

# An innovative formula and preparation plan of traditional Chinese medicine for repairing endometrial injury

Zhao Bofei<sup>1,a,\*</sup>

<sup>1</sup>Hebei University of Traditional Chinese Medicine, Shijiazhuang City, Hebei Province, China, 050200

<sup>a</sup>3557609728@qq.com

\*corresponding author

**Abstract:** This article reviews the research progress on the pathological mechanism and clinical impact of endometrial injury. Endometrial injury is a common gynecological disease, with a complex pathogenesis involving multiple aspects such as inflammatory response, fibrosis formation, and abnormal angiogenesis. This article explores in detail these pathological mechanisms and analyzes the serious impact of endometrial damage on female reproductive health, including infertility, recurrent miscarriage, and menstrual abnormalities. In addition, the article also introduces commonly used diagnostic methods and treatment strategies, providing reference for clinical practice. Finally, this article looks forward to future research directions and emphasizes the necessity of conducting in-depth studies on the mechanisms of endometrial injury and developing new treatment methods.

**Keywords:** Endometrial injury; Pathological mechanism; sterility; diagnosis; Treatment Plan

Endometrial injury (also known as Asherman syndrome) is one of the main causes of intrauterine adhesions, which refers to the partial or complete occlusion of the cervical canal or uterine cavity secondary to damage to the basal layer of the endometrium. Although Asherman syndrome is widely defined as adhesions in the uterine cavity after pregnancy, a more accurate definition would be complete closure of the uterine cavity accompanied by amenorrhea. If describing the varying degrees of adhesions in the uterine cavity that occur after trauma, including complete occlusion of the uterine cavity or cervical canal wall, "intrauterine adhesions" would be more appropriate. IUA cannot self repair and often leads to reduced menstrual flow or amenorrhea, periodic abdominal pain, miscarriage, or infertility. With the liberalization of China's family planning policy and the popularization of uterine cavity surgery, the incidence rate of IUA has increased year by year, and has gradually become the primary cause of secondary infertility. In recent years, with the increase of medical behaviors such as induced abortion and uterine cavity operation, the incidence rate of endometrial injury is on the rise, which has aroused widespread concern. Endometrial injury not only leads to menstrual abnormalities, but may also cause serious consequences such as infertility and recurrent miscarriage, seriously affecting the quality of life and fertility of patients.

It is crucial to conduct in-depth research on the pathological mechanisms of endometrial injury in order to develop effective prevention and treatment strategies. This article aims to systematically elucidate the pathological mechanism, clinical impact, diagnosis, and treatment methods of endometrial injury, providing comprehensive references for clinical doctors and researchers, as well as ideas for

future research directions.

### **1. Pathological mechanism of endometrial injury**

The pathological mechanism of endometrial injury is complex and involves multiple aspects. Firstly, inflammatory response plays a crucial role in endometrial injury. When the endometrium is traumatized or infected, it can trigger a local inflammatory response, releasing a large amount of inflammatory factors such as interleukin-6 (IL-6), tumor necrosis factor alpha (TNF -  $\alpha$ ), etc. These inflammatory factors not only exacerbate tissue damage, but also affect the repair process of the endometrium.

Secondly, fibrosis formation is another important characteristic of endometrial injury. During the process of injury repair, excessive fibrous tissue proliferation can lead to the formation of endometrial scars, disrupting the normal structure of the endometrium. This fibrosis process is mainly regulated by the transforming growth factor -  $\beta$  (TGF -  $\beta$ ) signaling pathway, which, when activated, can promote fibroblast proliferation and extracellular matrix deposition.

