potential role of diet. *Advances in Physiology Education, 49*(1), 12–25. https://doi.org/10.1152/advan.00198.2025
24. Wójtowicz, M., Małek, P., & Olszanecka-Glinianowicz, M. (2025). The role of dietary supplements in the treatment of endometriosis: A critical review. *Nutrients, 18*(8), 1274. https://doi.org/10.3390/nu18081274
25. Xholli, A., Cremonini, F., Perugi, I., Londero, A. P., & Cagnacci, A. (2023). Gut microbiota and endometriosis: Exploring the relationship and therapeutic implications. *Pharmaceuticals, 16*(12), 1696. https://doi.org/10.3390/ph16121696