

# Research Progress of Zhuang Medicine Combined with Nanogels in Mastitis

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**Abstract** Mastitis is a common and frequently-occurring disease among Chinese women, which seriously harms their mental and physical health. External application of Zhuang medicine has the effects of dredging collaterals, relieving pain, promoting blood circulation, removing blood stasis, and softening hardness to dissipate stagnation, and show definite curative effect in preventing and treating breast diseases. Nano-composite hydrogels have the advantages of small toxic and side effects, high bioavailability, high targeting and controllable drug release. Therefore, this paper summarized and analyzed relevant literature of Zhuang medicine in treating breast diseases and clinical research of nanogels, providing new ideas and scientific basis for the treatment of mastitis with Zhuang medicine combined with nanogels.

**Key words** Mastitis; Zhuang medicine; Nanogel; Overview

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Mastitis is an important factor that harms women's physical and mental health. Its typical symptoms are breast lump, redness, swelling, heat and pain, ulceration and pus discharge, and repeated occurrence. Studies have shown that its pathogenesis is related to lumen obstruction, bacterial infection, congenital dysplasia and other reasons. At the onset, it causes great pain to patients' physiology and psychology. Early detection, early diagnosis and early treatment are ideal treatment methods. However, most patients did not intervene in time or handle it improperly at the initial stage of illness, and the abscess was cut and drained after the formation of breast abscess<sup>[1]</sup>. In severe cases, the disease persists after repeated attacks and stimulation, leading to systemic purulent infection<sup>[2]</sup>, and even more, it will cause cancer or neoplastic lesions, which is life-threatening, so it is urgent to receive early treatment. The treatment methods of western medicine for mastitis are mainly antibiotic therapy and physical therapy, but there are recurrence, metastasis and related adverse reactions, which are not conducive to further diagnosis and treatment of patients. As a national medicine, Zhuang medicine fully embodies the value in treating mastitis. External treatments of Zhuang medicine, including external application, bath rubbing, hot application of medicine, fumigation and washing and egg rolling, are the better methods to treat mastitis with good curative effect, few side effects and green health. Studies have shown that preparing nano-composite hydrogels by embedding drugs directly into polymer nanoparticles and filling drug-loaded nanoparticles into hydrogels can greatly improve the drug loading of hydrogels, promote the transdermal absorption rate of drugs, and have remarkable clinical effects<sup>[3]</sup>. Therefore, exploring the characteristics of Zhuang

medicine, investigating the mechanism of Zhuang medicine combined with nanogels and applying it to clinic will be the main direction of mastitis prevention and treatment in the future.

## Understanding of Mastitis in Zhuang Medicine

Mastitis, called Beixi by Zhuang medicine<sup>[4]</sup> and Baezci by Zhuang language, refers to the acute purulent disease that occurs in the breast. Zhuang doctors believe that the important channels of the human body are three channels and two roads. The three channels, namely the air channel, cereal channel and water channel, and two ways, namely the loong road and fire road. The loong road is the road for blood circulation in human body, and the fire road is the road for sensing various information in human body and regulating human physiological functions<sup>[5]</sup>. Zhuang doctors divide the human body into upper, middle and lower parts. The upper part is the sky, the middle part is human and the lower part is the earth. Among them, the sky qi is mainly descending, the earth qi is mainly rising, and the human qi is mainly harmonious. Only when the three kinds of qi operate synchronously can normal physiological functions and life activities be maintained. According to the theory of diseases due to toxin or deficiency, Zhuang medicine believes that "toxin" is an important cause of diseases. The invasion of toxins into the human body and whether they cause illness depends on two factors: the degree of the toxicity and the strength of the body energy. The conflict between good and evil leads to the incompatibility of good and evil, which further leads to the blockage of the three channels and two roads and the asynchrony of the three kinds of qi, resulting in the occurrence of diseases<sup>[6]</sup>. Zhuang doctors believe that "the diseases are not born out of nothing, but the imbalance of qi and blood"<sup>[7]</sup>, and the occurrence of Beixi is mostly due to eating foods rich or strong in flavor and accumulating heat in the stomach, or worry and anger and liver qi stagnation, or nipple rupture and invasion of external pathogenic fire toxin, which result in

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breast vein obstruction and poor milk ejection, or accumulating damp-heat-fire toxin, which causes the condition that the loong road and fire road of the breast are blocked and the stagnated heat toxin and accumulated milk coagulate each other, resulting in swelling and carbuncle<sup>[8]</sup>.

## Application of Zhuang Medicine in Breast Diseases

Zhuang medicine is an integral part of Chinese ethnopharmacology and an important part of Chinese traditional medicine. Under the guidance of Zhuang medicine theory, it is applied to prevent and treat diseases, and has accumulated rich experience in preventing and treating breast diseases and shows unique curative effect and characteristic advantages<sup>[9]</sup>. The clinical medication of Zhuang medicine emphasizes removing toxins, tonifying deficiency and regulating the three channels and roads, and the prescription emphasizes the organic combination of male medicine, female medicine, main medicine, auxiliary medicine and carrying medicine. The medicines in prescriptions are simple and specialized, making good use of toxic and detoxifying medicines. Animal medicines are often used to tonify deficiency, and the application of warm medicines is emphasized, and fresh medicines are preferred, with unique experiences of "treating red with red" and "treating white with white"<sup>[10]</sup>.

