



## Potential of Herbal Therapy as an Alternative Approach to Improve Fertility in Reproductive Age Women: A Systematic Literature Study

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### ABSTRACT

Infertility in women of reproductive age is an increasing global health problem, with a prevalence reaching 10-15% in Indonesia. Herbal therapy has emerged as a promising alternative approach. This study aims to analyze the impact, effectiveness, optimal dosage, and types of herbs that affect ovum maturation and fertility in women of reproductive age with fertility problems. This study aims to analyze the impact, effectiveness, optimal dosage, and types of herbs that affect ovum maturation and fertility in women of reproductive age with fertility problems. This study is a systematic literature study. Data were collected from various scientific databases such as PubMed, Scopus, and Google Scholar, using keywords related to herbal therapy and female fertility. Inclusion criteria included articles in English, published in the last 10 years, and focused on herbal therapy for female fertility. Data analysis was conducted using descriptive qualitative methods. Herbal therapies have shown effectiveness in improving female fertility through various mechanisms, including hormone regulation, improving ovum quality, and improving the endometrial environment. Some herbs such as *Cuscuta chinensis*, *Angelica sinensis*, and complex herbs such as Si-Wu-Tang have shown promising results in increasing pregnancy rates and improving reproductive function. This study highlights the importance of exploring herbal therapies as potential alternatives to improve female fertility. The study findings demonstrate the effectiveness of various herbs in improving reproductive function. Further studies are needed to confirm long-term safety and optimize herbal-based treatment protocols for female infertility.

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## INTRODUCTION

Infertility in women of productive age is an increasing global health problem. Globally, the prevalence of infertility in women increased from 1366.85 per 100,000 in 1990 to 1571.35 per 100,000 in 2017, indicating an increase of 14.96% (Hui Sun et al., 2019). In Indonesia, the infertility rate is estimated to reach 10-15%, which means that there are around 4-6 million couples out of a total of 39.8 million couples of fertile age who experience infertility problems and require treatment (Safitriana, 2022; Astuti et al., 2024). The cause of infertility does not only come from female factors which contribute 40-50%, but men also contribute around 30%, the rest is caused by other factors (Safitriana, 2022).

Herbal medicine has gained significant attention in alternative medicine practices for infertility in women of reproductive age. Liuwei Dihuang Granule (LDG) herb has been shown to decrease the expression of infertility-related proteins, suggesting potential in the treatment of conditions such as KDS-YIN (Alifariki et al., 2022). The use of Chinese herbal combinations, such as Dang-Gui-Sha-Yao-San, has also been reported to improve endocrine conditions and reduce uterine muscle contractions that are important for ovulation (Hung et al., 2016). Many women prefer herbal medicine because it aligns with their personal values and beliefs, although the risk of side effects may arise from the use of certain herbs (Kaadaaga et al., 2014). Infertility in women of reproductive age is a complex health problem, influenced by various physical, psychological, and social factors. Hormonal disorders, such as polycystic ovary syndrome (PCOS) which affects 8-13% of women of reproductive age, are one of the main causes (Costello et al., 2019).

Conditions such as chronic endometritis can also contribute to difficulty conceiving, where treatment can increase spontaneous pregnancy rates (Cicinelli et al., 2017). Infertility in women of reproductive age is characterized by the inability to conceive after 12 months of regular unprotected intercourse and can be influenced by a variety of factors, including age, lifestyle, genetic abnormalities, and underlying health conditions (Borghet and Wyns, 2018; Carson and Kallen, 2021; Crawford and Steiner, 2015). Infertility has a significant negative impact on women of reproductive age, both physically and psychologically. Frequent menstrual disorders can affect women's well-being and potentially worsen infertility (Safitri, 2021). Age and ovulation disorders contribute to the incidence of infertility, so early detection is important for women (Sirait, 2024). Unhealthy lifestyles such as smoking and alcohol consumption are also associated with an increased risk of infertility (Nurbaida, 2023; JAMHARIYAH et al., 2022). Infertile women tend to have low self-acceptance, leading to infertility-related stress (Pelupessy, 2023; Windarti et al., 2019).

Previous studies have revealed the potential of herbal plants to improve female fertility. Some plants are rich in polyphenolic compounds such as isoflavones and flavonoids that are beneficial for women's reproductive health by regulating endocrine pathways, improving menopausal symptoms, and treating reproductive disorders such as PCOS, premature ovarian failure (POF), endometriosis, hyperprolactinemia, and hypothalamic dysfunction (Akbaribazm

et al., 2021). Meta-analysis showed that Chinese herbal medicine (CHM) has a 1.74 times higher probability of achieving pregnancy compared to Western medical therapy alone, and improves fertility indicators (Ried, 2015; Jiang et al., 2017). Various herbal treatments have been studied, showing benefits in increasing the number of high-quality oocytes and embryos, follicle development, ovulation, clinical pregnancy rate, blood circulation, clinical symptoms, live birth rate, and endometrial receptivity (Khan et al., 2022; Alifariki et al., 2022).

## LITERATURE REVIEW

Although there are various studies on the use of herbs for infertility in women of reproductive age, there are still research gaps that need to be filled. Most studies focus on traditional Chinese or Korean herbal medicine, while the potential of herbs from other countries, including Indonesia, has not been widely explored. In addition, existing studies are often small-scale or observational studies, so larger-scale randomized controlled clinical trials are needed to strengthen the evidence of the effectiveness and safety of herbal therapy. Therefore, this study was conducted to analyze and compile the latest scientific evidence on the impact, effectiveness, optimal dosage, and types of herbs that affect ovum maturation and fertility in women of reproductive age with fertility problems.

## METHODOLOGY

The method used in this study is a systematic literature review, where this study aims to critically and systematically review certain ideas or findings. This systematic review also uses the PRISMA guidelines.

### Search Strategy

In this study, the researcher examines the effect of herbs on infertility management. The data used is secondary data, because the researcher did not make direct observations. Data were obtained from the results of research that had been conducted by previous researchers through existing research journals. Journal search using databases with medium to high quality criteria, namely, Science Direct and Web of Science with relevant keywords such as "Women fertility", "female fertility", "female infertility", "women infertility", "Herbal", "Traditional Medicine". The articles used are research articles published in the last 10 years, namely 2014-2024.

