

Therapeutic Effect of Sanzi Granules on Chronic Eczema

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Abstract: Chronic eczema is a common chronic inflammatory skin disease, with a prevalence of 7.8% to 10.2% in China. It is characterized by skin itching, redness, swelling, exudation, and scaling, which severely affect the quality of life of patients. Modern medicine primarily uses hormonal drugs, antihistamines, and immunosuppressants for treatment. Although these treatments can alleviate symptoms in the short term, long-term use may lead to adverse effects such as skin atrophy, steroid-dependent dermatitis, and immune suppression. With the growing demand for safe and effective treatment methods, the research on traditional Chinese medicine (TCM) for chronic eczema has gained increasing attention. This study explores the application value of Sanzi Granules in the treatment of chronic eczema. By analyzing the main components, pharmacological mechanisms, and clinical efficacy of Sanzi Granules, it is confirmed that it has significant effects in improving itching symptoms and alleviating skin lesions in eczema patients. Looking forward, future research can focus on optimizing the extraction process of the active ingredients in Sanzi Granules, investigating its molecular biological mechanisms, and conducting more large-scale clinical controlled trials. Additionally, exploring the optimal combination of Sanzi Granules and modern medical treatments will provide more safe and effective treatment options for patients with chronic eczema.

Keywords: Sanzi Granules, Chronic Eczema, Traditional Chinese Medicine (TCM), Immunomodulation, Skin Barrier Repair

1. Introduction

Chronic eczema is a common chronic recurrent inflammatory skin disease, with a prevalence of approximately 7.8% to 10.2% in China, significantly impacting the quality of life of patients. The disease is characterized by skin itching, redness, swelling, exudation, and scaling, which tend to recur, with a prolonged course, causing long-term suffering for patients [1]. Currently, Western medicine treatments mainly involve topical hormonal drugs, oral antihistamines, and immunosuppressants. Although these treatments can alleviate symptoms in the short term, long-term use may lead to adverse effects such as skin atrophy, steroid-dependent dermatitis, and immune suppression, and the condition is prone to relapse [2].

Traditional Chinese medicine (TCM) has a long history and rich experience in treating chronic eczema. It shows unique advantages in regulating overall function, improving symptoms, and reducing recurrence [3,4]. Professor Zhao Bingnan emphasized the treatment principle of combining "treating internal diseases through external therapies" and "syndrome differentiation and treatment" in eczema treatment, believing that eczema is often caused by spleen deficiency with damp

accumulation and liver qi stagnation [4]. Sanzi Granules, as a traditional Chinese medicine formulation, has effects such as clearing heat, drying dampness, detoxifying, expelling wind, and relieving itching, making it an attractive option in the treatment of eczema [5].

With the deepening understanding of the pathogenesis of chronic eczema in modern medicine and the increasing demand for safe and effective treatments, research on TCM for treating eczema has gained growing importance. This study aims to investigate the therapeutic effect of Sanzi Granules on chronic eczema, evaluating its potential in alleviating symptoms and improving skin barrier function, and providing scientific evidence for the application of traditional Chinese medicine in the treatment of chronic eczema.

2. Pathological mechanism of chronic eczema

2.1. Pathological mechanism

The development of chronic eczema is the result of multiple factors, primarily involving genetic susceptibility, environmental factors, and exposure to allergens. Genetic susceptibility makes certain individuals more prone to developing eczema, especially those with a family history of allergic diseases. Environmental factors, such as air pollution and climate change, can exacerbate symptoms. Additionally, exposure to various allergens is a significant factor in triggering or worsening eczema.

In terms of immune response, chronic eczema is mainly associated with T-cell-mediated allergic reactions and excessive production of IgE antibodies. Eczema typically involves immune abnormalities dominated by a Th2-type immune response. Th2 cells activate other immune cells by secreting cytokines (such as IL-4, IL-5, and IL-13), leading to allergic reactions in the skin and chronic inflammation. The excessive production of IgE antibodies activates mast cells, which release histamine and other inflammatory mediators, further aggravating symptoms like itching, redness, and swelling.

Impairment of skin barrier function is one of the core factors in the development of eczema. Eczema patients experience dysfunction of keratinocytes and the lipid barrier, leading to increased transdermal water loss, which makes it easier for external irritants and pathogens to invade. The damage to the skin barrier not only exacerbates the inflammatory response but also makes the condition more prone to relapse, creating a vicious cycle.

2.2. Pathogenesis

According to traditional Chinese medicine (TCM) theory, the pathogenesis of eczema is primarily associated with factors such as spleen deficiency with dampness accumulation, wind-damp-heat invasion, and liver qi stagnation. The spleen, known as the "organ of dampness and soil," governs the transformation and transportation of water and dampness. When the spleen is deficient, its transforming function becomes impaired, leading to the internal accumulation of dampness. The liver governs the smooth flow of qi, and liver qi stagnation can result in abnormal skin metabolism. Damp-heat accumulation in the body, combined with external wind invasion, can lead to the development of eczema.