Tang<sup>[11]</sup> treated 60 cases of hyperplasia of mammary glands with Xiaoruyin, which was mainly composed of Zhuang medicines: Radix Notoginseng powder 9 g (taken with liquid medicine for three times), Chinese Ixora flower 20 g, Radix zanthoxyli 12 g, *Polygonum cuspidatum* 20 g, Corydalis bungeana 15 g, kiwifruit 15 g, Semen Vaccariae 15 g, Radix Angelicae Sinensis 6 g, Radix Paeoniae Alba 15 g, Trionycis Carapax 30 g, Herba Hedyotidis Diffusae 20 g, and Radix Glycyrrhizae 6 g. Cured; 28 cases showed disappeared breast pain and breast lump; marked effect was observed in 18 cases; and 10 cases were observed with a positive effect and 4 cases with no effect. Overall, satisfactory results were achieved. Qi *et al.*<sup>[12]</sup> used fresh Zhuang medicine dandelion to treat acute mastitis. Through the clinical observation of 58 patients, no adverse reactions and side effects were found in the treatment of acute mastitis with fresh dandelion, and no local allergic reactions were found. The course of treatment was short, the operation was simple, and the price was inexpensive, while the curative effect was remarkable. The medicine could be found all year round and it was very convenient to use. Wei *et al.*<sup>[13]</sup> proposed that Tadehagi triquetrum belongs to one of the commonly used Zhuang medicines, which is widely used in the folk and clinical practice of Zhuang nationality, and has shown remarkable effects in the aspects of oral administration and external treatment of various diseases. *T. triquetrum* can be made into plaster, herbal medicine, *etc.*, which can achieve the effects of clearing away heat and toxic materials, removing dampness, expelling wind and toxic materials, stopping itching and reducing skin infection rate, through bath rubbing, medicated dressing, hot application of

medicine, fumigation and washing. Zhang *et al.*<sup>[14]</sup> used the strong medicine Xianghua Breast-care Gel composed of Herba Hedyotidis Diffusae, dandelion, Rhizoma Sparganii, Rhizoma Curcumae, *etc.*, to carry out clinical experiments on rats with hyperplasia of mammary glands, and observe its effects on serum estrogen and progesterone levels and pathological breast tissues of rats with hyperplasia of mammary glands. It was found that the Zhuang medicine, Xianghua Breast-care Gel, could reduce the nipple diameter of model rats, regulate the level of E2 and P hormones in serum and improve the pathological morphology of breast tissue. The improvement of each index was statistically significant compared with the model group ( $P < 0.05$ ). It shows that Zhuang medicine has certain inhibitory effect on hyperplasia of mammary glands.

In a word, Zhuang medicine plays a positive role in the treatment of breast diseases, so we put forward the hypothesis that Zhuang medicine has a good effect on the treatment of mastitis. Based on the core theory of three channels and two roads in Zhuang medicine, compound gels of Zhuang medicine have been prepared according to the etiology and pathogenesis of mastitis, and play the role of Zhuang medicine in dispersing and dredging collaterals and removing toxins. The prescriptions are special for the disease. They regulate the balance of yin and yang in the body and grasp the key points in the process of regulating qi, removing toxins and tonifying deficiency, to alleviate and treat mastitis caused by various reasons.

## Drug Delivery Advantages of Nanogels

The nano-material is a new type of polymer material, which has attracted more and more attention as a carrier of drug delivery. A large number of studies have proved that it can improve the adhesion and permeability of drugs. In addition, nano-materials also have the advantages of high bioavailability, high targeting and controllable drug release<sup>[15]</sup>. With the development of nanotechnology, the process of drug loading by nano-carriers is simplified and they have strong biological affinity. They can not only improve the curative effect of drugs, but also reduce the side effects of drugs, and thus have bright application prospects.

How to build a nanogel drug-carrying system with strong drug-carrying ability, good chemical stability and easy modification by combining nano-materials with gels has attracted the attention of many scholars<sup>[16]</sup>.

## Clinical Application of Nanogels

In China, nanogel preparations of traditional Chinese medicine are gradually developed. They can penetrate the stratum corneum and be absorbed into the systemic circulation through the skin, so as to give full play to their efficacy, and they can be well used for the treatment of patients who cannot tolerate injections or oral drugs<sup>[17]</sup>.

Puerarin gel paste prepared by Gou<sup>[18]</sup> can improve the problems of puerarin's rapid absorption from gastrointestinal tract, but

its absorption degree is poor, its bioavailability is low, and there are many adverse reactions caused by injection, which provides basis for "external treatment of internal diseases".

