

Effects of herbal compounds on various aspects of endometriosis treatment: a systematic review

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Abstract. – OBJECTIVE: Endometriosis means the presence of tissue similar to normal endometrium outside the uterus. Although surgical, hormonal, and analgesic treatment relieves symptoms and improves fertility, it is associated with side effects and a high recurrence rate. Alternative medicines like medicinal plants have been used for the treatment of chronic diseases. Given the global importance of endometriosis as a chronic disease affecting over 15% of all women in their fertile period, this systematic review aimed to give a comprehensive view of research on medicinal plants.

MATERIALS AND METHODS: Comprehensive searches were performed on three databases, including PubMed/MEDLINE, Web of Science Core Collection (Indexes = SCI-EXPANDED, SSCI, A, and HCI Timespan), and Scopus, to identify papers published until June 2023. Keywords, such as "Endometriosis" and "Herbal Medicine", were used to search. A manual search of valid journals followed by a manual search of the references of the retrieved full-text articles was performed. All retrieved articles were imported into a database into Endnote X9. Articles that did not meet the inclusion criteria were excluded from the study, and the full texts of all the articles that met the inclusion criteria were assessed. Studies that evaluated the effects of herbal compounds on various aspects of endometriosis treatment were included in the review.

RESULTS: In total, 11 studies were included in the present study. The evidence showed that

in addition to safety, drugs available alongside treatments could play an effective role in improving the symptoms associated with endometriosis. In this study, the positive results of using Chinese treatments were reported in aspects such as fertility rate, pain, endometriosis recurrence rate, quality of life, sexual function, CA-125 level, and menopause symptoms.

CONCLUSIONS: A wide range of preclinical and clinical studies evaluated the effectiveness and safety of medicinal plants in the treatment of endometriosis symptoms. Thus, alternative treatments for endometriosis with no or low side effects should be included in the holistic treatment of endometriosis upfront. However, there is still a need for well-designed trials to investigate standard interventions and specific and safe doses of herbal medicines.

Key Words:

Endometriosis, Herbal medicine, Systematic review.

Introduction

Endometriosis, which can be defined as the presence of endometrial tissue outside the uterine cavity, is one of the most common benign gynecological disorders, with prevalence rates ranging between 0.2 and 71.4 among women in their fer-

tile life phase¹. This disease affecting women of reproductive age causes chronic pain that is not necessarily related to the depth or extent of tissue penetration. Back pain, reduced fertility, infertility, dysmenorrhea, dyspareunia, and dysuria, which are among the most common symptoms/signs of endometriosis, have adverse effects on the health and quality of life of affected women^{2,3}. Intra-pelvic endometriosis lesions commonly involve the ovaries, fallopian tubes, or uterine sacral ligaments, and extra-pelvic lesions usually affect the abdominal wall, digestive, and urinary tract. Traces of genetic, hormonal, and immune factors are thought to be involved in this multifactorial disorder⁴. The diagnosis of this disease is often delayed due to non-specific symptoms, so it usually leads to more difficult treatment, chronic pain, and infertility⁵.

Endometriosis is treated with surgical and/or medical methods. Nonsteroidal anti-inflammatory drugs (NSAIDs) combined oral contraceptives (OC), progestin, gonadotropin-releasing hormone agonists (GnRH-a), and aromatase inhibitors are the most common medical treatments for the disease. Concrete diagnosis can only be made by surgical biopsy, which is mostly performed by laparoscopy. In many cases, surgical resection is performed to remove endometriosis lesions, leading to improved fertility and relief of endometriosis symptoms, but it may be associated with complications and does not avoid the possibility of recurrence. Also, in the presence of ovarian endometriosis, surgery is associated with the possible decrease of ovarian reserve⁶⁻⁸. Alternative medicines like medicinal plants have been widely used in the treatment of chronic diseases for many years and are expanding due to their favorable effects. This treatment method uses different medical philosophies (such as Chinese, Indian, anthroposophic, etc.), herbs, dosages, and timings to relieve symptoms⁹. However, their concrete benefit is still under discussion, and there is no general commitment to a global point of view for medical professionals. Considering the importance of endometriosis and the negative aspects of patients suffering on the one side and the side effects of conventional medicine on the other side, the objectives of this systematic review were to give a comprehensive view of this disease by reviewing studies carried out on medicinal plants and their compounds and to clarify the need for future studies in this field.

Materials and Methods

Published articles that developed or validated herbal medicine on symptoms of endometriosis were searched for a systematic review.

Research Question

Following the PRISMA guidelines¹⁰, this study was conducted to answer the following research question: what are the effects of herbal treatments on symptoms and signs of endometriosis?

