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## **Does diet influence the development and treatment of endometriosis? - A literature review**

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**ABSTRACT:**

**Introduction and objective:**

Endometriosis is a chronic disease that can cause symptoms that significantly worsen the quality of life of patients. Treatment methods often fail to produce satisfactory results. Therefore, there is growing interest in the potential role of diet in prevention and management of endometriosis. The aim of the review is to analyze available scientific literature on the impact of diet on the development and alleviation of endometriosis symptoms and the possibility of its use in clinical practice.

**Brief description of the state of knowledge:**

Both nutrient deficiencies and excesses can affect health, with gene-nutrient interactions playing a key role in disease prevention and progression. Nutrition can alter gene expression and disease susceptibility, making the study of diet's influence on gynecological diseases like endometriosis important. Research suggests dietary changes can improve symptoms and quality of life for patients with endometriosis.

**Conclusions:**

This study confirms that consuming or limiting some of the nutrients can reduce the risk of developing endometriosis and alleviate its symptoms. However, there are many contradictions in the research. The role of diet and nutrition in endometriosis still remains an unexplored area that requires further investigation.

**Keywords:**

"endometriosis"; "endometriosis and diet"; "influence of diet in endometriosis".

## **Introduction**

Endometriosis is a chronic inflammatory disease caused by the presence of endometrial tissue outside the uterine cavity. It affects 6-10% of women of childbearing age. Lesions caused by endometriosis can be detected in asymptomatic women and are found in up to 50% of women with infertility. This disease can cause severe menstrual pain, pelvic pain, fertility problems and other symptoms that significantly affect the quality of patients' life. [1] So far, no reliable marker has been discovered to detect this disease, and imaging methods are not fully effective in diagnosing endometriosis. A breakthrough in recent years has been the use of high-resolution magnetic resonance imaging (MRI) with contrast of the urinary bladder, vagina and rectum, but the diagnosis of endometriosis is final only after surgical confirmation. [2] Despite progress in diagnostics, pharmacotherapy and surgery, this disease still poses a therapeutic challenge. There is an urgent need to expand knowledge about endometriosis and its treatment. [3] Endometriosis is an estrogen-dependent disease and the most commonly used treatments are combined oral contraceptives, progestogens or gonadotropin-releasing hormone agonists. Surgical removal of endometrial lesions is an alternative treatment method, but with low effectiveness. Additionally, there are conflicting opinions regarding second- and third-line treatment options. [4] Maintaining a healthy lifestyle and a balanced diet is crucial to preserve homeostasis and prevent various chronic diseases. Therefore, in addition to traditional treatment methods, there is growing interest in the potential role of diet in the treatment of endometriosis. There are reports that diet influences the development and course of endometriosis and may be one of the therapeutic strategies for this disease. [5]

## **State of knowledge**

Diet and nutrition have a significant impact on maintaining the overall health of the population, including women's health. Both deficiency and excess of nutrients can affect it. Interactions between genes and nutrients are important factors in prevention and course of diseases. Nutrition can alter gene expression as well as susceptibility to disease. For this reason, the influence of diet on the development and treatment of gynecological diseases, including endometriosis, is studied. [7] Endometriosis is a complex condition influenced by many factors, including genetic and immune pathways, excessive smooth muscle contraction, inflammatory processes, and the influence of environmental factors, including dietary habits and nutrients. The impact of diet on endometriosis is not fully understood, but research suggests that certain dietary changes may help improve symptoms and improve the quality of

life for some people with the disease. [6] According to research, nutrition in endometriosis should focus primarily on supplementing nutritional deficiencies, reducing excess estrogens, alleviating inflammation, reducing oxidative stress and limiting exposure to phytoestrogens and xenoestrogens. [7] Below there is an analysis of selected nutrients and their potential impact on endometriosis.