Research has shown that congenital uterine abnormalities and acquired uterine injury can cause endometrial abnormalities such as intrauterine adhesions (IUA) and endometrial thinning, such as congenital uterine malformations, previous cesarean sections, manual placental removal, myomectomy, miscarriage curettage, intrauterine device placement, endometrial infection, and scar formation. These can affect uterine dilation and embryo implantation, ultimately leading to gynecological complications such as endometrial infertility, recurrent miscarriage, menstrual abnormalities, and placental implantation. Intrauterine procedures are the most common factor causing damage to the endometrium, resulting in the opening of the endometrial sinusoids and exposure to the open environment after endometrial detachment. Intrauterine procedures carry external and vaginal microorganisms up to the uterine cavity, accelerating their growth in the oozing blood. The inflammatory stimulation and absorption of blood clots produced by these procedures can further cause complications such as tubal obstruction, intrauterine adhesions, endometriosis, and ultimately lead to infertility. According to WHO statistics, there are 36 to 53 million cases of pregnancy termination worldwide each year, with approximately 90% occurring in the early stages of pregnancy. In the past 20 years, the age of first sexual intercourse among adolescents has advanced, while the age of marriage and childbirth has shifted, resulting in the majority of adolescents experiencing unintended pregnancies ending in induced abortion. Among women undergoing abortion surgery, 47.5% are under the age of 25, with 49.7% having never given birth. In addition, 55.9% of women are not undergoing abortion surgery for the first time, and 45% of women have repeated abortions with intervals of only six months to one and a half years. Even 13.5% of women have undergone three or more abortions. Repeated induced abortions increase the risk of endometrial damage. A study has shown that the incidence of intrauterine adhesions after induced abortion in early pregnancy is about 6.3%. If the number of intrauterine operations is  $\geq 3$ , the incidence of moderate to severe intrauterine adhesions is as high as 80.6%. If the history of intrauterine adhesions is  $\geq 2$  years, the incidence of severe adhesions is 56.3%. The incidence of complications such as endometrial thinning and chronic endometritis caused by induced abortion has been increasing year by year.

In addition, microbial infections are considered the most common cause of chronic endometritis, with the most common bacteria causing chronic endometritis being Enterococcus, Enterobacteriaceae, Streptococcus, Staphylococcus, Gardnerella vaginalis, Mycoplasma, and other sexually transmitted infections such as Mycoplasma urealyticum, Chlamydia trachomatis, and Neisseria gonorrhoeae. And

among the pathogens that cause endometritis, many are opportunistic pathogens that reside in the vagina. When a woman's own immune system is weakened or the cleanliness of her intimate area is not maintained, the endometrium exposed to the bacteria is very susceptible to infection, especially during menstruation, when coagulated menstrual blood is a good culture medium for the bacteria. The mechanism of microbial infection leading to endometritis mentioned above, as well as pathological abnormalities of the endometrium, are also considered as one of the causes of endometritis, including pathological manifestations such as endometrial polyps, submucosal uterine fibroids, and endometrial hyperplasia. This sterile microenvironment change can also lead to population and functional disorders of immune cells in the endometrium, causing plasma cell infiltration. Aseptic inflammation caused by local pathological abnormalities in the endometrium alters the distribution of local immune cells in the endometrium, including an increase in the number of plasma cells in B lymphocytes and an imbalance in the ratio of Th2/Th1 cells and Th17/Treg cells in T lymphocytes. The proportion of Th1 cells increases, and the inflammatory response is activated, leading to miscarriage. More and more evidence suggests from different perspectives that abnormal cytokines, growth factors, and inflammatory factors in the endometrium affect its receptivity, leading to embryo implantation failure. Furthermore, many studies have shown that pathological factors such as the microbiome play an important role in the human reproductive system, particularly viral infections. The ability to conceive normally is closely related to the anatomy and function of the reproductive tract. These microorganisms have a certain negative impact on human reproductive function. Viral infection can cause inflammation of the reproductive tract, which can hinder the production, transportation, and binding of sperm and eggs, leading to infertility. In addition, viruses can also invade fetal tissues such as the placenta, affecting pregnancy and fetal development, leading to miscarriage or premature birth. Moreover, due to different physiological and anatomical factors, women are more susceptible to the invasion of viral microorganisms than men, so some studies suggest that viral microorganisms may be a possible environmental factor for human infertility. A study has found that viral infection is the main cause of idiopathic unexplained infertility. The correlation between viral infection and infertility has been reported in many studies, such as human papillomavirus (HPV), herpes simplex virus (HSV), human immunodeficiency virus (HIV), hepatitis B virus (HBV), hepatitis C virus (HCV), cytomegalovirus (CMV), and Zika virus (ZIKV).