Search Strategy

The present study was conducted to investigate the effect of herbal remedies on the symptoms of endometriosis. To answer the study question, PubMed/MEDLINE, Scopus, and Web databases were searched in June 2023. Keywords such as “Endometriosis”, “Herbal Medicine”, “Hawaiian Herbal Medicine”, “Medicine”, “Hawaiian Herbal”, and “Herbalism”, were used to search for related articles. To make the search more comprehensive, two investigators also performed a manual search of authentic journals, followed by a manual search of the references used in the retrieved full-text articles. All retrieved articles were imported into a database into Endnote X9. The search strategy was revised iteratively to maximize the sensitivity and specificity of articles.

Inclusion Criteria

We included original studies and randomized controlled trials (RCT) using samples with endometriosis published in English and using keywords in the title, abstract, or text.

Exclusion Criteria

Commentaries, editorials, systematic reviews, conference abstracts, opinion statements, practice guidelines, and case series or case reports were excluded from the study. Animal and laboratory studies were also excluded; non-herbal treatments like acupuncture, enema, or pressure points, lack of access to the full text of the article, or duplicate data in several articles were among other exclusion criteria.

Data Extraction

The articles were searched by one of the researchers (HS) and then were entered into the Endnote software (X9, Clarivate, London, UK). The study inclusion and exclusion criteria were independently checked by two researchers (ZM, LA) based on the titles and abstracts of the articles.

At this stage, the articles that did not meet the inclusion criteria were removed, and then the full text of all remaining articles that met the inclusion criteria was reviewed and analyzed. By assessing each article in detail, its results and conclusions were extracted. The following data were extracted using a standardized data collection form: the first author, year of publication, inclusion and exclusion criteria, sample size, intervention details (such as type of intervention, type of herb used, drug dose, duration of treatment, and type of placebo), and results. Disagreements in each phase were resolved by two referees through discussion or, if necessary, by a third referee (IA).

Types of Patients

In this systematic review, a clear diagnosis of endometriosis, confirmed by laparoscopic or laparotomy, was deemed essential.

Results

Selection of Studies

After searching the different databases, a total of 466 articles were retrieved and entered into the Endnote software. Of these, 316 articles were duplicates. 120 studies were excluded after reviewing their titles and abstracts. 19 articles were excluded for the following reasons: one was a non-English article, 11 articles were rat models, and one was out of alignment with the study's objective. Finally, 11 studies were included in the systematic review (Figure 1).

Included Studies

A total of 11 articles published between 2006 and 2023 were included in the study. These studies, with a sample size of 50-208, investigated the effects of herbal compounds for the treatment of endometriosis¹¹⁻²¹. The four studies compared herbal compounds with placebo^{16-18,22} and the rest with other available treatments ([Supplementary Table I](#)).

Fertility Rate

Pelvic anatomy changes, endocrine abnormalities and ovulation disorders, peritoneal function changes, hormonal disorders, and endometrial cell dysfunctions are some mechanisms involved in endometriosis-related infertility²³. According to the study by Zhao et al¹³, the pregnancy rate in the Chinese medical plants' group was not different from that in the GnRH-a injection group.

The pregnancy rate in infertile women was higher in the Chinese medical plant (CMP) group. The results of a study¹⁶ conducted on women aged 20-35 years in two intervention and control groups showed that after the surgery, the intervention group received one type of herbal medicine at the ovulation time. Based on the results of this study, the pregnancy rate in the intervention group during 6 menstrual cycles after laparoscopy was significantly higher than that in the control group. In addition, the live birth rate in the CMP group was significantly higher than that in the controls, but the adverse pregnancy outcomes, such as spontaneous abortion and misplaced pregnancy, were not significantly different between the two groups. The cumulative amount of dominant follicle, mature follicle, and cycles with ovulation in the CMP group was significantly higher than the control group¹⁶. Rostami et al¹⁷ studied 50 infertile women with stage III and IV endometriosis and showed that before and after 12 weeks of treatment with Astaxanthin, the number of transferred embryos was similar between the two groups, but the number of recovered oocytes, mature oocytes, and high-quality embryos in the Astaxanthin group was significantly higher than that in the control group. In a clinical trial²¹, Chinese researchers examined 156 infertile women with mild endometriosis after laparoscopy in three groups of OC, OC with Dan'e mixture (DEM, consisting of Radix Salviae Miltiorrhizae and Rhizoma Zedoariae), and no complementary treatment. According to the results of this study, in the 12-month follow-up, there was no statistically significant difference among the three groups in terms of the rates of pregnancy and live births.