### Study Selection

Studies are assessed based on significant and valid results related to the potential of herbal therapy in increasing the fertility of women of reproductive age. Studies that meet the criteria are studies that evaluate the effectiveness of herbal therapy in women of reproductive age with a diagnosis of infertility, either approved by a doctor or based on other standard diagnostic criteria. If there is any doubt about the validity of the research results, a discussion will be conducted in the research group. The statistical analysis used must be appropriate and strong to answer the research question regarding the effect of herbal therapy on increasing fertility. The research design used in each study must be in accordance with the research question and allow for accurate

conclusions. The discussion of the research must also be relevant to the topic of fertility and explain the results in detail, including the potential benefits of herbal therapy in increasing the chances of pregnancy. A systematic literature search was conducted to ensure the relevance of the selected studies, with limitations on manuscripts published in English and Indonesian. Studies that met the inclusion criteria and had valid statistical analysis were included, while studies using non-clinical or qualitative methods were excluded.

### Data Extraction

The extraction was carried out following a structure determined by the authors. The data taken were publication information, study design, study population, number of participants, acupressure points used, study time, measured outcomes, and main findings. The extracted data were classified based on impact, effectiveness, dosage, and type.

## RESULTS AND DISCUSSION

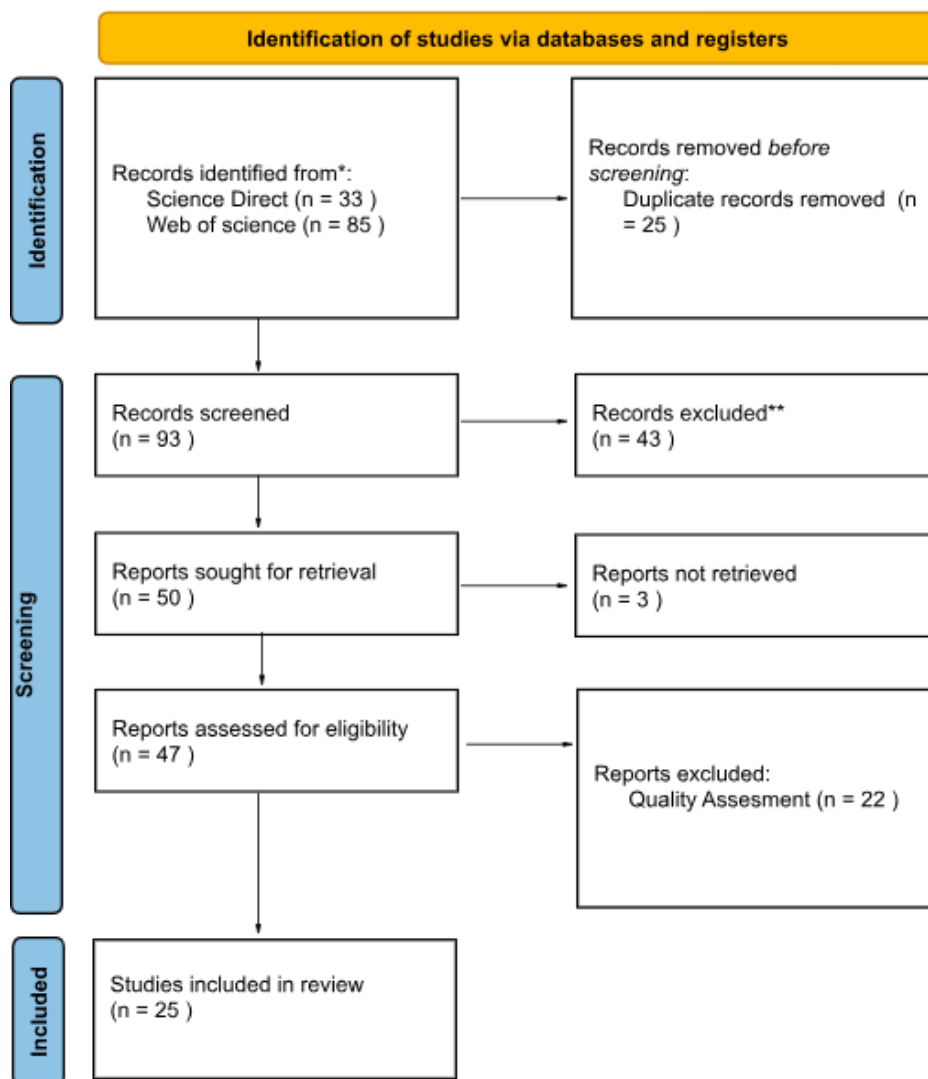


Figure 1. PRISMA diagram

The initial stage of the process involved identifying studies through searches of various databases and registers. Thirty-three records were obtained

from Science Direct, while another 85 records were obtained from Web of Science, resulting in a total of 118 records being identified. Before proceeding to the screening stage, 25 duplicate records from these 118 records were removed, leaving 93 unique records ready for further analysis.

In the screening stage, the remaining 93 records were screened for eligibility based on the inclusion and exclusion criteria established in the previous stage. Of the 93 records screened, 43 were excluded because they did not meet the inclusion and exclusion criteria. These criteria may include topic relevance, study design, population, or other factors deemed important to answering the research question. The results of the screening stage left 50 reports that were searched for further eligibility assessment.

Of the 50 reports searched, only 47 were successfully assessed for eligibility. A further 10 reports could not be retrieved because they were not downloadable. This could be due to a variety of factors, such as limited access, technical issues with the download link, or copyright restrictions that prevent full reports from being retrieved.

In the eligibility assessment stage, the 47 reports that were successfully retrieved were thoroughly evaluated against the established quality criteria. Of the 47 reports that were reviewed, 22 were deemed ineligible and were excluded from the review. These reports may have had methodological flaws, were not relevant to the research question, or did not meet other required quality standards.

The final outcome of this article selection process was a total of 25 studies that met all inclusion criteria and successfully passed each screening stage. These 25 studies will be included in a systematic review or meta-analysis for further in-depth analysis and synthesis. This number represents a small fraction of the total records identified in the initial stages, indicating the rigor of the selection process to ensure only high-quality studies are included in the review.

### **Impact of Herbal Therapy on Fertility of Women of Reproductive Age**

Table 1. Impact

No.	Group	Impact	Reference Source
1.	Improving the Quality of Ovaries and Follicles	Improve the quality of the ovaries	Choi, T. Y., Jun, J. H., Lee, H. W., Ang, L., Kim, E. S., Go, H. Y., You, S., & Lee, M.S. (2019).
		Increases ovarian growth, ovulation, and ovarian follicle maturity	Kim, K. H., Jang, S., Lee, J.A., Go, H. Y., Jung, J., Park,S., Lee, M. S., & Ko, S. G.(2018).
		Enhances the survival and development of small follicles in human ovarian tissue	Zhao, Y., Zhang, Y., Liu, D.,Feng, H., Wang, X., Su, J.,Yao, Y., Ng, E. H.