### **1. Vegetables and fruits**

According to one hypothesis, eating plenty of vegetables may help reduce the risk of endometriosis. It is believed that DNA methylation of specific genes involved in the pathogenesis of this disease may be responsible for this. However, there is also a suspicion that pollutants such as pesticides used to fertilize plants may be harmful to health and contribute to the development of endometriosis. [8] The effect of vegetable consumption on the development of endometriosis was examined in two main case-control studies, but the results were contradictory. One study observed a lower risk of endometriosis, while another study found no significant differences between women consuming large amounts of green vegetables and women consuming small amounts. [9][10] When examining the impact of fruits on the risk of developing endometriosis, it was discovered that fruits contain antioxidants that reduce free oxygen radicals. Owing to this fact, they can eliminate inflammation by reducing oxidative stress. There is a theoretical possibility that fruit consumption may lower the risk of developing endometriosis. Studies have shown that the consumption of fresh fruit was associated with a significant reduction in the risk of this condition. It has been observed that consuming citrus fruits may be particularly beneficial. It is suggested that beta-cryptoxanthin present in these fruits is responsible for this effect. [9][11] However, another study did not confirm this finding. It has been shown that a larger number of servings of fruit per day was associated with an increased risk of disease [10].

### **2. Vitamin D**

The endometrium is a tissue susceptible to changes in secretory activity under the influence of vitamin D, therefore the effect of this vitamin on endometriosis was studied. Vitamin D has many functions that suggest that its supplementation may reduce disease lesions or symptoms. It has been observed, among other things, that vitamin D may interact with pro-inflammatory cytokines and other molecules mediating inflammatory processes by reducing the production of interleukin-17 and interleukin-6, it may also act as a factor interfering with the activity of matrix metalloproteinase (MMP), it also has an effect on inhibiting angiogenesis by reducing

the expression of vascular endothelial growth factor-A (VEGF-A) genes, as well as inhibiting nuclear factor kappa B (NF- $\kappa$ B), which are involved in the pathway involved in neovascularization. [7] It has been observed that serum vitamin D concentrations are lower in women with endometriosis compared to women with mild endometriosis or without it. [12] Several clinical studies have been conducted to evaluate the effect of vitamin D on the symptoms of endometriosis. It has been noted that taking vitamin D can relieve pelvic pain in patients with endometriosis. Moreover, it lowers the total cholesterol to HDL ratio, lowers CRP and total antioxidant capacity, but has no effect on other clinical symptoms or metabolic profiles. [13] However, two other studies did not confirm this relationship. In one study of young women with endometriosis, vitamin D supplementation led to reduced pelvic pain; although, the results were similar to placebo. [14] In the second study, vitamin D treatment did not provide significant relief from painful periods and/or pelvic pain. [15]

### **3. Other vitamins**

Vitamins C, E, A are antioxidants and they have the ability to reduce the amount of free oxygen radicals, which may have anti-inflammatory effects. [8] Several animal studies have shown that the use of vitamin C can inhibit the formation of endometriosis and also cause regression of the disease. [16][17] In the case of vitamin E, significant discrepancies in research results are observed. One study suggested an increased contribution of vitamin E to antioxidant mechanisms in women with endometriosis, although other researchers either found no association between vitamin E levels and endometriosis or noted decreased serum vitamin E concentrations. However, the effect of simultaneous supplementation with vitamins C and E was positively assessed, which provided pain relief and reduced the level of oxidative stress and inflammatory markers. [7] Research on vitamin A suggests that its supplementation may reduce the incidence of endometriosis. [18] [19] Research on the effect of vitamin A in normal and endometriotic tissues is scarce and mainly focuses on the role of all-trans-retinoic acids (ATRA) in in vitro models. The results are very promising, but ATRA concentrations in these studies were much higher than those detected in human fluids and tissues. Therefore, these results should be treated with caution. [7]

