

# Research on Pharmacological Action of Commonly Used Topical Drugs for Vaginitis

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**Abstract:** The incidence of vaginitis is high, and it is easy to relapse. The main clinical manifestations are leukorrhagia, vulva and vaginal itching. The treatment method and drug selection are especially important. In this paper, the relevant literature reports of topical drugs for treating vaginitis in recent years were searched, the pharmacological effects of commonly used western medicine, Chinese medicine and Chinese patent medicine were summarized, and the existing shortcomings were pointed out. It is helpful to provide the basis for clinical research of external drugs for vaginitis in the future.

**Keywords:** Vaginitis, Topical Medications, Pharmacological Action, Research Progress

## 1. Introduction

Vaginitis is a common gynecological disease, characterized by the change of leucorrhea and pruritus vulvae. There are bacterial vaginitis, mycotic vaginitis, trichomonal vaginitis, atrophic vaginitis, vaginitis secondary to infection in adjacent parts of the vagina, etc. The reason is that the natural defense function of the vagina is damaged or the body's resistance is weakened in western medicine, which improves the conditions for the invasion of bacteria, fungi, trichomonas and viruses. Moreover, the vagina and urethra are close to the anus, which is prone to local dampness and pollution. In addition, women have frequent sexual life in the growing period, and the operation of uterine cavity is unfavorable to the access of cervix and vagina, which is easily damaged or infected by external pathogenic bacteria, leading to vaginitis [1]. In ancient Chinese medicine, there is no record of the name of vaginitis, and it can be classified as "pruritus vulvae" according to its clinical manifestations. The name of "pruritus vulvae" was put forward for the first time in "Emergency Prescription after Elbow". It is recorded in the Golden Mirror of Medical Cases: "The pruritus of female vulva is mostly caused by insects caused by damp heat and insect poison". Traditional Chinese medicine is due to vulva dystrophy or downward flow of damp-heat in liver meridian, or damp-heat infestation [2].

With a high incidence of vaginitis, traditional Chinese medicine and western medicine have their own advantages in treating this disease. Topical medicine has a good effect in treating this disease, which can be divided into three categories: western medicine, traditional Chinese medicine and Chinese patent medicine. And these drugs can be made into suppositories for vaginal use, or liquid medicine for local fumigation and washing. Vaginitis treatment and drug selection are particularly important. This paper focuses on summarizing and analyzing the pharmacological effects of commonly used external drugs for vaginitis for clinical reference.

## 2. Commonly used topical western medicine

The treatment of vaginitis is mainly to eliminate the inducement and change the vaginal microecology as the auxiliary. Western medicine is mainly used to fight bacteria, fungi, trichomonas and viruses. Clinical use of antibacterial, antifungal, trichomonal, antiviral, estrogen relief local treatment. Sometimes, drugs to improve vaginal microenvironment will be added for treatment.

### **2.1. Antibacterial drugs**

Antibiotics are mainly used to treat bacterial vaginitis. Currently, quinolones and lincomycin are the most commonly used drugs in clinics. Ofloxacin suppository or ofloxacin vaginal effervescent tablets and clindamycin phosphate suppository will be introduced in detail below.

Ofloxacin suppositories play an antibacterial role mainly by inhibiting the synthesis and replication of bacterial DNA. The main ingredient of Ofloxacin suppositories or ofloxacin vaginal effervescent tablets is ofloxacin, which belongs to the quinolone class of antibacterial drugs and has a broad-spectrum antibacterial effect. It is clinically used for the treatment of bacterial vaginosis and has a significant effect on gynecological infections caused by gram-positive and gram-negative bacteria [3].

Clindamycin phosphate suppository mainly inhibits the synthesis of bacterial protein and leads to bacterial death, the main component of which is clindamycin phosphate, is a kind of lincomycin, which has a good antibacterial effect on most anaerobic bacteria. In vitro bacteriostatic experiments have shown that it has a strong inhibitory effect on common anaerobic bacteria in the vagina.

### **2.2. Antifungal drugs**

Antifungal drugs are mainly used to treat fungal vaginitis. Including imidazole, triazole and polyene antibacterial agents. The representative drugs of imidazole include miconazole nitrate vaginal soft capsule, clotrimazole vaginal tablet/expansion suppository/cream/suppository, buconazole nitrate vaginal cream. The representative medicine of triazole is terconazole vaginal suppository, and the representative medicine of polyene is nystatin vaginal effervescent tablet.