## **2. Clinical impact of endometrial injury**

Endometrial injury has serious clinical impacts on female reproductive health. Firstly, it is one of the important causes of infertility. Damaged endometrium can affect embryo implantation, leading to infertility or repeated implantation failures. Research has shown that the incidence of infertility in patients with endometrial injury is significantly higher than that in the normal population.

Among them, there is another direct factor related to infertility - endometrial receptivity (ER), which refers to the ability of the endometrium to accept implanted embryos, and is an important evaluation indicator for assessing its role as an embryo's "biological receptor". Among them, the evaluation indicators include morphology, molecular biology, and proteomics. Although there are many methods to evaluate endometrial receptivity, endometrial thickness (ET) can be obtained through non-invasive ultrasound examination, which is the most commonly used evaluation index in clinical practice due to its convenient and effective characteristics. Successful embryo implantation requires two conditions: a well-developed embryo and a well tolerated endometrium. For humans, the period when embryos are most likely to implant is the luteal phase of the menstrual cycle (19-23 days of

menstruation), commonly known as the window of implantation (WOI). Embryo implantation is a complex process involving many hormones, growth factors, and cytokines. About 1/3 to 2/3 of human embryos ultimately fail implantation due to abnormal uterine receptivity. Although assisted reproductive technology (ART) has solved many problems leading to infertility, implantation failure caused by poor endometrial receptivity remains an important factor determining the success rate of ART. Numerous studies have confirmed that damaged endometrium is associated with low pregnancy rates, with a thickness of 6 mm required for successful embryo implantation.

Returning to endometrial injury, secondly, endometrial injury is closely related to recurrent miscarriage. The decreased receptivity and structural abnormalities of the endometrium increase the risk of miscarriage. Clinical observations have found that patients with a history of intrauterine procedures have a significantly increased probability of recurrent miscarriage, which is closely related to endometrial damage.

In addition, endometrial damage can also lead to menstrual abnormalities, such as oligomenorrhea and amenorrhea. This is due to the impaired regenerative ability of the endometrium, which cannot complete normal periodic changes. Severe endometrial damage may even lead to intrauterine adhesions, further exacerbating symptoms of menstrual abnormalities.

### **3. Diagnosis and Current Treatment Strategies for Endometrial Injury**

#### ***3.1 Diagnosis of endometrial injury***

This paragraph will discuss the diagnosis of such diseases from both traditional and modern medicine perspectives.

##### *3.1.1 Medical Imaging Indicators*

Endometrial thickness is an important indicator reflecting the functional status of the endometrium, and transvaginal ultrasound is a simple non-invasive examination method for evaluating endometrial thickness. Under normal conditions, the thickness of the endometrium is 1-4mm in the early stage of proliferation, >4-8mm in the middle stage of proliferation, >8-14mm in the late stage of proliferation, and 7-14mm in the secretory stage. Research has shown that achieving a thickness of 7mm in the late proliferative stage of the endometrium is a prerequisite for embryo implantation. For patients with late stage proliferative endometrial thickness less than 7mm, the menstrual recovery and pregnancy rate after hysteroscopic intrauterine adhesion separation surgery are significantly lower than those with postoperative endometrial thickness greater than 7mm.

##### *3.1.2 Traditional Chinese Medicine Diagnosis*

Referring to the Guiding Principles for Clinical Research of Traditional Chinese Medicine New Drugs, as well as the Seventh Edition of Traditional Chinese Medicine Gynecology and the Sixth Edition of Traditional Chinese Medicine Diagnosis, relevant diagnostic criteria have been developed, as shown in the appendix. Main symptoms: After uterine cavity surgery, the amount of menstrual fluid gradually decreases, or it can be cleared by intravenous drip, or even it cannot be stopped, with purple color and blood clots. Secondary symptoms: lower abdominal distension and pain, lumbosacral soreness, insomnia and forgetfulness, dizziness and tinnitus, premenstrual breast swelling, fatigue and weakness, dull or yellowish complexion, dark or black eye sockets or saddle spots. Tongue pulse: The tongue texture is light or pale red, or there are fatigue spots and obsession points, and the pulse is thin or damp. Individuals with the above primary and secondary symptoms can be diagnosed with the disease. In traditional Chinese medicine, uterine cavity adhesions belong to categories such as

