THE EFFICACY OF TURMERIC LONGA AND ALLIUM SATIVUM IN RELIEVING ENDOMETRIOSIS SYMPTOMS: AN INTEGRATIVE REVIEW

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ABSTRACT

Endometriosis is a prevalent situation in women of reproductive age, leading to disabling symptoms such as chronic pelvic pain and infertility, posing a major challenge to women's health. Therefore, seeking safe and effective treatments is necessary in order to relieve the effort and improve the quality of life of these victims. Medicinal plants and herbal medicines draw attention in this context; They are available and relatively safe alternative treatments. Therefore, the aim of this study was to investigate the potential effect of Curcuma longa L. and Allium sativum L. on the treatment and management of the signs and symptoms of endometriosis. This study conducted an integrative review to investigate how Curcuma longa and Allium sativum may help in the treatment of endometriosis symptoms. Through searches in databases such as PubMed and Scielo, recent studies on the use of these herbal medicines in the context of endometriosis were selected. The results showed that both turmeric and garlic have anti-inflammatory and antioxidant properties, which may be essential for reducing the pain and inflammation associated with this condition. In studies conducted with humans and animal models, a decrease in symptoms has been observed, highlighting the potential of these natural compounds as alternatives to synthetic medicines. Therefore, turmeric and garlic have studies that prove the relief of endometriosis symptoms, but we reinforce the importance of more research to confirm their efficacy and safety for clinical use.

Keywords: Women's health. Herbal. Treatment.

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INTRODUCTION

The appearance of endometriosis occurs when the endometrial tissue is located outside the uterus, resulting in an inflammatory response under hormonal influence. This condition affects women of reproductive age, presenting symptoms such as pelvic pain, dysmenorrhea, intestinal dysregulation, urinary changes, and infertility, which negatively impacts quality of life. Endometriosis is a risk factor for ectopic pregnancies, with a prevalence of about 10% among women aged 25 to 45 years. In addition, the balance between apoptosis and cell proliferation in the endometrium is crucial; In endometriosis, there is excessive proliferation and reduced apoptosis, favoring the growth of lesions. (TORRES and et.al., 2021; CACCIATORI and MEDEIROS, 2015; MARQUES, 2022; HWANG and et.al, 2016; AGUIAR, 2007).

During the menstrual cycle, this tissue can proliferate and flake off, causing pain and inflammation, and leading to the formation of pelvic adhesions that distort the anatomy and function of the pelvic organs. The disease manifests itself in three forms: superficial peritoneal, ovarian (with the formation of cysts on the ovaries), and deep (with lesions that cross the peritoneum). The most accepted theory about the origin of endometriosis is that of retrograde menstruation, proposed by John Sampson, who suggests that endometrial tissue recedes through the fallopian tubes to the peritoneal cavity. However, this theory faces questions, such as the occurrence of endometriosis in women without a uterus and in pre-menarcheal children, indicating that the etiopathogenesis of the disease is not yet completely understood. (MARQUES, 2022)

The current health scenario faces several challenges, leading to the search for methods that promote health, protect life, and help in the recovery from diseases. Among these responses, phytotherapy stands out, which aims at comprehensiveness in health actions, recognized since 1978 at the Alma-Ata Conference. Integrative and Complementary Health Practices (PICS) were made official in the SUS in 2006, including treatments such as homeopathy, acupuncture and phytotherapy, which add up to 29 practices by 2017. (MINISTRY OF HEALTH, 2002)[6]

Historically, the use of medicinal plants has been common in various cultures and is still an affordable option for many, with efficacy dependent on dosage and preparation.

Herbal medicines are derived from plants and have their safety and effectiveness documented by ANVISA. In addition to them, there are Traditional Herbal Products, which do not require clinical trials due to their prolonged and known use. (BRAZIL-RENISUS, 2018; BORTOLUZZI and et.al, 2020; RODRIGUES and et.al, 2019). It should be noted that food supplements, regulated by ANVISA, are used to complement the diet and cannot make therapeutic claims. Products containing isolated bioactive substances are not considered herbal medicines, as the beneficial action usually results from the interaction of phytocomplexes. (BRAZIL-DRC, 2014; ANVISA, 2018).

Phytotherapy can offer economical, safe and effective assistance, contributing to the treatment and prevention of diseases. Turmeric *(Curcuma longa)* and garlic *(Allium sativum)* are highlighted for their anti-inflammatory and antioxidant properties, being potentially effective in the treatment of endometriosis. Turmeric acts to protect tissue from oxidative damage and regulates cellular processes, while garlic favors apoptosis in endometriotic cells. (SILVA, 2023; SANTOS, 2023, MARMITT, 2019; SOUZA, 2019).