			Y., Yeung, W. S. B., Li, R. H.W.,Rodriguez-Wallberg, K. A., & Liu, K. (2022).
2.	Regulation of Reproductive Hormones	Increases levels of progesterone, 17 $\beta$ -estradiol, and dehydroepiandrosterone Increases estrogen receptor expression in the hippocampus, hypothalamus, and pituitary gland, as well as luteinizing hormone receptor expression in the ovaries.	Akbaribazm, M., Goodarzi,N., & Rahimi, M. (2021). Hung, Y. C., Kao, C. W., Lin, C. C., Liao, Y. N., Wu, B. Y.,Hung, I. L., & Hu, W. L. (2016).
		Regulates reproductive hormone disorders	Siyu, Y., Shixiao, Z., Congying, S., Xinqin, Z.,Zhen, H., & Xiaoying, W. (2024).
3.	Reduced Oxidative Stress and Inflammation	Reducing ROS (reactive oxygen species)	Akbaribazm, M., Goodarzi, N., & Rahimi, M. (2021).
		Tightly controlled ROS levels are essential for various signal transduction pathways of oocyte maturation, folliculogenesis, luteolysis, and fetoplacental development.	Bhardwaj, J. K., Panchal, H.,& Saraf, P. (2021).
		Protects reproductive cells from cell apoptosis by reducing reactive oxygen species (ROS) levels.	Hyun, J. Y., Jung, H. S., & Park, J. Y. (2024).
		Reduces ovarian inflammatory damage, oxidative stress, apoptosis and follicle atresia	Siyu, Y., Shixiao, Z., Congying, S., Xinqin, Z.,Zhen, H., & Xiaoying, W. (2024).
4.	Endometrial Environment Improvement	Increased LIF-mediated expression of integrins $\alpha$ V $\beta$ 3 and $\alpha$ V $\beta$ 5 on the surface of endometrial cells, which is associated with adhesion of trophoblastic cells to endometrial cells for blastocyst implantation.	Choi, H. J., Chung, T. W., Park, M. J.Jung, Y. S., Lee,S. O., Kim, K. J., & Ha, K. T. (2017).

		Increases blood flow to the cervical mucus and endometrium	Hyun, J. Y., Jung, H. S., & Park, J. Y. (2024).
		Increased endometrial thickness from $6.2 \pm 2.1$ mm to $9.6 \pm 1.0$ mm	Lin, J., Ma, H., Li, H., Han, J., Guo, T., Qin, Z., Jia, L., & Zhang, Y. (2022).
		Positively influences fertility indicators such as cervical mucus score and corresponding thickness of the endometrial layer	Ried, K. (2015).
5.	Increased Pregnancy Success	Increased pregnancy rates compared to the control group	Jiang, D., Li, L., & Zeng, B.Y. (2017).
		Shows the strongest relationship with pregnancy success (Si- Wu-Tang)	Liao, Y. H., Lin, J. G., Lin, C. C., Tsai, C. C., Lai, H. L., & Li, T. C. (2020).
		The pregnancy rate of the observation group was 43.3%, significantly higher than the control group ( $P < 0.05$ )	Lin, J., Ma, H., Li, H., Han, J., Guo, T., Qin, Z., Jia, L., & Zhang, Y. (2022).

Herbal therapy has been shown to improve ovarian and follicle quality. Jogyeongjongok-tang (Tiaojing Zhongyu Tang) has been reported to enhance ovarian growth, ovulation, and ovarian follicle maturity, leading to increased fertilization and embryo generation (Kim et al., 2018). In addition, curcumin can also enhance the survival and development of small follicles in human ovarian tissue, indicating its potential as an in-vitro drug to facilitate clinical treatment of infertility caused by POR (Poor Ovarian Response) and POI (Premature Ovarian Insufficiency) (Zhao et al., 2022). This improvement in ovarian and follicle quality is essential to improve pregnancy success in women with fertility disorders. Herbal therapy also plays a role in regulating reproductive hormones. Chamomile extract has been shown to increase levels of progesterone,  $17\beta$ -estradiol, and dehydroepiandrosterone (Akbaribazm et al., 2021). The well-established Luo recipe (罗氏促排卵汤) can modify serum levels of FSH, LH, and estrogen (Jiang et al., 2017).

In addition, Semen Cuscutae can increase the expression of estrogen receptors in the hippocampus, hypothalamus, and pituitary gland, and the expression of luteinizing hormone receptors in the ovaries (Hung et al., 2016). The regulation of these reproductive hormones is very important to overcome hormonal disorders that often occur in women with fertility problems. Oxidative stress and inflammation are important factors that can interfere with female

fertility. Herbal therapy has been shown to reduce reactive oxygen species (ROS) levels and maintain ROS levels under control, which are essential for various signal transduction pathways of oocyte maturation, folliculogenesis, luteolysis, and fetoplacental development (Akbaribazm et al., 2021; Bhardwaj et al., 2021). Herbal medicine can also protect reproductive cells from cell apoptosis by reducing ROS levels (Hyun et al., 2024) and reducing ovarian inflammatory damage, oxidative stress, apoptosis, and follicular atresia (Siyu et al., 2024). This reduction in oxidative stress and inflammation can create a more conducive environment for successful pregnancy. An optimal endometrial environment is essential for embryo implantation and successful pregnancy.

Herbal therapy can increase LIF-mediated expression of integrins  $\alpha V\beta 3$  and  $\alpha V\beta 5$  on the surface of endometrial cells, which are associated with trophoblastic cell adhesion to endometrial cells for blastocyst implantation (Choi et al., 2017). In addition, herbal medicine can also increase blood flow to the cervical mucus and endometrium (Hyun et al., 2024), and increase endometrial thickness from  $6.2 \pm 2.1$  mm to  $9.6 \pm 1.0$  mm (Lin et al., 2022). Fertility indicators such as cervical mucus score and appropriate endometrial thickness are also positively affected by herbal therapy (Ried, 2015). This improvement in the endometrial environment can increase the chances of successful embryo implantation and pregnancy.

The various positive effects of herbal therapy on ovum maturation and the endometrial environment ultimately aim to increase pregnancy success. The well-established Luo recipe has been shown to increase pregnancy rates compared to the control group (Jiang et al., 2017). Si-Wu-Tang, a Traditional Chinese Medicine (TCM) formula, showed the strongest association with pregnancy success (Liao et al., 2020). In one study, the pregnancy rate of the observation group receiving herbal therapy was 43.3%, significantly higher than the control group ( $P < 0.05$ ) (Lin et al., 2022). This increase in pregnancy success indicates the effectiveness of herbal therapy in overcoming fertility problems in women.