"abdominal pain in women", "insufficient menstruation", and "infertility". The operation of uterine cavity surgery damages the meridians of the uterus, blocks the meridians, causes local blood and qi circulation to be obstructed, and leads to qi stagnation and blood fatigue. Over time, it accumulates toxins and turns into heat. In addition, improper nursing in the later stage leads to qi and blood deficiency and invasion of evil toxins, which can cause damage to the uterus and cause stagnation in the Chong and Ren meridians. Blood fatigue and qi stagnation are mutually harmful, leading to poor blood and qi circulation in the Chong and Ren meridians. Over time, the imbalance of qi and blood in the organs and meridians can damage the kidney essence and kidney qi, resulting in this disease. In addition, patients are generally physically weak, with spleen and kidney deficiency being the main symptoms. Therefore, in terms of treatment, it is advisable to strengthen the spleen and kidneys, regulate qi and relieve fatigue.

### ***3.2 Existing treatment options for endometrial damage related diseases***

Previous treatments for promoting endometrial growth include high-dose estrogen and aspirin. There is still significant controversy over the dosage of hormone drugs used, and caution should be taken against the risks caused by long-term systemic use of high-dose hormones. Estrogen can promote the growth of the endometrium, while excessive growth can also induce the occurrence of endometrial cancer. The breast is another target organ of estrogen. The increase of estrogen content in serum stimulates the hyperplasia of breast tissue, which may lead to hyperplasia of breast, which is manifested as an increase in the incidence of breast nodules and breast cancer. In addition, estrogen is metabolized in the liver, and long-term use of estrogen can cause damage to liver function. Therefore, in clinical practice, regular monitoring of liver function is necessary when taking estrogen orally, which can greatly harm the physical and mental health of patients. Aspirin is a commonly used anti-inflammatory drug, but as a type of nonsteroidal anti-inflammatory drug, aspirin can cause damage to the gastric mucosa. Some patients may experience stomach pain when taking aspirin orally, and in severe cases, gastric ulcers and bleeding may occur. Aspirin has an anti platelet aggregation effect, and long-term use of this drug may increase the risk of bleeding and complications such as decreased coagulation function in patients.

On the other hand, the drugs commonly used in clinical practice to treat endometritis are mostly antibiotics, and the abuse of antibiotics can cause certain bacterial communities in the body to develop resistance, disrupt the normal bacterial environment in the body, lead to bacterial imbalance, and decrease the patient's physical condition. Therefore, higher specification antibiotics must be selected for further treatment to achieve therapeutic effects, leading to a vicious cycle. In severe cases, it can cause multiple infections in the body and even lead to death. Antibiotics are mostly metabolized through the liver and kidneys, and have a certain degree of liver and kidney toxicity. Some antibiotics have a long half-life in the body, so it is necessary to wait for a long time after taking medication before preparing for pregnancy. We know that the diagnosis of endometrial injury mainly relies on imaging examinations and hysteroscopy. Ultrasound examination is the most commonly used non-invasive diagnostic method, which can evaluate the thickness and morphology of the endometrium and has relatively high safety; Three dimensional ultrasound and uterine cavity acoustic contrast can more accurately display the morphology of the uterine cavity and the condition of the endometrium. Hysteroscopy can more accurately detect whether the endometrium is damaged or the degree of damage, and can directly observe the internal situation of the uterine cavity. The treatment method for moderate to severe intrauterine adhesions is hysteroscopic adhesiolysis (TCRA) and postoperative anti adhesion materials. The influencing factors of hysteroscopic surgery include the location and degree of

adhesions. Data shows that patients with severe intrauterine adhesions have a recurrence rate of up to 20% -62.5% after undergoing intrauterine adhesion separation surgery. For patients, the risks associated with surgery are more serious than those associated with medication, commonly including anesthesia accidents and bleeding at the surgical site, especially in the surgical field. Bleeding in the surgical field is a common complication during hysteroscopic surgery, especially in cases of severe endometriosis or severe pelvic adhesions, which may result in postoperative bleeding in the surgical field. In addition, there is still a risk of the condition not improving or even worsening after surgery. If the operator operates improperly, it may lead to the recurrence of intrauterine adhesions in the patient. Therefore, how to prevent various postoperative adhesion recurrence is an urgent problem that needs to be solved

In terms of treatment, the current approach mainly combines drug therapy with surgical treatment. Drug therapy includes estrogen, growth factors, etc., aimed at promoting endometrial regeneration and repair. Surgical treatment mainly involves separating adhesions and removing scars through hysteroscopy to restore the normal shape of the uterine cavity. In recent years, new treatment methods such as stem cell therapy and platelet rich plasma (PRP) have also been explored, providing new ideas for the treatment of endometrial injury.