Miconazole nitrate vaginal soft capsule, the main component of which is miconazole nitrate, is a broad-spectrum antifungal agent of imidazole. It can be used to treat vaginitis caused by candida and gram-positive bacteria, and has inhibitory effects on many fungi, as well as some cocci and bacilli. The mechanism of miconazole nitrate vaginal soft capsule is to inhibit the synthesis of fungal cell membrane.

Clotrimazole vaginal tablet swelling suppository cream suppository, whose main component is clotrimazole, is an imidazole broad-spectrum antifungal drug, which has inhibitory effects on many fungi, especially candida albicans, and has antifungal activities in vitro and in vivo, including skin fungi, yeast and mold [4]. The mechanism of which is to inhibit the synthesis of fungal cell membrane.

Tebuconazole nitrate vaginal cream, the main component of which is Tebuconazole nitrate, is a broad-spectrum antifungal agent of imidazole, which is mainly used to treat candidal vaginitis. The mechanism of tebuconazole nitrate vaginal cream is to inhibit the synthesis of fungal cell membrane.

Teconazole vaginal suppositories, the main component of which is Teconazole, is a triazole antifungal drug, which is used to treat candidal vaginitis. Compared with imidazoles, terconazole is strong and long-acting and does not affect the normal flora in the vagina. Its mechanism of action is to change the permeability of fungal cell membrane, which leads to the death of fungi.

Mycin vaginal effervescent tablets, the main component of which is mycin, is a broad-spectrum antibacterial drug of the polyene class for the treatment of candida vaginitis. It is sensitive to Candida and not easily resistant, and also has an inhibitory effect on trichomoniasis. In a word, mycin has the pharmacological effect of inhibiting and killing bacteria, fungi and protozoa.

### **2.3. Multi-antibody drugs**

Some anti-drugs can be used to treat mixed vaginitis caused by various pathogenic bacteria. It mainly includes metronidazole suppository or metronidazole vaginal effervescent tablet, tinidazole vaginal effervescent tablet or tinidazole vaginal tablet, ornidazole vaginal suppository, nifuratel nystatin vaginal soft capsule, and bisazoletail suppository. These six kinds of drugs will be introduced in detail below.

Metronidazole suppository or metronidazole vaginal effervescent tablet, the main component is metronidazole, belonging to nitroimidazole derivatives, which can effectively combat anaerobic bacteria and trichomonads. Compared with metronidazole suppository, metronidazole effervescent tablet can better contact vaginal mucosa, so it can significantly increase the drug concentration in the affected area, improve the therapeutic effect and increase the clinical cure rate [5].

Tinidazole vaginal effervescent tablets or tinidazole vaginal tablets, the main component of which is tinidazole, belong to nitroimidazole derivatives, which can effectively fight against most anaerobic

bacteria and trichomonads, and can be used for treating trichomonal vaginitis and bacterial vaginosis caused by sensitive anaerobic bacteria.

Ornidazole vaginal suppositories, the main component of ornidazole, belongs to the third generation of nitroimidazole derivatives, and can be used in the treatment of bacterial vaginosis and trichomoniasis vaginitis. However, studies have found that treatment with ornidazole suppositories alone is difficult to cure in the short term, and the recurrence rate is high [6].

Nifuratel-mycin vaginal soft gels, the main components of nitrofuratel and-mycin, of which nitrofuratel is a furan derivative, has a strong ability to fight bacteria and trichomoniasis, mycin is a polyene antifungal drug, has a broad spectrum of antifungal pharmacological effects, is most sensitive to *Candida*, but also inhibits trichomoniasis.

Shuangtai suppository is mainly composed of metronidazole, clotrimazole and chlorhexidine acetate, in which metronidazole is a derivative of nitroimidazole, which has the pharmacological action of resisting trichomonad and anaerobic bacteria; Isoxazole is a broad-spectrum antifungal agent of imidazole, which can inhibit many kinds of fungi. Chlorhexidine acetate is a quaternary ammonium salt cationic surfactant which can effectively inhibit gram-positive bacteria. The synergistic effect of these three ingredients can be used for vaginitis caused by various pathogen infections.