**Effectiveness of Herbal Therapy on Fertility of Women of Reproductive Age**

Table 2. Effectiveness

No.	Group	Impact	Reference Source
1.	Increased Fertility and Pregnancy	Increasing IVF success rates	Choi, T. Y., Jun, J. H., Lee, H. W., Ang, L., Kim, E. S., Go, H. Y., You, S., & Lee, M. S. (2019).
		Increase pregnancy and ovulation rates	Hung, Y. C., Kao, C. W., Lin, C. C., Liao, Y. N., Wu, B. Y., Hung, I. L., & Hu, W. L. (2016).
		Significant increase in pregnancy rate compared to placebo treatment	Hyun, J. Y., Jung, H. S., & Park, J. Y. (2024).

		The probability of achieving pregnancy with CHM therapy was 1.74 times higher than with clomiphene alone.	Jiang, D., Li, L., & Zeng, B. Y. (2017).
		The probability of achieving pregnancy with CHM therapy was 1.74 times higher than with WM therapy alone.	Ried, K. (2015).
		Increase pregnancy success (OR = 1.48; 95% CI = 1.31-1.66)	Liao, Y. H., Lin, J. G., Lin, C. C., Tsai, C. C., Lai, H.L., & Li, T. C. (2020).
		Shows positive effects on pregnancy in women with infertility..	Kim, K. H., Jang, S., Lee, J. A., Go, H. Y., Jung, J., Park, S., Lee, M. S., & Ko, S. G. (2018).
2.	Improvement of Reproductive Function	Regulates the female endocrine pathway	Akbaribazm, M., Goodarzi, N., & Rahimi, M. (2021).
		Improves menopausal symptoms	
		Improves ovarian function.	Choi, T. Y., Jun, J. H., Lee, H. W., Ang, L., Kim, E. S., Go, H. Y., You, S., & Lee, M. S. (2019).
		Improves the operation and distribution of essence, qi, blood and body fluids in the uterus.	Lin, J., Ma, H., Li, H., Han, J., Guo, T., Qin, Z., Jia, L., & Zhang, Y. (2022).
		Gives strength to the endometrium to grow	Lin, J., Ma, H., Li, H., Han, J., Guo, T., Qin, Z., Jia, L., & Zhang, Y. (2022).
		Enhancing follicle development after transplantation	Zhao, Y., Zhang, Y., Liu, D., Feng, H., Wang, X., Su, J., Yao, Y., Ng, E. H. Y., Yeung, W. S. B., Li, R. H. W., Rodriguez Wallberg, K. A., & Liu, K. (2022).
3.	Treatment of Reproductive Disorders	Treating polycystic ovary syndrome (PCOS)	Akbaribazm, M., Goodarzi, N., & Rahimi, M. (2021).
		Treating premature ovarian failure (POF)	
		Treating endometriosis	
		Treating hyperprolactinemia	
		Treating hypothalamic dysfunction	Siyu, Y., Shixiao, Z.,

		Treating hypothalamic dysfunction	Congying, S., Xinqin, Z., Zhen, H., & Xiaoying, W. (2024).
		Reducing symptoms of primary dysmenorrhea	
		Reducing PCOS symptoms	
		Reducing endometriosis symptoms	
		Reducing symptoms of luteal phase defect	
		Reduces symptoms of vulvovaginal candidiasis	
		Treating POI (Primary Ovarian Insufficiency)	
4.	Increased Hormones and Antioxidants	Increases estradiol concentration levels	Alrezaki, A., Aldawood, N., Alanazi, S., Arafah, M., Fabova, Z., Badjah, Y., Sirotkin, A. V., Alwasel, S., & Harrath, A. H. (2021). Alrezaki, A., Aldawood, N., Alanazi, S., Arafah, M., Fabova, Z., Badjah, Y., Sirotkin, A. V., Alwasel, S., & Harrath, A. H. (2021).
		Reduces infertility problems mediated by oxidative stress	Bhardwaj, J. K., Panchal, H., & Saraf, P. (2021).
5.	Reproductive Parameter Improvement	Improve cervical mucus scores	Hung, Y. C., Kao, C. W., Lin, C. C., Liao, Y. N., Wu, B. Y., Hung, I. L., & Hu, W. L. (2016).
		Reduce miscarriage rates	
6.	Specific Herbs	Shivlingi seeds as a fertility enhancer	Kadam, P. V., Bhapkar, P. V., Shaikh, S. K., Yadav, K. N., Giram, D. K., & Karanje, A. S. (2023).
		Curcumin is useful for in-vitro treatment of ovarian tissue.	Zhao, Y., Zhang, Y., Liu, D., Feng, H., Wang, X., Su, J., Yao, Y., Ng, E. H. Y., Yeung, W. S. B., Li, R. H. W., Rodriguez-Wallberg, K. A., & Liu, K. (2022).
7.	Effectiveness of Traditional Medicine	Traditional Korean Medicine (KM) is effective for treating infertility	Kim, E., Lee, H. W., Lee, M. S., Kim, N., Park, Y. H., & Choi, T. Y. (2022).

**Fertility and Pregnancy Improvement**

This group suggests that herbal medicine has significant potential to improve fertility and pregnancy rates. Several studies have shown that herbal medicine can improve IVF and ovulation success rates (Choi et al., 2019; Hung et al., 2016). Meta-analyses conducted by Ried (2015) and Jiang et al. (2017) found that Chinese Herbal Medicine (CHM) therapy had a 1.74 times higher probability of achieving pregnancy compared to conventional Western medicine or clomiphene alone. Liao et al. (2020) also reported a significant increase in pregnancy success with the use of Traditional Chinese Medicine (TCM). This effectiveness may be due to the ability of herbs to regulate the endocrine system, improve ovum quality, and improve the uterine environment. However, it should be noted that although these results are promising, further studies with more rigorous designs are needed to ensure long-term safety and efficacy.

### **Improvement of Reproductive Function**

Herbal medicine has been shown to improve various aspects of female reproductive function. Akbaribazm et al. (2021) reported that polyphenolic compounds in herbal plants can regulate women's endocrine pathways and improve menopausal symptoms. Choi et al. (2019) found that acupuncture and herbal medicine can improve ovarian function. Lin et al. (2022) explained that Chinese Herbal Medicine (CHM) can improve the operation and distribution of essence, qi, blood, and body fluids in the uterus, and provide strength to the endometrium to grow. Zhao et al. (2022) even reported that curcumin can promote follicle development after retransplantation. These effects suggest that herbs can work at multiple levels of the reproductive system, from hormonal regulation to tissue repair. However, the exact mechanisms of many of these effects still need further study for better understanding.