#### **4. Uterus gel**

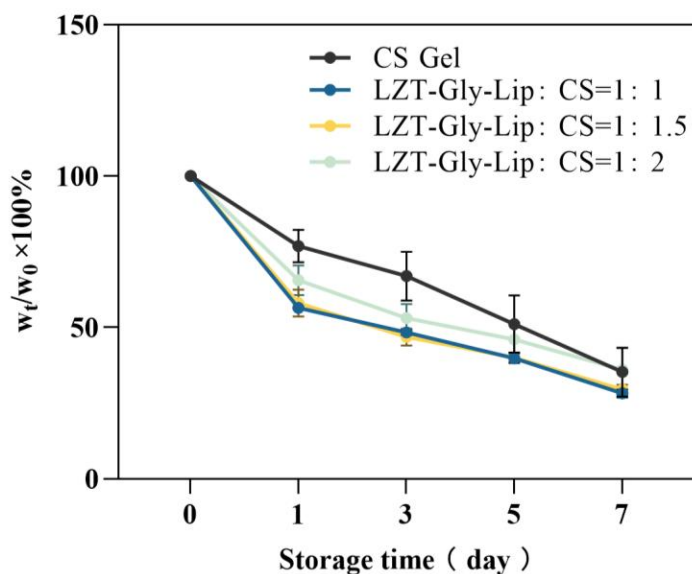
##### ***4.1 Aqueous gel matrix***

The methods that can be used clinically to prevent the recurrence of intrauterine adhesions include intrauterine devices, intrauterine adaptive balloons, rubber catheters, estrogen, anti-inflammatory/reparative drugs, growth factors, and amniotic membrane. Intrauterine devices and intrauterine adaptive balloons can reduce the recurrence rate of intrauterine adhesions to some extent, but there is no significant difference in reproductive outcomes. Strictly speaking, the formation of more severe connective tissue and scars is irreversible. The above-mentioned methods for preventing intrauterine adhesions are difficult to achieve biodegradability, non toxicity, appropriate residence time in the body, promotion of endometrial repair, and glandular regeneration as a whole. It is still necessary to find multiple effective methods to promote endometrial repair and better prevent the recurrence of intrauterine adhesions. The key to prevent recurrence of intrauterine adhesions is to reconstruct the endometrium with normal functions. The latest breakthrough in the treatment of recurrent intrauterine adhesions at home and abroad is to use biodegradable materials to prepare hydrogels to prevent recurrence of adhesions, mainly including physical barrier hydrogels and carrying hydrogels (endometrial regeneration drugs, growth factors, stem cells, etc.). The advantage is that it can promote endometrial regeneration and reduce contact with adherent tissues, including promoting cell regeneration and proliferation, reducing fibrosis and reducing inflammation recurrence.

Hydrogels are three-dimensional porous reticular polymers obtained by crosslinking hydrophilic polymers, which are considered to be the most potential materials to replace extracellular matrix. In addition to highly similar structure to extracellular matrix, hydrogels can also form high-performance artificial extracellular matrix while continuously modifying and processing. Due to the existence of hydrophilic groups (such as carboxyl, hydroxyl, etc.), the hydrogel has a certain swelling property. Some studies have shown that the hydrogel can absorb thousands of times of its dry mass of water, and keep its structure stable without being damaged, with excellent drug loading capacity. At the same time, hydrogels have good biocompatibility and meet the basic requirements of tissue engineering. In recent years, they have been widely used in bone repair, cardiovascular stents and skin dressings. The excellent performance of the hydrogel for endometrial repair can support it to carry estrogen, active

substances, drugs and stem cells, and transport therapeutic substances to the interior of the uterus; Its special three-dimensional structure can isolate the wound surface while avoiding adhesion recurrence, and as a carrier, it can better promote endometrial repair and reconstruction of normal functional morphology.