#### **2.4. Drugs to improve the microenvironment**

In the treatment of vaginitis, drugs are commonly used to improve the vaginal microenvironment, which is often used as an adjuvant treatment for vaginitis. Including vaginal lactic acid bacteria capsule and recombinant human interferon a-2 b gel, which will be described in detail below.

*Lactobacillus vaginalis* viable capsule, the main component of which is *Lactobacillus* viable, can effectively supplement the number of viable lactobacilli in women's vagina, and its metabolites such as lactic acid and hydrogen peroxide can maintain the normal acidic environment of vagina and inhibit the growth of pathogenic bacteria.

Recombinant human interferon a-2 gel, the main component is recombinant human interferon a - 2 b, has a broad spectrum of antiviral, antibacterial, inhibition of cell proliferation and regulation of immunity. Studies have shown that interferon can inhibit the growth of virus and trigger a series of immunomodulatory effects, such as enhancing the phagocytosis of macrophages, enhancing the cytotoxicity and natural killing ability of lymphocytes on target cells.

#### **2.5. Relieving low estrogen drugs**

The representative drug for relieving low estrogen is estriol suppository, main component of estriol, as the natural estrogen, can promote the angiogenesis of vaginal mucosa and the healing of vaginal epithelial injury. Local application by women can relieve vaginal discomfort caused by insufficient secretion of endogenous estrogen, normalize the epithelial cells, and restore the physiological pH value of vagina, thus enhancing local resistance to pathogens.

### **3. Common traditional Chinese medicine used in vaginitis**

External washing of traditional Chinese medicine for treating vaginitis has been recorded in ancient books and record, and its application in gynecology first can be found in Synopsis of the Golden Chamber. Fumigation and washing of traditional Chinese medicine can warm up the meridians and collaterals, and promote the penetration and absorption of drugs. The effective ingredients in the fumigant are absorbed and then enter the blood circulation.

Over the years, according to the relevant literature of external treatment of vaginitis by traditional Chinese medicine, combining with the clinical medication rules and the characteristics of clearing away heat and toxic materials, it is analyzed that most external drugs are mosquito repellent and antipruritic drugs, and the combined application is common. Bitter drugs, *Stemona Cortex*, *Phellodendri* and *Fructus Cnidii*, which are used together with various drugs, are commonly used traditional Chinese medicine, and they are also used as processing agents for the effective ingredients of traditional Chinese medicines. The details are introduced as following.

### **3.1. Multi-flavored traditional Chinese medicine combined application**

It is common to treat vaginitis with multiple traditional Chinese medicines combined with external washing. By searching the relevant literature in recent years, it is found that there are many studies on Cnidium powder. The main ingredients of Fructus Cnidii powder are Fructus Cnidii, Radix Sophorae Flavescentis, Radix Stemonae, Alumen, Fructus Zanthoxyli, Cortex Phellodendri, Kochiae Fructus, etc. The whole formula has the effects of clearing away heat, promoting diuresis, killing insects and relieving itching. Fructus Cnidii and Radix Sophorae Flavescentis can kill insects, eliminate dampness and relieve itching; Radix Stemonae and alum can kill insects, Zanthoxylum bungeanum can kill insects and relieve itching, Cortex Phellodendri can clear away heat and promote diuresis, purge fire and detoxify, and Kochia scoparia can clear away dampness and heat, expel wind and relieve itching.

### **3.2. Commonly used single-flavor Chinese medicine**

#### **3.2.1. Cnidium monnieri**

Cnidium monnieri was first published in Shennong Materia Medica. Materia Medica Congxin: Cure damp, women's pruritus, decoct soup and bathe, stop wind and relieve itching. Modern pharmacological research shows that Cnidium monnieri has significant effects on the central nervous system, and have pharmacological effects of antibacterial, antiviral, anti-inflammatory and antipruritic. Studies have shown that osthole, the active component of osthole, can inhibit calcium influx, increase the content of cyclic guanylic acid, and affect the content of PG NO MDA and the activity of nitric oxide synthase, thus achieving anti-inflammatory effect.