In a study¹⁹ that compared two herbal diets with Mifepristone in infertile women with endometriosis, no statistically significant difference was observed between the two groups in terms of the rates of pregnancy and spontaneous abortion. In this study, the follicle diameter was greater in the herbal treatment group, but this difference was not significant.

Recurrence Rate of Endometriosis

The exact causes of endometriosis recurrence are unclear. Various clinical and surgical factors might contribute to endometriosis recurrence. Whether the recurrence of endometriosis is caused by the remaining cells after surgery or is caused by new lesions is debated²⁴. The result of a prospective, multi-center-controlled trial¹² showed that the recurrence rate of stage III and

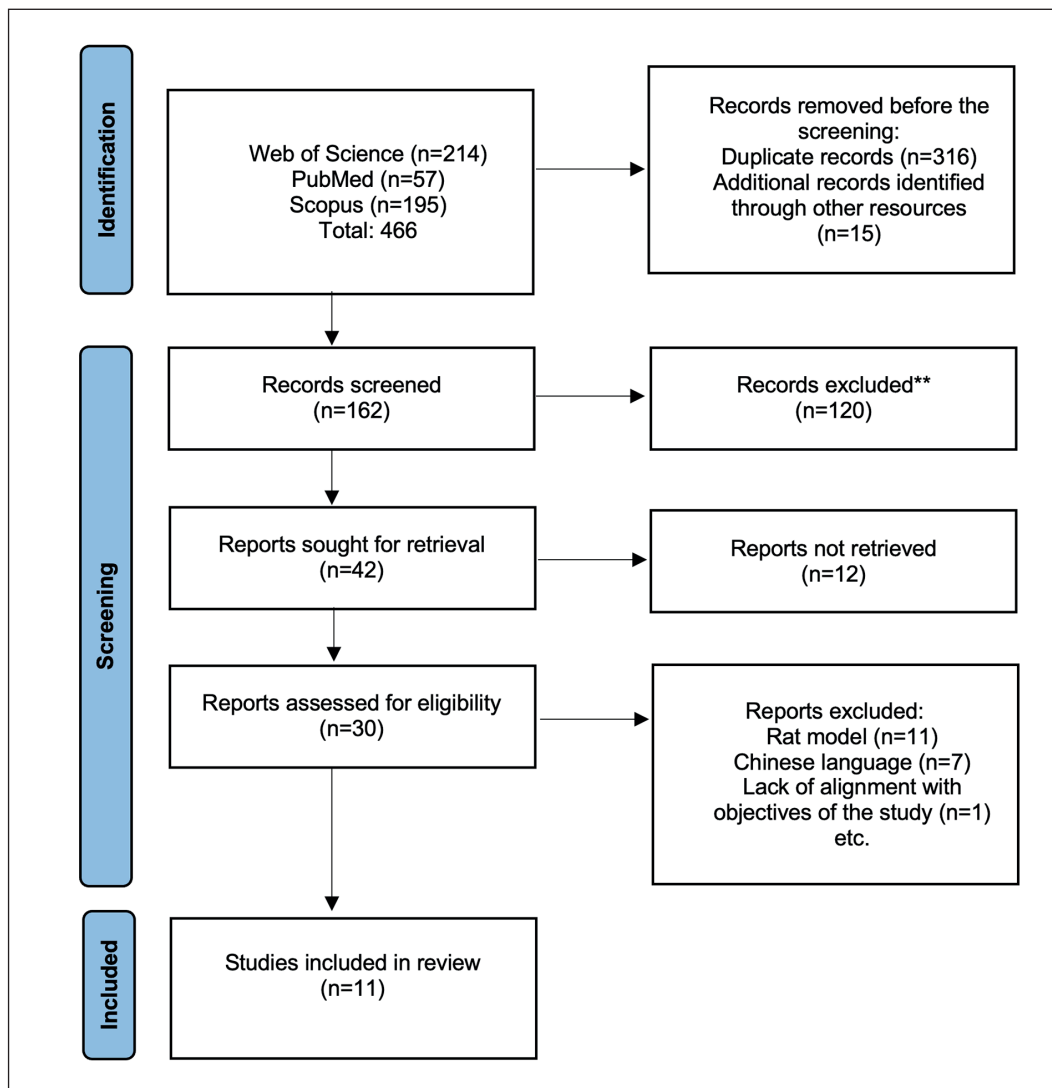


Figure 1. Flowchart of the selected study.