The hydrogel has good stability at 4 °C, which can better meet the requirements of drug storage, transportation and use. At the same time, it is also important to have a certain moisture retention at room temperature, because the water loss and weight loss caused by water evaporation at room temperature will lead to poor drug delivery effect, limiting the application of hydrogel



As shown in the figure, for the weight change of the prepared hydrogel within 7 days, the weight-loss test results show that the higher the concentration of CS, the better the moisturizing performance of the hydrogel. Among them, the moisturizing effect of water gel increases with the increase of CS content within 5 days. On the first day, the weight loss rate of hydrogel was the highest. The weight loss rate of blank CS hydrogel patch was  $23.1 \pm 4.4\%$ , that of LYT GlyLip: CS was 1: 2 was  $34.4 \pm 4.0\%$ , and that of LYT Gly Lip: CS was 1: 1 and 1.5 was  $43.5 \pm 0.3\%$  and  $42.0 \pm 3.6\%$ , respectively. Within 7 days, the overall weight loss rate of the hydrogel decreased, and on the 7th day, the weight loss rate of the hydrogel with LYT Gly Lip: CS of 1: 2 was basically the same as that of the white C hydrogel patch, which was  $64.0 \pm 5.8\%$  and  $64.7 \pm 6.6\%$ , respectively, lower than that of LYT Gly Lip: The weight loss rate of hydrogel with CS of 1:1 and 1.5 is  $71.8 \pm 1.0\%$  and  $70.5 \pm 1.3\%$  respectively.

#### 4.2 gel mainly composed of Chinese herbal extracts

In this paper, a traditional Chinese medicine gel matrix scheme was proposed for endometrium injury such diseases: *Salvia miltiorrhiza*, *Chuanxiong*, *Rehmannia glutinosa*, *Paeonia lactiflora*, *Angelica sinensis*, *Patrinia villosa*, *Spatholobus spatholobi*, *Zelan*.

Among them, *Danshen*, as an active medicine, may improve the permeability of the endometrium and promote the repair process by activating blood vessels; *Chuanxiong*, as a live grass or plant medicine, may have a relaxing and contractionary effect on the muscles, helping to repair the endometrium; *Rehmannia glutinosa*, *Paeonia lactiflora*, and *Angelica sinensis*: as active medicines, these two may provide a relaxing or dilating effect, promoting repair.

By analyzing and comparing multiple drug formulations on target analysis platforms such as TCMSP, it was ultimately confirmed that this formulation scheme has a wide range of applicability and the best target matching effect.

#### *4.2.1 Extraction of active ingredients from traditional Chinese medicine*

There are several common methods for extracting traditional Chinese medicine ingredients, including: 1. Biological enzymatic extraction: using enzymatic reactions to destroy the cell walls and interstitium of traditional Chinese medicine, reducing mass transfer resistance. Gentle, efficient, specific, and simple. Can improve the extraction rate and antioxidant activity of various active ingredients; Some microbial fermentation techniques can promote the release and transformation of components. 2. Ultra high pressure extraction: Using high-pressure fluid to act on a mixture of traditional Chinese medicine, causing cell rupture and releasing effective ingredients. Can protect components that are sensitive to heat, unstable, and prone to oxidation. Improve efficiency and quality, save energy and solvents, and reduce pollution. 3. Boiling and extraction: Boil crude Chinese medicine powder in water to extract effective ingredients. Suitable for water-soluble and moisture stable medicinal herbs. It is one of the commonly used methods for preparing various pharmaceuticals. 4. Ultrasonic extraction: Ultrasonic waves are used to generate cavitation, mechanical and thermal effects in liquids, destroy cell walls, and release and dissolve active ingredients. Short time, high efficiency, and low temperature. It has good effects on various compounds. 5. Supercritical fluid extraction: Separate the desired components from liquid or solid materials using supercritical fluid. Efficient, fast, and powerful penetration. Can be extracted and distilled simultaneously, and can be directly analyzed and detected

This article uses boiling and ethanol soaking extraction methods to prepare traditional Chinese medicine extract extracts. Mix the Chinese herbal extracts and additives with the blank gel in proper proportion, add sodium hydroxide solution drop by drop, measure the pH value, stop dropping until the pH of the gel is about 7, and record the amount of sodium hydroxide added; Then add 1,2-propanediol drop by drop, adjust the viscosity of gel, record the amount of 1,2-propanediol added, and finally prepare the traditional Chinese medicine gel.