In this sense, this study aimed to verify from the literature the efficacy of *Allium sativum* and *Curcuma longa* in relieving the symptoms of endometriosis through an integrative review.

MATERIAL AND METHODS

It was an integrative review of an exploratory nature, which implies the analysis of the bibliographic collection to enrich the discussion on methods, research results and directions for future studies on the subject. The electronic databases Pubmed and Scielo were used to access the publication database from 2007 to 2024. They were searched using the keywords 'endometriosis' or 'endometriosis' and/or '*Curcuma longa'* and/or '*Allium sativum' as descriptors.*

Studies that investigated phytotherapy as an integrative approach to endometriosis were included in this research, especially highlighting the therapeutic effects of herbal medicines such as *Curcuma longa* and *Allium sativum*. The analysis focused on research published over the past seventeen years and available in Portuguese, English, and Spanish, to ensure the inclusion of recent and widely accessible data. In addition, only

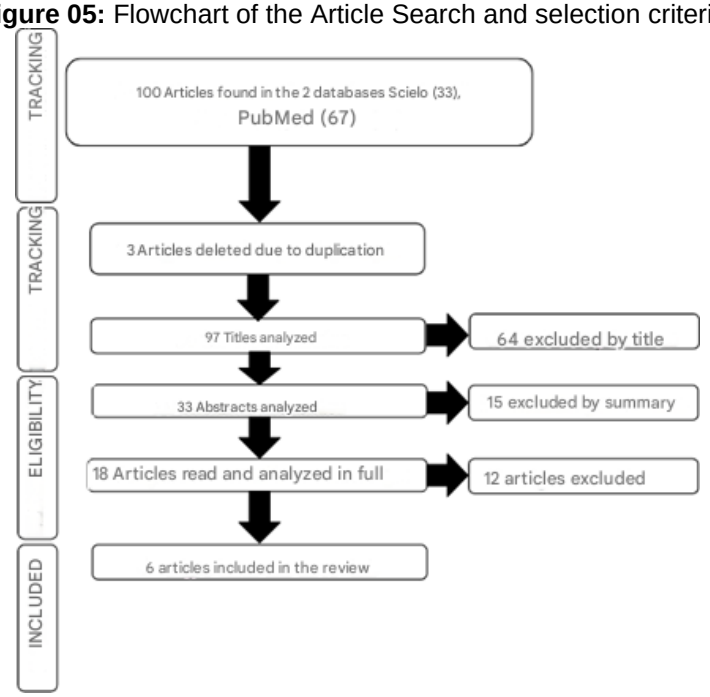
studies that presented promising results on the efficacy of phytotherapy and that contributed to the advancement of scientific knowledge in the area were considered.

On the other hand, studies that do not focus on phytotherapy as an intervention for endometriosis were disregarded. This includes research that has not explored the relationship between the bioactive compounds present in *C. longa* and *A. sativum* and their specific therapeutic effects on endometriosis. Excluding these studies, the review focuses on evidence that directly links herbal compounds to the benefits observed in the patients' condition.

RESULTS AND DISCUSSION

We identified 100 articles that met the inclusion criteria. After eliminating duplicates and articles considered irrelevant, 6 records were selected (Figure 5).

Figure 05: Flowchart of the Article Search and selection criteria.



Source: Authors, 2024.

The review of the 6 articles selected for this study revealed a distribution of publications over the years, with one article dated 2009, one from 2012, one from 2013, one from 2017, one from 2019 and one from 2021. This pattern suggests a relatively

recent activity in the field investigated, indicating that the theme may be emerging or not yet widely explored.

Figure 06 - Selection of studies for the elaboration of the results and discussion, taking into account the titles, purposes and findings of the articles.

Reference	Article Title	Goal	Findings
Swarnakar and et al, 2009.	Curcumin stops endometriosis through Of Negative regulation Of matrix metalloproteinase-9 activity.	To study the effect of curcumin on surgically developed endometriosis in mice.	The activity of MMP-9 increased as the severity endometriosis, and the treatment with curcumin reversed [illegible] activity to levels close to control.
Jana et al, 2011.	Curcumin as an agent anti-endometriotic drug: Implication of MMP-3 and the intrinsic apoptotic pathway.	Investigate the role of MMP-3 in apoptosis during endometriosis, as [illegible] check if Curcumin [illegible] endometriosis, modulating MMP-3 and the apoptotic pathway.	Curcumin treatment has shown efficacy by shifting the peak from expression of MMP-3 from the 7th to the 15th day, in addition to presenting obliteration of the glandular regions.
Kim Hyung and et al, 2013.	Extract of aged black garlic hexane	Investigate the effects of the extract garlic hexane	Treatment of TNF-α-activated HESCs with HEABG reduces the