IV endometriosis in two groups of CMPs and the Goserelin acetate in post-operative patients was not different from each other. Based on syndrome differentiation, Zhao et al¹³ recommended multiple drug regimens twice a day for 21 days and compared them with GnRH-a injection. According to the results of this study, there was no difference between the two groups in terms of the recurrence rate and time of pelvic endometriosis¹³. In another study, Ruan et al¹⁵ did not observe any significant difference in the recurrence rate among the three groups of SanJieZhenTong (SJZT) capsules, GnRH-a, and OC. Ding et al¹⁹ examined patients with grade III endometriosis after surgical treatment in two groups of Yiweining and Gestrinone. The results showed no sta-

tistically significant difference between the two groups in terms of recurrence rates, but the rates in the two groups were lower than those in the control group.

Pain

Periodic bleeding from lesions and subsequent inflammation at the site of the lesion and peritoneal cavity causes chronic pain in the endometriosis²⁵. The results of a three-group study¹⁵ showed that SJZT capsules provided more effective pain relief in women with moderate to severe endometriosis compared to GnRH-a and OC. A study¹⁸ conducted in Iran investigated the pain relief associated with endometriosis in the garlic tablets group compared to a placebo. The results showed that the consu-

mption of 400 mg garlic tablets significantly reduced lower back pain, dysmenorrhea, dyspareunia, and the overall pain score compared to the placebo group. By comparing the amount of pelvic pain and visual analog scale (VAS) score in the OC and OC with Dan'e mixture groups of infertile women with mild endometriosis after laparoscopy treatment, Zhu et al²¹ showed no significant difference between the two groups.

Quality of Life

The symptoms of endometriosis, especially pain, could have adverse effects on the patient's quality of life. Comparing the quality of life in the two groups of Chinese medical plants and GnRH-a showed that the quality of life in both groups improved significantly, and the treatment with Chinese medical plants was more effective than the other group¹⁴. Based on the results of the study by Ruan et al¹⁵, SJZT capsules improved the quality of life of women with moderate to severe endometriosis compared to GnRH-a and OC.

Menopause Symptoms

The postoperative use of GnRH-a in endometriosis patients could cause premenopausal symptoms by reducing estrogen levels. In the study by Chen et al¹¹, three groups of Kuntai (which is a combination of 6 Chinese medicines: Radix Rehmanniae Preparata, Rhizoma Coptidis, Radix Paeoniae Alba, Donkey Hide Gelatin, Radix Scutellariae, and Poria), Tibolone and control were compared. The results showed that Kuntai, by having a similar effect as Tibone, improved premenopausal symptoms, such as hot flashes and sweetening, in the 8th to 12th weeks of treatment. Kuntai capsule was also able to reduce premenopausal symptoms in women by improving ovarian function¹¹.

Sexual Function

Sexual dysfunction in women with endometriosis is higher than that in healthy women. These women face disorders in all areas of sexual function, such as desire, arousal, orgasm, lubrication, satisfaction, and pain^{26,27}. Based on the results of a three-group study, SJZT capsules improved sexual function in women with moderate to severe endometriosis more than GnRH-a and OC¹⁵.

CA-125 Level

Although the current guidelines by the European Society of Human Reproduction and Embryology (available at: [ne/Endometriosis\) do not recommend evaluating biomarkers for both the diagnosis and follow-up of endometriosis, the CA-125 level is elevated in some cases of advanced endometriosis. Some studies suggested a potential relationship between CA-125 level and the stage of endometriosis. According to the results of a study by Weng et al¹², after treatment, the serum CA-125 levels in the Chinese herbal medicine group were significantly lower than those in the Goserelin acetate group.](https://www.eshre.eu/Guideli-</p></div><div data-bbox=)

Safety

According to Chen et al¹¹ study, the incidence of adverse symptoms, such as vaginal bleeding, nose spot, and breast pain in the Kuntai group was lower than that in the Tibolone group. No adverse symptoms were seen in another study conducted in China¹². Meanwhile, in Zhao et al¹³ study, the adverse outcomes in the Chinese herbal medicine group were significantly lower than those in the GnRH-a group. This result was confirmed in Ruan et al¹⁵ study, and also side effects, such as hot flashes, insomnia, and arthralgia in the SJZT capsules and OC groups were lower than those in the GnRH-a group. The safety of herbal medicines was also investigated in another study¹⁶, and no significant adverse outcomes were reported. A study¹⁹ performed in China examined liver and kidney function and reported the safety of herbal medicines. In another study²⁰, the rate of adverse outcomes in the herbal treatment group was lower than that of the Gestrinone group.