First, the salvia miltiorrhiza, ligusticum chuanxiong, prepared rehmannia root, white peony root, angelica, patrinia, spatholobus suberectus, and eupatorium eupatorium are mixed according to the prescription ratio (using the equipment: a hydrogel raw material proportioning device for repairing endometrial damage), and crushed into powder with a crusher. Next, the formula was extracted using three methods: decoction extraction, ultrasonic extraction, and ultra-high pressure extraction. The specific extraction methods are as follows:

(1) Boiling and extraction: Dissolve 50g of medicinal powder in 1000mL of water, boil for 2 hours, and stir continuously. Filter the boiled liquid using a 0.45  $\mu$  m aqueous filter membrane to obtain the decoction extract.

(2) Ultrasonic extraction: Dissolve 50g of drug powder in 500mL of 75% ethanol solution, and sonicate at 500w for 1 hour in an 80 °C water bath. Filter the extracted liquid using a 0.45  $\mu$  m organic filter membrane, and blend the filter residue into 500mL of water. sonicate at 500w for 1 hour in an 80 °C water bath. Filter the extracted liquid using a 0.45  $\mu$  m aqueous filter membrane, collect the filtrate twice, and mix to obtain the ultrasonic extraction solution.

(3) Ultra high pressure extraction: Dissolve 50g of medicinal powder in 500mL of 75% ethanol



solution, extract for 3 minutes under a pressure of 300MPa and cycle three times. Filter the extracted liquid using a 0.45 μ m organic filter membrane, and mix the filter residue into 500L of water for extraction under the same conditions. Filter the extracted liquid using a 0.45 μ m aqueous filter membrane, collect the filtrate twice, and mix to obtain the ultra-high pressure extraction solution.

#### 4.2.2 Preparation scheme of water-based gel matrix

Refer to Kangduo Preparation of recombinant collagen I hydrogel and its application in skin wound healing In the third chapter, the preparation scheme of type I collagen hydrogel is combined with the resources of our school to prepare the hydrogel.

### 5. Conclusion and Prospect

With the increasing attention paid by the country to fertility related issues, the requirements for the fertility of women of childbearing age have also been further enhanced. How to provide better treatment plans and methods for patients with endometrial injury, thereby improving the receptivity of the endometrium, restoring endometrial function, and increasing embryo implantation rate, clinical pregnancy rate, and improving pregnancy has become an urgent task. However, the current treatment measures have poor efficacy, and Chinese medicine has broad development prospects in endometrial injury repair. Through preliminary exploration, it was found that traditional Chinese medicine is effective in repairing the endometrium. Based on this, relevant research on the effect of effective ingredients in traditional Chinese medicine on endometrial repair was conducted. In summary, this article provides a treatment plan and traditional Chinese medicine formula, and confirms its feasibility, but its mechanism of action still needs further research. In future research, the mechanism of action can be further explored through in vivo experiments, or the fertility of the experimental model can be evaluated through long-term experimental cycles. It is hoped that future experiments can provide more comprehensive research supplements for the clinical application of the proposed scheme.