### **Treatment of Reproductive Disorders**

Herbal medicine has shown potential in treating various reproductive disorders. Akbaribazm et al. (2021) reported that herbs can treat polycystic ovary syndrome (PCOS), premature ovarian failure (POF), endometriosis, hyperprolactinemia, and hypothalamic dysfunction. Okafor et al. (2023) found that herbal medicine can reduce symptoms of primary dysmenorrhea, PCOS, endometriosis, luteal phase defect, and vulvovaginal candidiasis. Siyu et al. (2024) also reported that herbal medicine can treat Primary Ovarian Insufficiency (POI). The effectiveness of herbs in treating these disorders may be due to their ability to balance hormones, reduce inflammation, and improve reproductive organ function. However, it is important to note that the use of herbs for reproductive disorders should be done under the supervision of a health professional, as some herbs may have interactions with conventional drugs or unknown side effects.

### **Hormone and Antioxidant Enhancement**

Herbs have been shown to have the ability to influence hormone levels and increase the body's antioxidant capacity. Alrezaki et al. (2021) reported that high doses of sage extract can significantly increase estradiol concentration levels. Bhardwaj et al. (2021) found that natural antioxidant compounds in herbs can reduce infertility problems mediated by oxidative stress. This increase in hormones and antioxidant capacity can have positive effects on fertility by improving egg quality, increasing endometrial receptivity, and protecting reproductive cells from oxidative damage. However, it should be noted that

hormonal balance is very important in the reproductive system, and significant changes in hormone levels can have side effects. Therefore, the use of herbs for this purpose should be done with caution and under professional supervision.

### **Improvement of Reproductive Parameters**

Herbs have been shown to improve various reproductive parameters that are important for fertility. Hung et al. (2016) reported that the use of Chinese herbal medicine combined with clomiphene citrate can improve cervical mucus scores and reduce miscarriage rates. Improvement of cervical mucus scores is very important because good quality cervical mucus facilitates sperm passage and increases the chances of fertilization. Reducing miscarriage rates is also a valuable effect, especially for women who have had recurrent miscarriages. These effects may be due to the herb's ability to balance hormones, increase uterine vascularization, and strengthen the immune system. However, it should be noted that further studies are needed to understand the exact mechanisms behind these effects and to confirm the safety of long-term use.

### **Specific Herbs**

Several specific herbs have been identified to have positive effects on fertility. Kadam et al. (2023) reported that shivlingi seeds act as a fertility enhancing herb in Ayurveda. Zhao et al. (2022) found that curcumin may be useful for the in-vitro treatment of human ovarian tissue and may enhance follicle development after retransplantation. The effectiveness of these specific herbs suggests the potential for developing more targeted treatments for specific fertility problems. However, it is important to note that the effects of herbs may vary depending on the dosage, preparation method, and individual factors. Therefore, further research is needed to optimize the use of these specific herbs in the treatment of infertility.

### **Effectiveness of Traditional Medicine**

Traditional medicine, especially Traditional Korean Medicine (TCM) and Traditional Chinese Medicine (TCM), has shown effectiveness in treating infertility. Kim et al. (2022) reported that infertility therapy using KM may be a successful option for treating infertility when used alone or as an adjunct to IVF and IUI. Choi et al. (2019) also reported that KM has become very common as a primary or additional therapy for infertile patients and can increase the success rate of IVF. The effectiveness of this traditional medicine may be due to its holistic approach that not only targets symptoms but also seeks to balance the entire body system. However, it should be noted that standardization and quality control in traditional medicine can be challenging, and further research is needed to understand its mechanisms of action and optimize its use in modern infertility treatment.

## **Herbal Therapy Dosage for Fertility in Women of Reproductive Age**

Table 3. Dosage

No.	Group	Dose	Impact	Source (APA Style)
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1	Single Herbal Extract	Licorice extract 3,000 mg kg <sup>-1</sup> day <sup>-1</sup> for 6 weeks	Reduces endometrial implants in an animal model of endometriosis by inhibiting COX-2 and IL-6, strengthening the HPG axis, and reducing VEGF expression	Akbaribazm,M., Goodarzi, N., & Rahimi,M. (2021).
		High dose sage extract	Improves ovarian function by stimulating folliculogenesis and steroidogenesis.	Alrezaki, A., Aldawood, N., Alanazi, S., Arafah, M., Fabova, Z., Badjah, Y., ... & Harrath, A. H. (2021).
		Consumption of <i>E. angustifolia</i> for 10 weeks	There was no significant effect on the levels of the hormones studied or their ratios.	Jalalvand, F., Rezaei, A., Badehnoosh, B., Yaseri, M., Qorbani, M., Emaminia, F., & Shabani, M. (2021).
2	Herbal Combination with Supplements	5 mg/kg body weight nicotine and 60 mg/kg tocotrienol rich fraction (TRF)	Increased pregnancy rates to 83.3% in mice, compared to 33.3% in mice given nicotine alone	Bhardwaj, J. K., Panchal, H., & Saraf, P. (2021).
3	Chinese Herbal Blend	An average of 5.81 kinds of Chinese herbs in one recipe	No specific impacts mentioned	Hung, Y. C., Kao, C. W., Lin, C. C., Liao, Y. N., Wu, B. Y., Hung, I. L., & Hu, W. L. (2016).

		Bu Shen Huo Xue decoction (BSHXD) for 14 days, starting from the 5th day of the menstrual cycle, for 4 treatment cycles.	Increases follicle development, endometrial thickness, and serum estradiol levels in the preovulatory phase.	Jiang, D., Li, L., & Zeng, B. Y. (2017).
4	Herbal Combination with Acupuncture	Herbal medicine for 4 menstrual cycles, acupuncture and moxibustion 3 times (day 3, 8, 14 of menstrual cycle) for 4 menstrual cycles	Evaluate clinical pregnancy rate, implantation rate, ongoing pregnancy rate, and live birth rate.	Kim, S. H., Jo, J., & Kim, D. I. (2017).
5	Specific Herbal Blend	Mentha Spicata + Zingiber Officinale + Cinnamomum Zeylanicum + Citrus Sinensis: 700 mg per day for 3 months	Increase serum antioxidant levels, decrease MDA levels, decrease FBS, regular menstrual cycles, ovulation, and pregnancy	Okafor, I. A., Obi, N. P., & Ibeabuchi, K. C. (2023).
		700 mg herbal blend capsules per day for three months	No specific impacts mentioned	Zhou, K., Zhang, J., Xu, L., & Lim, C. E. D. (2021).
6	Single Compound	Curcumin 50 $\mu$ M for in-vitro culture and 100 $\mu$ M for in-vitro culture before transplantation	No specific impacts mentioned	Zhao, Y., Zhang, Y., Liu, D., Feng, H., Wang, X., Su, J., ... & Liu, K. (2022).