	Reduces the cell proliferation and attenuates expression from ICAM-1 and VCAM-1 in human endometrial stromal cells activated by TNF-α.	Aged Black (HEABG) in proliferation and expression Of Molecules ICAM-1 and VCAM-1 adhesion in human endometrial stromal cells (HESCs), activated by tumor necrosis factor-α (TNF-α) and isolated from patients with endometriosis.	expression of ICAM-1 and VCAM-1 (mRNA [illegible] cell proliferation, the cell cycle progression and IL-6 secretion.
Cao et al, 2017.	Effect Curcumin inhibitory in human endometrial cells endometriosis through Of regulation of the factor from vascular endothelial growth.	Investigate the association between the endometriotic stromal cells and curcumin, in addition to from clarify The underlying mechanism of action.	Or treatment with Curcumin reduced the growth of ectopic human stromal cells [illegible]

Jelodar, 2019.	Serum CA-125 antigen assessment, Resistin, Leptin, Homocysteine and total antioxidant capacity in model Endometriosis in rats treated with curcumin.	Examine the Changes in serum levels of CA125 antigen, leptin, resistin, homocysteine and total antioxidant capacity (TAC) in model endometriosis in Rats and The effect of the treatment with	The Leptin was significantly higher in the treated group with curcumin, except compared to group from danazol. There were no significant differences in the levels from resistin, homocysteine and CA-125.
		curcumin in these factors.	
Amirsalar and et al, 2021.	Or effect of garlic tablets In Related pains Endometriosis: A Randomized Controlled Clinical Trial by placebo	Evaluate the effectiveness of garlic on the symptoms of endometriosis.	It was noticed that the group that received garlic, had a significant reduction in pain, but the group that received only placebo showed an increase in pain.

Source: Authors, 2024.

There is a growing interest among professionals from different areas in the investigation of endometriosis and herbal therapies as complementary treatments, driven by the clinical importance of this gynecological condition. Endometriosis, with its complex nature, attracts the attention of scientists from various sectors who seek to understand its causes, risk factors, and the impact of genetic variables on predisposition to the disease. This multidisciplinary interest demonstrates not only the complexity of endometriosis, but also the understanding that significant advances are only possible through collaboration between different areas of knowledge, from basic research to clinical practice, with the aim of improving the quality of life of affected women. (AGUIAR, 2007)

A study conducted by Bortoluzzi (2020) set out to identify and evaluate the most prevalent herbal medicines in the context of the treatment of certain conditions. Within the scope of her research, the author outlined the objective of mapping not only the most frequently used herbal compounds, but also of examining the quality of these products with regard to the control of raw materials. The results of his investigation highlighted the importance of not considering herbal medicines simply as formulations that encompass isolated substances of different origins or associations with plant extracts or encapsulated ones. Instead, they stressed the need to understand that the therapeutic efficacy of these products is intrinsically related to the integrity and quality of the raw materials used in their composition.

The use of herbal medicines has been used to relieve the symptoms of endometriosis. According to Rodrigues (2019), a herbal medicine is a product derived from active plant raw material, excluding isolated substances, intended for the prevention, treatment or interruption of symptoms, encompassing herbal medicine and traditional herbal product. It can be classified as simple, when the active ingredient comes from a single medicinal plant species, or compound, when derived from multiple plant species. The study by Silva (2023) had as its main objective to analyze medicinal plants and herbal medicines that reduce pain in women with endometriosis. The result showed that medicinal plants and herbal medicines are natural alternatives, with low economic cost and similar effect to drugs, such as anti-inflammatories.

According to the author Torres (2024), a large part of the world's population resorts to medicinal plants, as it is a viable and low-cost resource. In addition, they are efficient for women's health, such as menstrual discomfort and hormonal changes in the body.

Turmeric *(Curcuma longa)* and garlic *(Allium sativum)* are highlighted for their anti-inflammatory and antioxidant properties, being potentially effective in the treatment of endometriosis. Turmeric acts to protect tissue from oxidative damage and regulates cellular processes, while garlic favors apoptosis in endometriotic cells. (SILVA, 2023; SANTOS and et.al, 2023; MARMITT and et.al, 2016; SOUZA, 2019)

After analyzing the six studies, it was found that two investigated garlic and four turmeric. Thus, three authors carried out their studies in animal models (two in mice and one in rats), one *in vitro* and one *in vivo* (women).