### References

- [1] Zhu Yingying *Effect of cross-linked sodium hyaluronate gel in uterine cavity combined with oral estrogen and progesterone on prevention of re adhesion after hysteroscopic separation of intrauterine adhesion* [J]. *Clinical Rational Drug Use*, 2025, 18 (08): 95-97. DOI: 10.15887/j.cnki.13-1389/r.2025.08.027
- [2] Zhang Guanwen, Zhang Wanlin, Wang Mingyi, etc *Physiological repair mechanism of endometrium* [J]. *Advances in modern obstetrics and gynecology*, 2025,34 (02): 150-154. DOI: 10.13283/j.cnki.xdfckjz.2025.02.009
- [3] Yang Yi *Analysis of the application of estradiol tablets/estradiol didroxyprogesterone tablets combined with estradiol gel in promoting endometrial repair in high-risk induced abortion patients* [J]. *Heilongjiang Medical Journal*, 2025, 38 (01): 149-151. DOI: 10.14035/j.cnki.hljyy.2025.01.051
- [4] Wu Yuanfang *The effect of sodium hyaluronate gel on the morphology, menstruation and re adhesion of uterine cavity in patients with intrauterine adhesion after hysteroscopy* [J]. *Heilongjiang Medical Journal*, 2025, 38 (01): 141-143. DOI: 10.14035/j.cnki.hljyy.2025.01.048
- [5] Hong Guizhen, Mo Guihua, Wang Chunling, etc *Application of uterine balloon combined with cross-linked sodium hyaluronate gel for uterine cavity in patients after cold knife separation of uterine cavity adhesion* [J]. *Chinese Medical Journal*, 2025, 60 (02): 168-171
- [6] Sun Yuchen, Shi Yaxin, Shi Wei *Research progress on the treatment of endometrial dysfunction with blood derived stem cells combined with kidney tonifying and blood activating traditional Chinese medicine* [J/OL]. *Chinese General Practice*, 1-8 [March 26, 2025] <http://kns.cnki.net/kcms/detail/13.1222.R.20241231.1455.022.html>.
- [7] Lin Lijun, Wu Guohua, Peng Changsheng, etc *Application of biomaterial based hydrogel delivery system in intrauterine adhesion* [J]. *China Family Planning and Obstetrics and Gynecology*, 2024,16 (12): 45-49
- [8] Li Jiaming, Yang Chao, Ma Li *Strategies for preventing and treating endometrial injury* [J]. *Basic Medicine and Clinical Medicine*, 2024, 44 (09): 1308-1313. DOI: 10.16352/j.issn.

1001-6325.2024.09.1308

- [9] Chen Min Construction of Endometrial Disease Prediction Model and Study on Traditional Chinese Medicine Diagnosis and Treatment Rules [D]. Yangzhou University, 2024. DOI: 10.27441/d.cnki.gyzdu.2024.001936
- [10] Ding Ze, Zhang Yaofeng, Ma Bei, et al. Study on the anti-inflammatory effect of 1 drug loaded water gel on bovine endometrial epithelial cells [J]. Modern Animal Science and Technology, 2024, (02):30-32.DOI:10.19369/j.cnki.2095-9737.2024.02.009.
- [11] Wang Shaoqing Study on the effect of kidney tonifying and blood activating formula on endometrial repair in patients with intrauterine adhesions based on Wnt/ $\beta$  - catenin signaling pathway [D]. Hunan University of Traditional Chinese Medicine, 2023. DOI: 10.27138/d.cnki.ghuzc.2023.000494
- [12] Kangduo Preparation of recombinant collagen I hydrogel and its application in skin wound healing [D]. South China University of Technology, 2023. DOI: 10.27151/d.cnki.ghnlu.2023.005405
- [13] Han Xiao Design and performance study of "Liuzi Decoction" compound Chinese medicine liposome gel patch [D]. South China University of Technology, 2023. DOI: 10.27151/d.cnki.ghnlu.2023.003099
- [14] Li Yue Study on the repair of endometrial damage by hydrogel loaded with hyperoside nanoparticles [D]. Guangzhou University of Traditional Chinese Medicine, 2022. DOI: 10.27044/d.cnki.ggzdu.2022.000248
- [15] Huang Huihuan Effect of estradiol gel on promoting endometrial repair and preventing uterine adhesion after induced abortion [J]. China Minkang Medical Journal, 2021,33 (23): 57-59
- [16] Liu Qingwu, He Xiujuan, Zhang Jinchao, etc Research progress of extracellular matrix in skin tissue wound repair [J]. Journal of Medical Research, 2019, 48 (09): 21-24
- [17] Chen Jia, Liu Qingwu, He Xiujuan, etc Research progress of extracellular matrix in skin wound repair [J]. Chinese Journal of Clinical Pharmacology and Therapeutics, 2019, 24 (06): 716-720
- [18] Liu Liwen Clinical study on the effect of traditional Chinese medicine nourishing kidney and nourishing membrane formula on the repair of intrauterine adhesions and pregnancy outcomes [D]. Hunan University of Traditional Chinese Medicine, 2015
- [19] Xiong Feng Research and development of epistaxis hemostasis gel [D]. Changchun University of Traditional Chinese Medicine, 2010