### Single Herbal Extracts

The use of single herbal extracts represents a more focused approach in addressing fertility issues and reproductive disorders. Licorice extract, for example, has been shown to be effective in reducing endometrial implants in an animal model of endometriosis (Akbaribazm et al., 2021). Its mechanism of action involves inhibition of COX-2 and IL-6, enhancement of the HPG axis, and reduction of VEGF expression. On the other hand, high-dose sage extract has shown potential in improving ovarian function through stimulation of folliculogenesis and steroidogenesis (Alrezaki et al., 2021). However, not all single herbal extracts show significant effects, as seen in the case of *E. angustifolia* consumption for 10 weeks which did not affect the levels of the studied hormones (Jalalvand et al., 2021). This variation in results may be due to differences in the type of herbs, dosage, and duration of treatment, as well as the specific conditions targeted.

### **Combination of Herbs with Supplements**

The combination approach of herbs with supplements shows promising potential in improving fertility. A study conducted by Bhardwaj et al. (2021) demonstrated that the combination of nicotine with tocotrienol-rich fraction (TRF) significantly increased pregnancy rates in rats. The increase from 33.3% to 83.3% indicates a strong synergistic effect between herbs and supplements. This approach may be effective in overcoming the negative effects of certain substances (in this case nicotine) on fertility. However, it should be noted that this study was conducted in an animal model, and further research is needed to confirm its efficacy and safety in humans. The combination of herbs with supplements opens up opportunities for the development of more comprehensive and personalized therapies in treating fertility issues.

### **Chinese Herbal Blends**

The use of Chinese herbal blends in the treatment of fertility and reproductive disorders demonstrates a more holistic approach. Hung et al. (2016) reported the use of an average of 5.81 types of Chinese herbs in a single prescription, indicating the complexity of the formula used. Although the specific effects were not mentioned in this study, the complexity of the formula may be intended to address multiple aspects of reproductive health simultaneously. On the other hand, Bu Shen Huo Xue decoction (BSHXD) used for 4 cycles of treatment showed more specific effects, namely increased follicle development, endometrial thickness, and serum estradiol levels in the preovulatory phase (Jiang et al., 2017). This approach reflects the philosophy of traditional Chinese medicine that emphasizes the balance and harmony of the body's systems as a whole. However, variations in composition and duration of treatment between studies suggest the need for standardization and further research to understand the mechanism of action and optimal effectiveness of this Chinese herbal mixture.

### **Combination of Herbs with Acupuncture**

The approach that combines the use of herbal medicine with acupuncture shows the integration between herbal medicine and other traditional medicine techniques. Kim et al. (2017) reported the use of herbal medicine for 4 menstrual cycles, combined with acupuncture and moxibustion performed 3 times during the menstrual cycle. This study aimed to evaluate various aspects of fertility, including clinical pregnancy rate, implantation rate, ongoing pregnancy rate, and

live birth rate. This integrated approach reflects an attempt to address fertility issues from multiple perspectives, combining the pharmacological effects of herbs with the physiological effects of acupuncture. Although specific outcomes are not mentioned in the summary provided, this approach suggests potential for a more comprehensive treatment. However, the complexity of this combined intervention also poses challenges in isolating and understanding the specific contribution of each component to the overall outcome.

### Specific Herbal Blends

The use of specific herbal blends represents a more focused approach while still utilizing the synergy between herbs. Okafor et al. (2023) reported the use of a blend of *Mentha Spicata*, *Zingiber Officinale*, *Cinnamomum Zeylanicum*, and *Citrus Sinensis* at a dose of 700 mg daily for 3 months. The reported outcomes were quite comprehensive, including increased serum antioxidant levels, decreased MDA and FBS levels, and improved menstrual cycles, ovulation, and pregnancy. These multifaceted effects suggest the potential of herbal blends in addressing multiple factors that affect fertility. On the other hand, Zhou et al. (2021) also reported the use of herbal blend capsules at the same dose (700 mg per day for three months), although the specific effects were not mentioned. This similarity in dose and duration may indicate standardization in the approach to using specific herbal blends. However, differences in the results reported also suggests the need for further research to understand the factors that influence the effectiveness of these herbal blends.

### Single Compounds

The use of single compounds such as curcumin represents a more focused and specific approach to addressing fertility issues. Zhao et al. (2022) reported the use of curcumin at a dose of 50 µM for in-vitro culture and 100 µM for in-vitro culture prior to transplantation. Although specific effects were not mentioned in the summary provided, the use of curcumin in an in-vitro context suggests its potential in the research and development of assisted reproductive techniques. Curcumin, known to have anti-inflammatory and antioxidant properties, may play a role in protecting reproductive cells from oxidative stress during the in-vitro process. This approach reflects a trend in reproductive research that seeks to optimize culture conditions to improve the success of assisted reproductive techniques. However, it should be noted that the use of single compounds such as these may have limitations in addressing the complexity of the overall fertility problem, and may be better suited as part of a more comprehensive approach.

## Types of Herbs for Fertility in Women of Reproductive Age

Table 4. Types

No	Impact	Types of Herbs	Source
1.	Controlling female reproduction through the nervous system	<i>Senecio biafrae</i> (Asteraceae)	Alrezaki, A., Aldawood, N., Alanazi, S., Arafah, M., Fabova, Z., Badjah, Y., Sirotkin,

			A. V., Alwasel, S., & Halim Harrath, A. (2021).
2.	Improving menstrual cycles in women with PCOS	Cinnamon (Cinnamomum zeylanicum)	Bhardwaj, J. K., Panchal, H., & Saraf, P. (2021).
3.	Treating female infertility	Cuscuta chinensis Lam. (Tusizi)	Hyun, J. Y., Jung, H. S., & Park, J. Y. (2024).
		Angelica gigas Nakai (Danggui)	Hyun, J. Y., Jung, H. S., & Park, J. Y. (2024).
		Cyperus rotundus L. (Xiangfuzi)	Hyun, J. Y., Jung, H. S., & Park, J. Y. (2024).
		Shivlingi Beej (biji)	Kadam, P. V., Bhapkar, P. V., Shaikh, S. K., Yadav, K. N., Giram, D. K., & Karanje, A. S. (2023).
4.	A symbol of love, happiness, wisdom and female fertility	Elaeagnus angustifolia (buah)	Jalalvand, F., Rezaei, A., Badehnoosh, B., Yaseri, M., Qorbani, M., Emaminia, F., & Shabani, M. (2021).
5.	Increases ovarian growth, ovulation, and ovarian follicle maturity	Jogyongjogok-tang (Tiaojing Zhongyu Tang)	Kim, K. H., Jang, S., Lee, J. A., Go, H. Y., Jung, J., Park, S., Lee, M. S., & Ko, S. G. (2018).
6.	Relaxes uterine muscles, balances hormone secretion and controls endometrial tissue proliferation.	Onkyung-tang (Wenjing Tang)	Kim, K. H., Jang, S., Lee, J. A., Go, H. Y., Jung, J., Park, S., Lee, M. S., & Ko, S. G. (2018).