The study by Amirsalar et al (2021), investigated the use of herbal medicines in the management of endometriosis, focusing on the effectiveness of *Allium sativum L*. in reducing the symptoms of this condition. 120 participants were randomly divided into two groups: one received garlic tablets, at a concentration of 400mg, while the other received a placebo. To assess the efficacy of the treatment, the Visual Analogue Scale (VAS) was used on four occasions over three months. The results showed a significant reduction in pain intensity in the group that received *Allium sativum*, with the average pain decreasing from 6.51 to 1.83. In contrast, the placebo group showed an increase in pain intensity, showing that garlic may be effective in reducing pain associated with endometriosis.

Kim et al. (2013) evaluated the effects of aged black garlic hexane extract (HEABG) on human endometrial stromal cells activated by TNF-α, collected from patients with endometriosis. The research demonstrated that HEABG was effective in reducing both cell proliferation and expression of the adhesion molecules ICAM-1 and VCAM-1. The results showed that the extract was able to decrease the activation of the ERK and JNK signaling pathways, in addition to inhibiting the transcription factors NF-κB and AP-1, which are involved in the inflammatory response and cell proliferation, characteristic of endometriosis.

In this way, the study suggests that HEABG may be a possible natural treatment to prevent and fight endometriosis, showing promise in reducing inflammation and multiplication of endometrial stromal cells.

In this sense, *Allium sativum L.,* as it is recognized for its antimicrobial, antioxidant, and anti-inflammatory properties, can bring benefits when used to relieve the symptoms of endometriosis. Sulfur compounds present in garlic, such as allicin, have been shown to be effective in reducing inflammation and oxidative stress, factors that are key in the pathogenesis of endometriosis. *Allium sativum* can also help improve blood circulation and modulate the immune response, which can be beneficial for patients suffering from endometriosis. *Allium sativum* acts in the body through allicin, a compound released when we cut or mash it. This compound has a natural effect against bacteria, viruses, and fungi, helping to protect the body from infection. Allicin also functions as an antioxidant, defending cells from damage and contributing to overall health. (SOUZA, 2019)

Curcuma longa l. It has a more active ingredient, curcumin, a powerful compound with a range of health benefits, such as anti-inflammatory, antioxidant, and antibacterial properties. By reducing the production of oxidative molecules, curcumin helps protect the body's cells against aging and diseases related to cellular stress. In addition, it plays a role in relieving pain and modulating inflammatory processes, which makes *Curcuma longa* a promising option for chronic conditions, especially endometriosis.(SANTOS and et.al., 2023; MARMITT and et.al, 2016)

Cao et al. (2017), evaluated the effect of curcumin on endometrial stromal cells, collected from patients with endometriosis. As a result, curcumin treatment helped to reduce proliferation, especially at the concentration of 50 μmol/l affecting the decrease in the number of stromal cells collected from endometriotic tissue, increasing the number of cells in the G1 phase of the cell cycle, which indicates a decrease in cell division. In addition, curcumin causes apoptosis of such endometrial cells, 4.7% reveal early apoptosis, while 28.4% have late apoptosis.

One of the reasons for this effect is the compression of the expression of vascular endothelial growth factor (VEGF), a protein considered critical for the process of angiogenesis and the growth of endometriotic cells. With these results, it was possible to conclude about the opportunity to name curcumin as a drug for the treatment of endometriosis, whose main action is to inhibit growth and induce the programmed death of normal and malignant cells associated with the disease. (CAO et al., 2017)

Swarnakar and Paul (2008), studied the effect of curcumin on surgically developed peritoneal endometriosis in female mice. In this sense, the scientists analyzed in endometriotic tissues, the changes in matrix metalloproteinase (MMP)-9 and tissue metalloproteinase inhibitor (TIMP)-1, after the mice received the curcumin treatment. Thus, curcumin being distributed in doses of 16, 32, and 48 mg/kg body weight, once daily, for 10 days, as well as intraperitoneal vehicle insertion, demonstrated a gradual decrease in MMP-9 secreted activity by 50%, 70%, and 80%. In the same way, he found promising results in synthesized MMP-9, with a decrease of 60%, 70% and 90%. Thus, it is evident that curcumin becomes a great ally in relieving painful symptoms of endometriosis.