Hou<sup>[19]</sup> synthesized a kind of nano-silver sol in a green and environment-friendly way, and prepared an antibacterial nano-silver gel for gynecological external use, which has obvious antibacterial effect, and is safe, non-toxic, non-irritating, non-allergenic, practical, stable and reliable. The nano-silver gel prepared by this method is put into a special vaginal applicator to treat gynecological inflammation such as vaginitis, cervicitis and cervical erosion, so it also has high development value and application prospect.

Jin<sup>[20]</sup> treated 150 cases of bacterial vaginitis with antibacterial nano-silver gel for women. Among them, 78 cases in the experimental group were treated with the antibacterial nano-silver gel for women, and 72 cases in the control group were treated with metronidazole gel. The total effective rates of the experimental group and the control group were 100% and 91.67%, respectively. The therapeutic effect of the antibacterial nano-silver gel for women on bacterial vaginitis was better than that of the control group, and it was concluded that the therapeutic effect of the antibacterial nano-silver gel for women on bacterial vaginosis was remarkable.

In the treatment of gynecological diseases by vaginal mucosal administration, Li<sup>[21]</sup> constructed a new vaginal mucosal drug delivery system, a post-expansion nanogel foam agent, based on nano-gel technology. Drugs entered the vagina in the form of foam by using the polymer gel foam technique, and the slow expansion process and deformation promoted the even spreading and distribution of drugs in the vaginal cavity. The system is safe and non-irritating to vaginal mucosa, which improves the compliance of patients and the permeability of drugs, is conducive to the formation of drug "reservoir effect" in tissues, and also increases the bio-availability of drugs.

Wang<sup>[22]</sup> loaded glycyrrhetic acid into alginate zinc nanogel to prepare glycyrrhetic acid-alginate zinc nanogel, which was then loaded with paeoniflorin to prepare glycyrrhetic acid-mediated paeoniflorin-alginate zinc nanogel. *In-vitro* safety evaluation and pharmacological activity research showed that it had good biocompatibility and anti-inflammatory and antioxidant activity.

It can be seen that the application of nanogels in medical field is worth popularizing. With the deepening of research, their excellent medical characteristics will surely occupy an important position in the future medical excipients.

## Conclusions

In recent years, the incidence of mastitis has increased. At the onset, patients show redness, swelling, heat and pain in their breasts, and even purulent, and many women suffer from it. Western medicine therapy is mainly hormone therapy and surgical therapy. However, it show the characteristics of expensive treatment cost and painful treatment process, and patients are prone to drug resistance, large side effects, easy recurrence, poor progno-

sis, low acceptance and low medical compliance. Surgical treatment has wounds, risks, long recovery period and aesthetic impact. Under the background that women's thoughts, economy and rights are gradually moving towards equality and freedom, women's aesthetic concepts have changed and their demands and expectations for a "perfect" body have gradually turned to more conservative traditional medicine which cures diseases in a comfortable and high-quality state.

Zhuang medicine has unique advantages in treating mastitis. Based on the core theory of three channels and two roads in Zhuang medicine, compound preparations of Zhuang medicine have been prepared according to the etiology and pathogenesis of mastitis, and show the effects of dispersing and dredging collaterals and removing toxins. The prescriptions are special for the disease. They regulates the balance of yin and yang in the body and grasp the key points in the process of regulating qi, removing toxins and tonifying deficiency, to alleviate and treat mastitis caused by various reasons. Studies have proved that the clinical application of nanogels has greatly improved the cure rate. For the first time, we combined nanogels with the compound preparations of Zhuang medicine to develop new types of gels of Zhuang medicine. The combination of the two brings out the best in each other, so that drugs can penetrate through the skin directly to the affected area, promote the smoothness of lymphatic vessels and accelerate lymphatic reflux. Meanwhile, it can also avoid the first-pass effect of oral drugs and the damage of gastrointestinal digestive juice and digestive enzymes to drugs, improve the speed and effectiveness of transdermal drug delivery, and thus improve the curative effect of drugs. The external application of Zhuang medicine can stimulate the loong and fire roads scattered in human breasts, dredge the qi and blood of the two roads, and get rid of toxins. On the basis of inheriting the culture of Zhuang medicine and combining with modern high technology, the treatment efficiency of mastitis is improved to the greatest extent, which not only meets the needs of patients for treating mastitis, but also promotes the development and application of nano-gels in the field of ethnic medicine, opening up new ways for clinical treatment of mastitis. Composite nanogels have great research prospect and application potential in the treatment of mastitis, and it is believed that it will become a new trend in the future. However, at present, the research in this direction is relatively lacking, and the research from multiple angles, deep levels and wide fields needs to be further strengthened. Which Zhuang medicine to chose, how to make the formula and how to develop comfort and mild products with high drug loading, good permeability and strong skin friendliness combining with nanogels, are the breakthrough points, and also the research focus of Zhuang medicine development. It is anticipated that Zhuang medicine nanogels will have further development in the treatment of mastitis.

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enterohepatic circulation's metabolism, the effect has certain limitations. Aromatherapy still has broad application prospects.

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