In addition, foreign reports of the anti-inflammatory and analgesic effects of Cnidium monnieri have a great relationship with inhibiting peripheral inflammatory substances and affecting the central nervous system. In addition, it can also be combined with other coumarins to block the signal transduction pathway caused by substances P, and replace the itching consciousness, thus achieving the effect of relieving itching. Snake nitristin can also inhibit the release of the inflammatory factor TNF- $\alpha$  by macrophages by down regulating iNOS and COX-2 protein expression levels [7].

#### **3.2.2. Matrine**

Matrine was first published in Shennong Materia Medica and South Yunnan Materia Medica: It can cure skin pruritus, tinea and sore caused by blood wind, and Sophora flavescens, a traditional Chinese medicine, has the effect of clearing away heat, drying dampness and killing insects. In the external treatment of gynecological diseases, Sophora flavescens has the functions of anti-mycoplasma, killing trichomonad and relieving itching. Studies have shown that Sophora flavescens has a strong inhibitory effect on the pathogenic bacteria of vaginitis. Sun Jiehui et al [8]. observed the effect of different doses of c Compound Kushen lotion on local skin itching were observed in experimental animal models. The results showed that Compound Kushen lotion had obvious antipruritic effect, which may be related to its anti-inflammatory effect by increasing the level of interleukin -10, an anti-inflammatory factor. This also indicated that IL-5 plays an important role in the development of skin inflammation. Zhao Rui and others[9] experimentally studied the effect of matrine on Trichomonas vaginalis cultured in vitro was studied, and the results showed that matrine could kill Trichomonas vaginalis. Tao et al. [10] observed the effect of matrine on Trichomonas vaginalis cultured in vitro was studied, and the results showed that matrine could kill Trichomonas vaginalis.

#### **3.2.3. Stemona**

Stemona was first published in Bielu of famous doctors. Modern research shows that Stemona has antibacterial, antifungal, pest control, sedative and analgesic effects. Stemona extract or decoction is commonly used to drive out trichomonas vaginalis. When treating trichomonas vaginalis, it can be used alone or combined with auricular bone, Sophora flavescens and other decoction. Jin Lingjia et al. [11] screened anti-inflammatory components of Baibu, and the results showed that several compounds of Baibu had anti-inflammatory effects and inhibition of phosphatase 2 was the possible anti-inflammatory mechanism of Baibu.

#### **3.2.4. Phellodendri chinensis cortex**

Cortex Phellodendri is first recorded in Shennong's Herbal Classic. s .It shows that the main woman leakage red and white, Yin wound erosion sores Phellodendri Chinensis Cortex has the effect of clearing heat, dampness, detoxification and curing sores. Modern studies show that it has antiviral microbial regulation immune anti-ulcer and other pharmacological effects. Studies have shown that the anti-

inflammatory effects of *Phellodendri Chinensis Cortex* is related to the inactivation of NF- $\kappa$  B and MAPKs to inhibit the production of NO and the expression of iNOS, as well as the inhibition of IL-6, IL-1  $\beta$  and MCP-1 and other cytokines [12]. Liu Chunping [13] extracted berberine hydrochloride from *Phellodendri Chinensis Cortex*, and measured its inhibitory effect on the common skin fungi *Trichophyton rubrum* and *Trichophyton rubrum*. Microspores of dogs, Microspores of gypsum and *Trichophyton floccosum*. The results showed that berberine hydrochloride had antibacterial effect on common dermatophytes. Studies have shown that *Phellodendri Chinensis Cortex* has immunosuppressive effects that may be related to some of its components, such as yellow cedar base, which exhibits strong corticosterogen-like effects [14].

### 3.2.5. *Dandelion*

Dandelion is first recorded in Shennong's Herbal Classic. *Materia Medica Justice*: Treating all the symptoms of sores, carbuncle, redness, swelling, heat and poison, which can be taken and applied, quite fulfilling the efficacy of dandelion in clearing away heat, detoxifying, swelling and resolving hard masses. Modern pharmacological research shows that it has the pharmacological effect of anti-ulcer bacteria. It can inhibit gram-positive bacteria, gram-negative bacteria, fungal spirochetes and viruses [15]. Studies have shown that dandelion saponin can block the NF- $\kappa$  B signaling pathway. Inhibition of NO synthesis and INOS gene expression in RAW 264.7 cells induced by LPS, as well as inhibition of TNF-IL-6A expression and secretion of TNF -  $\alpha$  IL - 6 can achieve anti-inflammatory effects in vitro [16]. It has been confirmed that dandelion leaf extract can reduce the expression of iNOS and COX-2 in lipopolysaccharide induced RAW 264.7 inflammatory cells and inhibit the activation of mitogen-activating proteins [17].