Discussion

Endometriosis is an estrogen-dependent disease, and therefore, it often affects women of reproductive age. This common disease imposes a heavy burden on patients and society and harms mental health, relationships, and the overall quality of life of women and their families. As it also hurts the society's environment, it becomes a significant factor for global health policy²⁸. In addition to infertility, chronic pelvic pain, and disorders of involved organs, this disease can lead to adverse pregnancy outcomes, and also women with a history of endometriosis are at an increased risk of spontaneous abortion, ectopic pregnancy, gestational diabetes, and hypertensive disorders^{29,30}. Although medical and surgical treatments often reduce pain, they are associated with high complication rates of conventional therapy and adverse side effects, as well as the recurrence of the disease, leading to the frustration and discontinuation of treatment in many

women³¹. The problems of the existing treatments and the increase in awareness of the disease could lead to efforts being made to obtain better treatments for this disease.

The side effects of existing drugs and the effectiveness of herbal products in managing some women's problems have made herbal medicine be used as an alternative treatment in health systems. Today, medicinal plants and herbal products are used to manage many diseases like endometriosis. Medicinal plants and their active compounds may affect processes including invasion, adhesion, angiogenesis, immune system inflammation, and oxidative stress. These drugs can reduce aberrant lesions and prevent the progression of endometriosis by preventing inflammation and inducing apoptosis³².

In the present study, we systematically reviewed the results of 12 studies that investigated the effects of herbal medicines on symptoms of endometriosis. The evidence from previous studies in the literature shows that in addition to safety, herbal medicines could play an effective role in improving the symptoms of endometriosis. In the study, the positive effects of Chinese treatments on fertility rate, pain, endometriosis recurrence rate, quality of life, sexual performance, CA-125 levels, and menopausal symptoms were confirmed.

Sexuality is affected by various biological, psychological, cultural, social, and economic factors, and therefore, these factors determine the quality of sexual performance in each person^{33,34}. Stretching of pelvic endometriosis nodules during intercourse causes deep sexual pain. Dyspareunia and post-coital pains decrease the frequency of sexual intercourse and subsequently decrease arousal and orgasm^{35,36}. Although the result of the study by Ruan et al¹⁵ showed the effectiveness of herbal treatment in improving sexual function, the determination of the effect is limited due to the multifactorial nature of sexual dysfunction.

In a systematic review of 11 randomized clinical trials, Zheng et al³⁷ reported that Chinese herbal medicine could improve ovarian function by increasing estradiol levels. The authors also considered Chinese herbal medicine as a safe method for the treatment of endometriosis. In another study, Cao et al²² used Chinese herbal medicine capsules to treat patients with premature ovarian failure. In this study, Yangyin Shugan formula improved ovarian function and reduced menopausal symptoms in patients by reducing follicle-stimulating hormone (FSH) levels and improving anti-müllerian hormone (AMH) levels²². Chinese medicine seems to play an important role

in improving the ovarian function of women with endometriosis by having a synergistic effect on the regulation of estrogen and serotonin.

Chinese medical plants can play an important role in improving pain by affecting target proteins and pathways related to hormone regulation, central analgesia, spasmolysis, inflammation, and the immune system¹⁵. Compounds in Chinese medicine, such as ursolic acid, rosmarinic acid, ferulic acid, caffeic acid, and oleanolic acid, could regulate pain receptors. On the one hand, Chinese herbs can also reduce pain by regulating neurotransmitters. On the other hand, an increase in the level of pro-inflammatory cytokines has been observed in endometriosis lesions. These cytokines can cause chronic pelvic pain³⁸.

In a systematic review and meta-analysis, Dong et al³⁹ assessed 11 articles and concluded that Chinese herbal medicine could play an effective role in the treatment of endometriosis-related infertility and improving pregnancy rates. In a systematic review study conducted on 1,851 infertile women at the mid-fertility stage, the fertility rate in the Chinese herbal medicine group was reported to be twice as high as that in the group receiving infertility treatment or *in vitro* fertilization (IVF)⁴⁰. In addition to restoring balance in the body, this treatment helps fertility by regulating the hormonal cycle during menstruation, creating a physiological environment to facilitate conception, implantation, and preservation of the embryo, and improving the blockage of the fallopian tube⁴¹. Xia et al⁴² found that some Chinese herbal formulas could have a positive effect on the treatment of infertility by increasing blood flow in the uterus and ovaries and improving the growth and development of follicles compared to clomiphene citrate.