7.	Achieving optimal health in women of childbearing age	Angelicae sinensis radix	Lei, H. L., Wei, H. J., Ho, H. Y., Liao, K. W., & Chien, L. C. (2015).
		Lycii fructus	
		Zizyphi fructu	
		Si-Wu-Tang	
8.	Increase pregnancy success	Si-Wu-Tang	Liao, Y. H., Lin, J. G., Lin, C. C., Tsai, C. C., Lai, H.L., & Li, T. C. (2020).
		Gui-Zhi-Fu-Ling-Wan	
		Jia-Wei-Xiao-Yao-San	
		Dang-Gui-Sha-Yao-San	
9.	Traditional medicine for reproductive health	Curcumin (dari <i>Curcuma longa</i> )	Zhao, Y., Zhang, Y., Liu, D., Feng, H., Wang, X., Su, J., Yao, Y., Ng, E. H. Y., Yeung, W. S. B., Li, R. H. W., Rodriguez-Wallberg, K.A., & Liu, K. (2022).

The use of traditional Asian herbs in the treatment of female infertility has been practiced for a long time and is still relevant today. Some prominent herbs in this category include *Cuscuta chinensis* Lam. (Tusizi), *Angelica gigas* Nakai (Danggui), and *Cyperus rotundus* L. (Xiangfuzi), which are considered to be the most commonly used herbs for treating female infertility (Hyun et al., 2024). *Senecio biafrae* (Asteraceae) is also known for its ability to control female reproduction through the nervous system (Alrezaki et al., 2021). Meanwhile, cinnamon (*Cinnamomum zeylanicum*) has been reported to improve menstrual cycles in women with polycystic ovary syndrome (PCOS) (Bhardwaj et al., 2021). The use of these herbs reflects the holistic approach of traditional Asian medicine towards women's reproductive health.

Several complex herbal formulations have been shown to be effective in improving fertility. *Jogyongjongok-tang* (Tiaojing Zhongyu Tang) has been

reported to promote ovarian growth, ovulation, and ovarian follicle maturation, leading to fertilization and increased embryo generation. On the other hand, Onkyung-tang (Wenjing Tang) works by relaxing uterine muscles, balancing hormone secretion, and controlling endometrial tissue proliferation (Kim et al., 2018). Other formulations such as Si-Wu-Tang, Gui-Zhi-Fu-Ling- Wan, Jia-Wei-Xiao-Yao-San, and Dang-Gui-Sha-Yao-San have strong associations with pregnancy success (Liao et al., 2020). The complexity of these formulations suggests a comprehensive approach in addressing various aspects of female fertility. Several herbs are widely used by women of childbearing age to achieve optimal health, especially in Chinese society. *Angelicae sinensis radix*, *Lycii fructus*, *Zizyphi fructu*, and *Si-Wu-Tang* fall into this category (Lei et al., 2015). The use of these herbs is not only aimed at treating infertility, but also at maintaining overall reproductive health. This approach reflects the preventive philosophy of traditional Chinese medicine, where maintaining general balance and health is considered as important as treating specific conditions.

Some herbs have symbolic value in certain cultural contexts. For example, the fruit of *Elaeagnus angustifolia* is believed to symbolize love, happiness, wisdom, and female fertility in Iranian traditions and folklore (Jalalvand et al., 2021). Similarly, Shivlingi Beej (seed) is commonly used for the treatment of female infertility in traditional Indian medicine (Kadam et al., 2023). The use of these herbs suggests that in many cultures, infertility treatment is not only seen as a medical process, but also has deep spiritual and cultural significance.

Several studies have focused on single compounds extracted from herbal plants. Curcumin, derived from *Curcuma longa*, has been used as a traditional medicine for centuries and is now the subject of modern research in the context of reproductive health (Zhao et al., 2022). This approach reflects an attempt to understand the specific mechanisms behind the effectiveness of traditional herbs and the potential development of new herbal-based medicines. Such research may pave the way for better integration between traditional and modern medicine in treating fertility issues. Although many of these herbs have a long history of use in traditional medicine, it is important to note that their effectiveness and safety in the context of modern medicine still require further research.

### **Mechanism of Action of Herbal Therapy**

Based on information from various studies mentioned in the document, several mechanisms of action of herbal therapy that affect the process of ovum maturation and fertilization can be explained as follows:

#### **Stimulation of Folliculogenesis and Steroidogenesis:**

Some herbs, such as sage extract, have been reported to improve ovarian function by stimulating folliculogenesis (formation of follicles) and steroidogenesis (production of steroid hormones). This process is very important for optimal ovum maturation. This mechanism is explained in the study of Alrezaki et al. (2021), although the specific molecular details are not mentioned in the document.

#### **Effect on the Hypothalamic-Pituitary-Gonadal (HPG) Axis:**

Licorice extract, as reported by Akbaribazm et al. (2021), can strengthen the HPG axis. This axis regulates the production and release of hormones that are

crucial for ovum maturation and ovulation. Strengthening the HPG axis can optimize the reproductive cycle and increase fertility.

**Growth Factor and Cytokine Modulation:**

Some herbs work by inhibiting or modulating certain factors. For example, licorice extract has been reported to inhibit COX-2 and IL-6, and reduce the expression of vascular endothelial growth factor (VEGF). Although these effects have been primarily studied in the context of endometriosis, modulation of these factors may influence the ovarian environment and the process of ovum maturation.

**Increased Endometrial Thickness:**

Some herbal formulas, such as Bu Shen Huo Xue decoction mentioned by Jiang et al. (2017), may increase endometrial thickness. Although this does not directly affect ovum maturation, a healthy endometrium is essential for implantation and successful pregnancy after fertilization.

**Increased Estradiol Levels:**

Herbal therapies such as Bu Shen Huo Xue decoction have also been reported to increase serum estradiol levels in the preovulatory phase. Estradiol plays an important role in follicle maturation and preparation of the endometrium for implantation.