### 3.2.6. *Cortex dictamni*

It was first published in Shennong *Materia Medica*, which is used to treat female yin swelling and pain, and cortex dictamni has the effect of clearing away heat and toxic substances, eliminating dampness and expelling wind. Modern pharmacological studies have shown that its water-soaking agent has antifungal, antibacterial and antipyretic pharmacological effects. Huang Hanhui et al. [18] studies have shown that cortex dictamni extract can inhibit histamine and 5-hydroxytryptamine in swollen and inflammatory tissues of rat feet, suggesting that this may be one of the anti-inflammatory mechanisms of cortex dictamni extract. The anti-inflammatory mechanism is also related to the inhibition of the expression level of iNOS and COX-2, which can inhibit the activation of NF- $\kappa$ B in RAW 264.7 cells by inhibiting the degradation and phosphorylation of I $\kappa$ B and reducing the production of NO and PGE 2, and then the expression level of iNOS and COX-2 is inhibited. Its anti-inflammatory effects may also be realized by decreasing the activation of NF- $\kappa$ B through the IKK and MAP kinase signaling pathways [19].

### 3.2.7. *Zanthoxylum bungeanum*

The medicinal use of *Zanthoxylum bungeanum* was first recorded in the Shennong *Materia Medica*. On the Medicinal Properties, It can be mainly used for treating women's menstrual obstruction, postpartum bloody dysentery and dysentery for many years, as well as promoting hair growth and treating abdominal cold pain. *Zanthoxylum bungeanum* has the effects of warming middle warmer, relieving pain, killing insects and relieving itching. Modern pharmacological research shows that it has antifungal, analgesic, anti-inflammatory and insecticidal effects. Wu Shijun et al. [20] Studies have shown that pepper oil can inhibit gram-negative bacteria, gram-positive bacteria and fungi. The Studies of Zheng Jin et al. [21] have shown that the volatile oil and water-soluble components of *Zanthoxylum bungeanum* can reversibly block the impulse conduction of the isolated nerve trunk of toad and reduce the excitability of the nerve trunk, which may be the physiological basis for local anesthesia of *Zanthoxylum bungeanum*.

### 3.2.8. *Houttuynia cordata*

It was first recorded in the famous doctors' Book. *Diannan Materia Medica* shows it that treat lung cough with purulent blood, phlegm have a foul smell, e. Hot poison, cure furuncle Has qingrejiedu the effect of anti-abscess. Modern pharmacology study shows that *h. Cordata* has disease-resistant original microbes adjust the pharmacological effects of immune enhancement immunity. For example, by regulating the expression levels of TNF- $\alpha$ , IL-6 and other pro-inflammatory factors, *Houttuynia cordata* Thunb can improve the immune suppression of the body by increasing the expression of IFN- $\gamma$  [22]. Studies have shown that *Houttuynia cordata* Thunb can regulate the expression of cytokine mRNA by affecting inflammatory cytokines, such as prostaglandin, NO, chemokines, and the binding activity of nuclear factors and cyclooxygenase, so as to achieve anti-inflammatory effects [23].

### 3.2.9. Honeysuckle

Honeysuckle was first seen in the Records of famous Doctors. *Compendium of Materia Medica*: "once recorded all rheumatism, as well as all kinds of swollen poison, carbuncle, scabies, bayberry sore and other evil sores, which have the functions of clearing away heat and toxic materials". Honeysuckle has the effect of clearing away heat and toxic materials and dispelling wind-heat. Modern pharmacological research shows that it has anti-inflammatory and anti-viral pharmacological effects. Studies have shown that phenolic acids in *Flos Lonicerae* can inhibit lipopolysaccharide and induce RAW 264.7 cells to release nitric oxide, tumor necrosis factor TNF- $\alpha$  and interleukin -6, thus achieving anti-inflammatory effect. Honeysuckle decoction has a good phagocytic function for mouse leukocyte inflammatory cells, which can effectively help the body to improve immune function, strengthen the inhibition of various inflammatory factors, control their expression, and finally achieve anti-inflammatory effects [24]. The study of Anqi Zeng et al. [25] showed that *Flos Lonicerae* extract could inhibit LPS-induced NO secretion in RAW 264.7 cells, down-regulate the release of cytokines such as IL-1, IL-6 and TNF- $\alpha$ , and down-regulate the contents of iNOS, COX-2 and NF- $\kappa$ B p 65, so as to achieve anti-inflammatory effect.