Strengths and Limitations

The strengths of this systematic review included a detailed search strategy and the evaluation of the effects of herbal therapy on various symptoms of endometriosis. The main limitations of this study were the lack of conclusive evidence in previous studies, small sample size, confounding factors, heterogeneity of interventions and the type of intervention, control group, different characteristics of participants, different definitions of outcome, poor reporting of details, limited human studies, the existence of studies in other languages including Chinese, and the lack of access to many full-text articles. In addition, although there is some evidence that shows the

direct or indirect effect of COVID-19 on endometriosis symptoms, the evidence shows that the incidence of endometriosis symptoms such as pelvic pain, dysmenorrhea, and dyspareunia has increased during the COVID-19 pandemic⁴³. Therefore, some of the women in this systematic review may have experienced exacerbation of symptoms related to endometriosis. This means that it is not possible to accurately determine the effect of all medicines, including herbal medicines, in improving this disease during the COVID period. These limitations did not allow us to perform a pooled data analysis due to the high heterogeneity of the study designs and reduced the authors' ability to conclude the effectiveness of herbal therapy in relieving endometriosis-related symptoms. In addition, although most of the herbal treatments were associated with a good safety profile, some specific compounds may need further studies to evaluate the safety profile in women searching for pregnancy (for potential teratogenic effects) and the long-term outcomes in both mothers and offspring. Moreover, future studies should aim to evaluate the effects of hormone therapy combined with herbal therapy on symptoms and signs of endometriosis.

Conclusions

So far, various approaches have been proposed to reduce the symptoms of endometriosis. The side effects of existing treatments have led researchers to use new, safe, alternative, and effective treatments in this regard. The mechanism of action in some drugs is still debated, but a wide range of preclinical and clinical studies evaluated the effectiveness and safety of medicinal plants in the treatment of endometriosis symptoms and signs. However, there is still a need for well-designed trials to investigate standard interventions and specific and safe doses of herbal medicines so that useful and comprehensive information can be provided to the pharmaceutical industry and health policymakers.

Conflict of Interest

There is no conflict of interest to declare.

Informed Consent

Since this study is a systematic review, it was impossible to obtain informed consent from patients included in those study.

Ethics Approval

Not applicable due to the design of the study.

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Authors' Contributions

Z.M, H.S, L.A, G.M, G.G and I.A contributed to the design and implementation of the research project. Z.M, H.S, L.A., A.S.L, A.MM, and I.A conducted the analysis of results. Z.M, L.A, A.S.L, A.MM, G.M, G.G and I.A prepared the manuscript. All authors discussed the results and contributed to the final manuscript.

Data Availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

References

- 1) Ghiasi M, Kulkarni MT, Missmer SA. Is Endometriosis More Common and More Severe Than It Was 30 Years Ago? *J Minim Invasive Gynecol* 2020; 27: 452-461.
- 2) Van Niekerk L, Weaver-Pirie B, Matthewson M. Psychological interventions for endometriosis-related symptoms: a systematic review with narrative data synthesis. *Arch Womens Ment Health* 2019; 22: 723-735.
- 3) Della Corte L, Di Filippo C, Gabrielli O, Reppuccia S, La Rosa VL, Ragusa R, Fichera M, Commodari E, Bifulco G, Giampaolino P. The Burden of Endometriosis on Women's Lifespan: A Narrative Overview on Quality of Life and Psychosocial Wellbeing. *Int J Environ Res Public Health* 2020; 17.
- 4) Bokor A, Topbas Selcuki NF. Extrapelvic endometriosis. *Endometriosis and Adenomyosis: Global Perspectives Across the Lifespan*. Springer 2022: 243-249.
- 5) Gruber TM, Mechsner S. Pathogenesis of endometriosis: the origin of pain and subfertility. *Cells* 2021; 10: 1381.