**Antioxidant Effects:**

Some herbs, such as the mixture used in the study by Okafor et al. (2023), increase serum antioxidant levels (CAT, GPx, SOD) and decrease MDA levels. Oxidative stress can affect ovum quality, so increasing antioxidant status may support healthy ovum maturation.

**Normalization of Menstrual Cycle:**

Herbal therapies that help normalize the menstrual cycle, as reported in the PCOS study by Okafor et al. (2023), may optimize the timing of ovulation and increase the chances of fertilization.

**Effects on the Ovarian Microenvironment:**

Although not specifically described in the document, some herbal effects at the cellular and molecular levels may affect the ovarian microenvironment, which in turn may support optimal ovum maturation.

Based on the results of this systematic literature review, herbal therapy shows promising potential as an alternative approach to improve fertility in women of reproductive age. Various types of herbs and traditional formulations have shown positive effects on various aspects of reproductive health, including hormone regulation, ovum maturation, and increasing pregnancy success. The mechanisms of action of herbal therapy include stimulation of folliculogenesis and steroidogenesis, strengthening of the hypothalamic-pituitary-gonadal axis, modulation of growth factors and cytokines, and increasing endometrial thickness (Akbaribazm et al., 2021; Alrezaki et al., 2021; Jiang et al., 2017). The efficacy of herbal therapy is reflected in increased pregnancy rates, improved reproductive function, and treatment of various reproductive disorders such as PCOS and endometriosis (Ried, 2015; Liao et al., 2020; Okafor et al., 2023).

Although these results are promising, it should be noted that most of the evidence comes from observational studies or small-scale clinical trials. Further studies with more rigorous designs, including large-scale randomized controlled

clinical trials, are needed to validate these findings and ensure the long-term safety and efficacy of herbal therapies. Standardization of herbal formulations and dosages is also a challenge that needs to be addressed to improve the reproducibility of results and facilitate wider clinical application (Kim et al., 2022; Choi et al., 2019).

The diversity of herbs used, from single herbs to complex concoctions, demonstrates the flexibility of this approach in addressing various aspects of infertility (Hyun et al., 2024; Hung et al., 2016; Kim et al., 2018). However, this also poses challenges in identifying specific active components and their precise mechanisms of action. Further research is needed to unravel the interactions between the various components in complex herbal concoctions and how they synergize to improve fertility.

Integration of herbal therapies with conventional medicine is also a promising area for further exploration. Several studies have shown that the combination of herbal therapy with assisted reproductive techniques such as IVF can increase success rates (Choi et al., 2019; Hung et al., 2016). However, further research is needed to optimize this integration protocol and understand the potential interactions between herbs and conventional medicines.

Although herbal therapies show great potential, it is important to consider the safety of their use. Some herbs may have side effects or interact with other medications (Kaadaaga et al., 2014). Therefore, the use of herbal therapies to improve fertility should be carried out under the supervision of a health professional trained in complementary and alternative medicine.

Overall, this systematic literature review highlights the potential of herbal therapies as a promising approach to improving fertility in women of reproductive age. However, further research is needed to confirm the effectiveness, ensure safety, and optimize the protocol for the use of herbal therapies in infertility management. With a better understanding of the mechanisms of action and proper standardization, herbal therapies may become a valuable component in a holistic approach to improving women's reproductive health (Zhao et al., 2022; Siyu et al., 2024).

## **CONCLUSION AND RECOMMENDATION**

This systematic literature review suggests that herbal therapy has significant potential as an alternative approach to improving fertility in women of reproductive age. A variety of herbs and herbal complexes have been shown to have positive effects on various aspects of fertility, including hormone regulation, improving ovum quality, and improving the endometrial environment. The diverse mechanisms of action of herbal therapies reflect a holistic approach to reproductive health.

However, despite these promising results, several limitations remain to be considered. Variability in dosage and duration of treatment, as well as the lack of information on long-term safety, suggest the need for further research. In addition, the majority of studies have focused on traditional Chinese medicine, suggesting the need to expand research to herbal medicine systems from other cultures.

To advance this field, controlled clinical trials with larger sample sizes and more rigorous designs are needed. Future research should also focus on

optimizing treatment protocols, evaluating long-term safety, and exploring the potential integration of herbal therapies with conventional medicine.

In conclusion, although herbal therapies show promising potential to improve fertility in women of reproductive age, further research is needed to fully understand and optimize their use in clinical practice. A careful, evidence-based approach is needed when considering the use of herbal therapies for infertility, and collaboration between herbal and conventional medicine practitioners may provide a more comprehensive approach to addressing infertility issues.

Based on the results of this systematic literature study, there are several suggestions that can be put forward for the development and implementation of herbal therapy in improving the fertility of women of reproductive age. Given the effectiveness shown by various herbs such as *Cuscuta chinensis*, *Angelica sinensis*, and Si-Wu-Tang complex herbs in improving fertility, it is recommended to develop a standardized herbal therapy protocol. This protocol should include the type of herb, optimal dosage, and appropriate duration of use. This standardization is important to ensure consistency in therapy delivery and facilitate evaluation of effectiveness in clinical settings.

In addition, given the potential of herbal therapy in regulating hormones, improving ovum quality, and improving the endometrial environment, it is recommended to explore the possibility of integrating herbal therapy with conventional medicine. This integrative approach can utilize the advantages of both methods to optimize infertility treatment outcomes. However, further research is needed to ensure the safety and effectiveness of this combination of therapies. Although the results of the study indicate the effectiveness of herbal therapy, long-term studies are still needed to ensure the safety of its use.

Given the potential of herbal therapy as an alternative in treating infertility, it is recommended to develop education and training programs for health practitioners, especially midwives and obstetricians and gynecologists. The program should include knowledge about the various types of effective herbs, their mechanisms of action, appropriate dosages, and potential interactions with conventional medicines. Furthermore, based on the findings of this study, it is recommended to develop evidence-based clinical guidelines for the use of herbal therapies in the management of female infertility. These guidelines should include specific recommendations for different types of fertility problems, taking into account the effectiveness and safety of each herb or herbal combination.

By implementing these suggestions, it is hoped that the use of herbal therapies to improve female fertility can be carried out more effectively, safely, and integrated into the reproductive health care system. This can ultimately provide a wider treatment alternative for women of reproductive age who experience fertility problems, as well as open up new opportunities for more holistic and evidence-based infertility management.

## **FURTHER STUDY**

This research still has limitations so further research is still needed on this topic “Potential of Herbal Therapy as an Alternative Approach to Improve Fertility in Reproductive Age Women: A Systematic Literature Study”.

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