Endometriosis has symptoms such as pelvic pain, dysmenorrhea, intestinal dysregulation, urinary changes, and infertility, which negatively impacts quality of life. In

endometriosis, there is excessive proliferation and reduced apoptosis, favoring the growth of lesions. (TORRES and et.al., 2021; CACCIATORI and MEDEIROS, 2015; MARQUES, 2022; HWANG and et.al, 2016; AGUIAR, 2007). The study by Cacciatori et al (2015) with 1000 patients found that the most common symptoms of endometriosis were dysmenorrhea (79%) and pelvic pain (69%). In group A, pain during sex (dyspareunia) was the most frequent symptom, while in group B, with more severe lesions, difficulty getting pregnant (subfertility) and the presence of ovarian masses were the most common symptoms that led to the diagnosis. In this sense, the use of turmeric to relieve these symptoms is currently promising.

The study by Jana et al (2011) verified the role of MMP-3 in apoptosis during endometriosis, as well as whether curcumin had the power to reverse endometriosis by modulating MMP-3 and the apoptotic pathway. In the results, the mouse model of endometriosis, which was designed through intraperitoneal inoculation of endometrial tissues in females, demonstrated that on the 15th day, there was an increase in MMP-3 expression. In addition, cells positive for *Terminal Deoxynucleotidyl Transferase dUTP Nick-End Labeling* (TUNEL) were also identified with a progression, which possibly generated a destruction of local immune cells. On the other hand, when they underwent treatment with curcumin, it was noticed that there was a reversal of endometriosis, inhibiting NF-κB translocation and MMP-3 expression. In addition, an acceleration of apoptosis was observed in endometriomas predominantly the mitochondrial pathway mediated by cytochrome-c. However, curcumin's role has been effective in controlling endometriosis symptoms.

The research conducted by Jolodar and Azimifar (2019), investigated the serum levels of biomarkers in a mouse model of endometriosis treated with curcumin. The results indicated that although leptin in the curcumin-treated group was significantly higher compared to the other groups except the danazol group, there were no relevant differences in resistin, homocysteine, and CA-125 levels between the groups. In addition, the Total Antioxidant Capacity (TAC) was significantly higher in the control group compared to the treated groups.

These findings suggest that, despite curcumin's potential to prevent the growth of endometriosis, it did not promote significant changes in the biomarkers studied, indicating

that monitoring these parameters may not be a reliable indicator of endometriosis status in the rat model.

The positive results of these herbal medicines suggest that herbal medicine may be a viable option for managing endometriosis symptoms, highlighting the importance of exploring and validating alternative therapeutic approaches to improve patients' quality of life. (MARQUES, 2022)

The research corroborates that phytotherapy stands out for the use of medicinal plants and phytochemicals, especially those that contain phenolic compounds, such as flavonoids and phenolic acids. These compounds are known for their anti-inflammatory, pro-apoptotic, and antioxidant properties, which can help reduce inflammation and proliferation of endometrial tissue. In addition, some phytochemicals have phytoestrogenic effects, which means they can influence estrogen activity in the body. This is particularly relevant for endometriosis, as estrogen plays a crucial role in the pathology of the disease. The phytoestrogenic effects of these compounds may help balance hormone levels and modulate endometrial tissue activity, offering a potentially effective approach to treating endometriosis. (BRAZIL, 2014)

Estrogen plays a crucial role in the development of endometriosis, as it favors the proliferation of endometriotic cells and prevents their programmed death, or apoptosis. This hormone is produced locally in the lesions, mainly by the aromatase enzyme, which ends up creating a vicious cycle with prostaglandin E2, further intensifying the production of estrogen. In addition, there is an imbalance in the 17β-HSD enzymes, which maintains high levels of estradiol in the lesions, thus managing to promote the growth and resistance of the endometriotic tissue. These mechanisms explain why treatments reduce or block the action of estrogen are effective, helping to relieve the symptoms of endometriosis and reduce the size of the lesions caused by the pathology. (AGUIAR, 2007)

CONCLUSION

This study highlighted the great therapeutic potential of *Curcuma longa* and *Allium sativum L*., especially in the treatment of endometriosis. Based on a detailed analysis of the literature, it was evident that these herbal medicines have significant anti-inflammatory and antioxidant properties, helping to relieve symptoms such as chronic pelvic pain and

intestinal dysregulation. In addition, the isolated or combined use of these plants can be a more natural and safer alternative compared to synthetic medicines, which are often accompanied by unpleasant side effects.

Despite these advances, more studies are still needed to fully understand the impact of these herbal medicines. Well-designed clinical trials are essential to confirm their efficacy and safety, as well as to explore how, exactly, these substances act in the body. Understanding these mechanisms can open doors to more personalized and effective treatments, bringing new perspectives to those living with endometriosis.

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