- 6) Kalaitzopoulos DR, Samartzis N, Kolovos GN, Mareti E, Samartzis EP, Eberhard M, Dinas K, Daniilidis A. Treatment of endometriosis: a review with comparison of 8 guidelines. *BMC Womens Health* 2021; 21: 1-9.
- 7) Muñoz-Hernando L, Muñoz-Gonzalez JL, Marqueta-Marques L, Alvarez-Conejo C, Tejerizo-García A, Lopez-Gonzalez G, Villegas-Muñoz E, Martin-Jimenez A, Jiménez-López JS. Endometriosis: alternative methods of medical treatment. *Int J Womens Health* 2015: 595-603.
- 8) Pacchiarotti A, Iaconianni P, Caporali S, Vitillo M, Meledandri M, Monaco G, Sergio C, Boza M, Sacucci P. Severe endometriosis: low value of AMH did not affect oocyte quality and pregnancy outcome in IVF patients. *Int J Womens Health* 2020; 24: 11488-11495.
- 9) Flower A, Liu JP, Lewith G, Little P, Li Q. Chinese herbal medicine for endometriosis. *Cochrane Database Syst Rev* 2012; 5: CD006568.
- 10) Moher D, Shamseer L, Clarke M, Ghersi D, Liberati A, Petticrew M, Shekelle P, Stewart LA, Group P-P. Preferred reporting items for systematic review and meta-analysis protocols (PRISMA-P) 2015 statement. *Syst Rev* 2015; 4: 1.
- 11) Chen JM, Gao HY, Ding Y, Yuan X, Wang Q, Li Q, Jiang GH. Efficacy and safety investigation of Kuntai capsule for the add-back therapy of gonadotropin releasing hormone agonist administration to endometriosis patients: a randomized, double-blind, blank-and tibolone-controlled study. *Chin Med J* 2015; 128: 427-432.
- 12) Weng Q, Ding ZM, Lv XL, Yang DX, Song YZ, Wang FF, Ye YH, Qu F. Chinese medicinal plants for advanced endometriosis after conservative surgery: a prospective, multi-center and controlled trial. *Int J Clin Exp Med* 2015; 8: 11307.
- 13) Zhao RH, Hao ZP, Zhang Y, Lian FM, Sun WW, Liu Y, Wang R, Long L, Cheng L, Ding YF. Controlling the recurrence of pelvic endometriosis after a conservative operation: comparison between Chinese herbal medicine and western medicine. *Int J Clin Exp Med* 2013; 19: 820-825.
- 14) Zhao RH, Liu Y, Tan Y, Hao ZP, Meng QW, Wang R, Long D, Ding YF, Song DR, Xu C, Ren ZZ, Yang YH, Wang AM. Chinese medicine improves postoperative quality of life in endometriosis patients: A randomized controlled trial. *Chin J Integr Med* 2013; 19: 15-21.
- 15) Ruan JY, Zheng YX, Tian Q, Ke JY, Wang L, Du Y, Zhu ZL, Yi XF, Xu CJ. Efficacy and safety of sanjiezhentong capsules, a traditional chinese patent medicine, on long-term management of endometriosis: A randomized controlled trial. *Chin J Integr Med* 2021; 5: 15-22.
- 16) Zhao RH, Liu Y, Lu D, Wu Y, Wang XY, Li WL, Zeng C, Meng QW, Lian FM, Zhou J. Chinese medicine sequential therapy improves pregnancy outcomes after surgery for endometriosis-associated infertility: a multicenter randomized double-blind placebo parallel controlled clinical trial. *Chin J Integr Med* 2020; 26: 92-99.
- 17) Rostami S, Alyasin A, Saedi M, Nekoonam S, Khodarahmian M, Moeini A, Amidi F. Astaxanthin ameliorates inflammation, oxidative stress, and reproductive outcomes in endometriosis patients undergoing assisted reproduction: A randomized, triple-blind placebo-controlled clinical trial. *Front Endocrinol* 2023; 14: 1144323.
- 18) Amirsalari S, Behboodi Moghadam Z, Taghizadeh Z, Jafar Abadi MN, Sabaghzadeh Irani P, Goodarzi S, Ranjbar H. The Effect of Garlic Tablets on the Endometriosis-Related Pains: A Randomized Placebo-Controlled Clinical Trial. *Evid Based Complement Alternat Med* 2021; 2021: 5547058.
- 19) Ding Z, Lian F. Traditional Chinese medical herbs staged therapy in infertile women with endometriosis: a clinical study. *Int J Clin Exp Med* 2015; 8: 14085-14089.
- 20) Yang DX, Ma WG, Qu F, Ma BZ. Comparative study on the efficacy of Yiweining and Gestrinone for post-operational treatment of stage III endometriosis. *Chin J Integr Med* 2006; 12: 218-220.
- 21) Zhu S, Liu D, Huang W, Wang Q, Wang Q, Zhou L, Feng G. Post-laparoscopic oral contraceptive combined with Chinese herbal mixture in treatment of infertility and pain associated with minimal or mild endometriosis: a randomized controlled trial. *BMC Complement Altern Med* 2014; 14: 222.
- 22) Cao X, Huang X, Liu J, Ma F, Zeng Y, Chen C, Wang J, Nie G, Wang X. A randomized, double-blind, placebo-controlled trial of Chinese herbal medicine capsules for the treatment of premature ovarian insufficiency. *Menopause (New York, NY)* 2018; 25: 918-926.
- 23) Bulletti C, Coccia ME, Battistoni S, Borini A. Endometriosis and infertility. *J Assist Reprod Genet* 2010; 27: 441-447.
- 24) Nirgianakis K, Ma L, McKinnon B, Mueller MD. Recurrence Patterns after Surgery in Patients with Different Endometriosis Subtypes: A Long-Term Hospital-Based Cohort Study. *J Clin Med* 2020; 9: 496.
- 25) Maddern J, Grundy L, Castro J, and Brierley SM. Pain in Endometriosis. *Front Cell Neurosci* 2020; 14: 590823.
- 26) Fritzer N, Haas D, Oppelt P, Hornung D, Wöfler M, Ulrich U, Fischerlehner G, Sillem M, Hudelist G. More than just bad sex: sexual dysfunction and distress in patients with endometriosis. *Eur J Obstet Gynecol Reprod Biol* 2013; 169: 392-396.
- 27) Fairbanks F, Abdo CH, Baracat EC, Podgaec S. Endometriosis doubles the risk of sexual dysfunction: a cross-sectional study in a large amount of patients. *Gynecol Endocrinol* 2017; 33: 544-547.
- 28) Nnoaham KE, Hummelshoj L, Webster P, d'Hooghe T, de Cicco Nardone F, de Cicco Nardone C, Jenkinson C, Kennedy SH, Zondervan KT, Study WERFG. Impact of endometriosis on quality of life and work productivity: a multicenter study across ten countries. *Fertil Steril* 2011; 96: 366-373.e368.
- 29) Brosens I, Brosens JJ, Fusi L, Al-Sabbagh M, Kuroda K, Benagiano G. Risks of adverse preg-