### **4. Saturated fat**

Saturated fats, which are found mainly in animal products such as red meat, ham and butter, are associated with few health benefits. They may contribute to increased levels of estradiol and steroid hormones in the blood and are therefore associated with the risk of estrogen-

dependent diseases. [20] There are studies in which an increased risk of endometriosis was observed in people consuming beef and other red meats and ham, while the consumption of butter was not associated with a significant increase in the risk of endometriosis. [9][21] In another study, the conclusions were completely different. It has been observed that the consumption of butter causes an increased risk of endometriosis, while the consumption of red meat is not associated with such a risk. [22] Another study showed no significant correlation between endometriosis and red meat consumption. [23]

## **5. Trans fats**

Trans fats can be found in processed and deep-fried foods and are generally considered harmful to health. They are associated with higher levels of inflammatory mediators such as TNF-alpha, interleukin 6 and C-reactive protein, which increases inflammation. [8] One study found that people who consumed the most transunsaturated fats had a 48% greater risk of endometriosis than those who had the lowest transunsaturated fat intake. [24] However, other studies did not observe a significant effect of trans fats on the occurrence of endometriosis. [8]

## **6. Dairy**

According to research, consuming dairy products may reduce the risk of endometriosis. [25] It was found that people who ate 2 or more servings of yogurt per week as teenagers had a 29% lower risk of being diagnosed with endometriosis compared to those who ate less than 1 serving per week. Additionally, women who consumed 1 or more servings of ice cream per day during puberty had a 38% lower risk of being diagnosed with endometriosis compared to women who consumed less than 1 serving of ice cream per week. [26] However, two other studies did not prove that milk consumption was correlated with the occurrence of endometriosis. [9][16]

## **7. Coffee**

There is a hypothesis that the consumption of coffee and caffeinated beverages increases the availability of estrogens and estrones in the follicular phase, and also leads to an increase in the concentration of sex hormone binding protein (SHBG) and a decrease in the bioavailability of testosterone. These data allow us to hypothesize that the consumption of coffee and caffeine-containing beverages may be associated with the occurrence of estrogen-dependent diseases. Therefore, the influence of coffee consumption on the risk of developing endometriosis is being investigated. [8] This was not clearly proven in the meta-analyses. [27]

[28] However, it has been noted that high caffeine consumption (>300 mg/day) may be associated with the disease. [29]

## **8. Resveratrol**

Resveratrol is an organic substance obtained from plants. High levels of resveratrol can be found in grapes, wine, berries and nuts. [5] The effect of resveratrol on alleviating the symptoms of endometriosis has been studied, with conflicting results. One study found that resveratrol was no better than placebo for treating pain in endometriosis. Other studies suggested the positive effects of resveratrol. It was observed that resveratrol enhanced the effect of oral contraceptives in the treatment of dysmenorrhea associated with endometriosis by further reducing the expression of aromatase and cyclooxygenase-2 in the endometrium. [30] [31]

## **Conclusions**

Research confirms that consuming or limiting specific nutrients can reduce the risk of developing endometriosis and alleviate its symptoms. However, there are many contradictions related to the effects of specific products. It should be also emphasized that diet alone is not a sufficient treatment, but it may be an important element of a comprehensive approach to the treatment of endometriosis. Therefore, education about nutrition seems to be a promising strategy in controlling this disease. Studying the relationship between diet and endometriosis may reveal new preventive and therapeutic approaches beyond hormonal treatments. The role of diet and nutrition in endometriosis still remains an unexplored area that requires further research. Conducting randomized, controlled trials on a larger scale may help better establish the protective or harmful effects of different diets on the development and treatment of endometriosis.

## **Author's contribution:**

Conceptualization: Justyna Szpyra, Łukasz Gawlik, Piotr Jagodowski; methodology: Jagna Golemo, Julia Dębińska, Magdalena Górka; writing - rough preparation: Justyna Szpyra, Magdalena Celichowska, Gabriela Dziuba; supervision: Łukasz Gawlik, Piotr Jagodowski; writing - review and editing: Aleksandra Bogóń, Magdalena Ostojka.

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