## 4. Commonly used Chinese patent medicines for external treatment of vaginitis

Chinese patent medicine refers to the finished product which is made of traditional Chinese medicine and can be used at any time according to certain treatment principles. It has the advantages of convenient application and remarkable curative effect. Among them, there are many researches on Jieryin Lotion and Honghe Fujie Lotion. These will be described in detail below.

The main ingredients of Jieryin lotion are osmanthus wormwood leaves, living stone calamus *Atractylodes*, peppermint, *Phellodendri*, *Radix Scuariae*, and so on. This formula has the effect of clearing heat and draying-dampness, killing insects and relieving itching. The wormwood has the effect of killing insects and dampness and relieving itching. The mugwort leaves have the effect of warming and stopping cold, removing dampness and relieving itching for external use. The independent living has the effect of removing wind, dehumidifying and relieving pain. The stone calamus has the effect of opening up the body and awakening the spirit of dampness. The *Atractylodes* has the effect of removing wind, dampness and dampness, and the mint promotes and disperses rash. The effect of removing wind and anti-itching, yellow cedar, skullcap has the effect of clearing heat, dryness and dampness, diarrhea and detoxification, and bitter ginseng has the effects of clearing heat, dryness and wetness, killing insects and antipruritics. Modern pharmacological studies have shown that the whole party shares the effect of anti-pathogenic microorganisms, dehumidification and antiprurise. Indications for women under wet tropics, symptoms see genital itching redness and swelling, with a large amount of under belt, suitable for fungal, trichomoniasis and non-specific vaginitis or a combination of pathogenic factors caused by infection vaginitis.

The active ingredient of Honghe Jiefu Xiye is hawthorn kernel dry distillation liquid, which has the effects of clearing heat and toxic materials, killing insects and relieving itching. In vitro pharmacodynamic tests showed that it can inhibit the growth of *Candida albicans*, and in vitro tests can also inhibit the growth of bacteria. Chen Huiping et al. [26] studies have shown that the red nucleus female cleaning lotion can make the vaginal irrigation solution in patients promote macrophage phagocytosis and enhance NK cell activity, as well as clear and block the invasion of pathogenic microorganisms, and play an important role in the local immune function of the vaginal mucosa. The results suggest that Honghe Fujie Xiye can enhance the local immune function of vagina of patients. Li Yanxiang et al. [27] experimental results suggest that Honghe Fujie Xiye can slow down the formation of agar granuloma, reduce the quality of agar granuloma and obviously inhibit chronic inflammation; Honghe Fujie Xiye can increase the itch threshold of guinea pigs to histamine phosphate by 3 ~ 5 times, which has obvious antipruritic effect. It has obvious therapeutic effect on fungal vaginitis in rabbits. In conclusion, Honghe Fujie Xiye has significant anti-inflammatory, antipruritic and antibacterial effects.

## 5. Conclusion

The pharmacological action of external drug treatment for vaginitis is mainly to treat pathogenic bacteria, fungi, trichomonads and viruses, improve the low female status, relieve symptoms, clear away heat and dampness, relieve itching and inflammation, and kill insects, supplemented by improving vaginal micro ecology and enhancing resistance. The clinical treatment of vaginitis is mainly antibiotic

treatment, and the combination of traditional Chinese and western medicine is effective in treating vaginitis. The choice of drugs is especially crucial for treatment. It is necessary to seek advantages and avoid disadvantages, and choose the most appropriate drugs to achieve the effect of improving the cure rate and avoiding recurrence. With the emergence of drug-resistant strains, the incidence of refractory or recurrent vaginitis has been increasing year by year. Therefore, it is still the focus of future research to develop a long-acting treatment with a high cure rate.

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