- nancy outcome in endometriosis. *Fertil Steril* 2012; 98: 30-35.
- 30) Liu ZZ, Tang SJ, Chen X, Wang JY, Zhang YL. Effects of endometriosis on pregnancy outcomes in Fujian province. *Eur Rev Med Pharmacol Sci* 2023; 27: 10968-10978.
- 31) Tandoi I, Somigliana E, Riparini J, Ronzoni S, Candiani M. High rate of endometriosis recurrence in young women. *J Pediatr Adolesc Gynecol* 2011; 24: 376-379.
- 32) Zheng W, Wu J, Gu J, Weng H, Wang J, Wang T, Liang X, Cao L. Modular characteristics and mechanism of action of herbs for endometriosis treatment in Chinese medicine: a data mining and network pharmacology-based identification. *Front Pharmacol* 2020; 11: 147.
- 33) Bolin A, Whelehan P, Vernon M, Antoine K. *Human sexuality: Biological, psychological, and cultural perspectives*: Routledge; 2021.
- 34) Reed MA. *Female Sexual Dysfunction*. *Clin Plast Surg* 2022; 49: 495-504.
- 35) Pluchino N, Wenger JM, Petignat P, Tal R, Bolmont M, Taylor HS, Bianchi-Demicheli F. Sexual function in endometriosis patients and their partners: effect of the disease and consequences of treatment. *Clin Plast Surg* 2016; 22: 762-774.
- 36) La Rosa VL, De Franciscis P, Barra F, Schiattarella A, Tropea A, Tesarik J, Shah M, Kahramanoglu I, Ponta M, Ferrero S. Sexuality in women with endometriosis: a critical narrative review. *Minerva Med* 2019; 111: 79-89.
- 37) Zheng X, Wang F, Liu C, Gu J, Zhu Y, Zhou J, Qu F. Effects of Chinese Herbal Medicine on ovarian functions in the patients with endometriosis: A systematic review and meta-analysis of randomized controlled trials. *Eur J Integr Med* 2022; 51: 102125.
- 38) Li G, Liu A, Lin M, Liao S, Wen Z. Chinese herbal formula siwutang for treating primary dysmenorrhea: A systematic review and meta-analysis of randomized controlled trials. *Maturitas* 2020; 138: 26-35.
- 39) Dong P, Ling L, Hu L. Systematic review and meta-analysis of traditional Chinese medicine compound in treating infertility caused by endometriosis. *Ann Palliat Med* 2021; 10: 12631-12642.
- 40) Ried K, Stuart K. Efficacy of Traditional Chinese Herbal Medicine in the management of female infertility: a systematic review. *Complement Ther Med* 2011; 19: 319-331.
- 41) Jiang D, Li L, Zeng BY. Chapter Ten - Treatment of Chinese Herbal Medicine for Female Infertility. In: Zeng B-Y, Zhao K, editors. *Int Rev Neurobiol* 2017; 135: 233-247.
- 42) Xia JF, Inagaki Y, Zhang JF, Wang L, Song PP. Chinese medicine as complementary therapy for female infertility. *Chin J Integr Med* 2017; 23: 245-252.
- 43) Kabani Z, Ramos-Nino ME, Ramdass PV. Endometriosis and COVID-19: a systematic review and meta-analysis. *Int J Mol Sci* 2022; 23: 12951.