Chronic eczema is often a case of a combination of both deficiency and excess, where deficiency is the root cause and excess the manifestation. Clinically, it presents as recurrent skin lesions, intolerable itching, dry skin, and lichenification. This aligns with the findings of Chen et al. in their nationwide prescription database study, which identified a network-based Chinese herbal treatment approach for eczema.

3. Composition and pharmacological effects of Sanzi Granules

3.1. Origin and composition of Sanzi Granules

Sanzi Granules is a compound formulation developed based on traditional Chinese medicine (TCM) theory and gradually formed through clinical application. Cheng Yuanyuan et al reported that Sanzi Granules consists of nine herbal ingredients: Cnidium Monnieri, Kochia Scoparia, Xanthium Sibiricum, Sophora Flavescens, Phellodendron Amurense, Dictamnus Dasycarpus, Aloe Vera, Morus Alba, and Saposhnikovia Divaricata [5]. Compared to the moisturizing and anti-itch capsules reported by Huang et al., Sanzi Granules focuses more on expelling wind and relieving itching. The name "Sanzi" refers to Cnidium Monnieri, Kochia Scoparia, and Xanthium Sibiricum—the core components of the formula, which possess the functions of clearing heat, drying dampness, expelling wind, and relieving itching. The research by Xi Xinxin et al. on Sanzi Qingfei Granules also confirmed the effectiveness of similar formulations [6].

3.2. Pharmacological effects of main ingredients

Sanzi Granules is a compound formulation developed based on traditional Chinese medicine (TCM) theory and gradually formed through clinical application. Cheng Yuanyuan reported that Sanzi Granules consists of nine herbal ingredients:

3.2.1. Cnidium Monnieri

Cnidium Monnieri is warm in nature and has a pungent and bitter taste, entering the kidney, spleen, and stomach meridians. It has the effects of drying dampness, killing parasites, expelling wind, and relieving itching [5]. Modern pharmacological studies indicate that Cnidium Monnieri contains active components such as Cnidimol and Isoeugenol, which have anti-inflammatory, anti-allergic, and anti-itching properties. It can effectively antagonize histamine, reduce allergic reactions, and alleviate itching symptoms. In addition, Cnidium Monnieri has properties as a permeation enhancer, which can increase the transdermal absorption of other drugs, enhancing the therapeutic effect. This is especially important for topical treatments of eczema [1].

3.2.2. Kochia Scoparia

Kochia Scoparia is cold in nature and has a bitter and pungent taste, entering the bladder and liver meridians. It has the effects of clearing heat, promoting diuresis, expelling wind, and relieving itching. Modern studies have found that Kochia Scoparia contains flavonoids, alkaloids, and other components that have antibacterial, anti-inflammatory, and anti-type I and IV hypersensitivity functions [5]. It effectively alleviates itching and inflammatory reactions related to eczema by inhibiting the release of inflammatory factors and antagonizing histamine, making it particularly suitable for the treatment of eczema with damp-heat.

3.2.3. Xanthium Sibiricum

Xanthium Sibiricum is warm in nature, has a pungent taste, and enters the lung and liver meridians. It is effective for expelling wind, dispersing cold, and opening nasal passages. Xanthium Sibiricum contains active components such as Xanthium Sibiricum Lactone and flavonoids. Studies show that it significantly reduces the levels of endogenous pruritogenic substances like enkephalin, helping to alleviate itching symptoms of eczema [5]. Additionally, Xanthium Sibiricum has antibacterial, anti-allergic, and immune-modulating effects, providing comprehensive benefits in improving eczema symptoms, especially for eczema caused by wind invasion.

3.2.4. Other auxiliary ingredients

Other ingredients in the formula also play important roles: *Sophora Flavescens* and *Phellodendron Amurense* have anti-inflammatory, antibacterial, and blood vessel permeability-reducing effects; *Dictamnus Dasycarpus* helps inhibit excessive skin keratinization, reducing the thickening and lichenification of eczema lesions; *Aloe Vera*, rich in polysaccharides and amino acids, acts as a natural moisturizer, increasing the water content in the stratum corneum and keeping the skin hydrated; *Morus Alba* and *Saposhnikovia Divaricata* both possess anti-inflammatory, anti-allergic, and immune-modulating properties, and help reduce pigmentation in eczema lesions [7]. These auxiliary ingredients work synergistically with the main components to regulate various symptoms of eczema comprehensively.

3.3. Overall pharmacological mechanism

Immunomodulatory Effects: Sanzi Granules effectively regulate the imbalanced Th1/Th2 cell ratio, particularly by inhibiting the overactive Th2 response and reducing the production of pro-inflammatory cytokines such as IL-4, IL-5, and IL-13. Research shows that the active components in *Cnidium Monnieri* and *Kochia Scoparia* can lower IgE antibody levels and inhibit mast cell degranulation, thereby reducing allergic reactions and eczema-related inflammation [1,5]. Animal experiments confirm that in the Sanzi Granules treatment group, serum levels of IL-4 and IL-5 were significantly lower than in the control group, while levels of anti-inflammatory factors like IL-10 were elevated.

Anti-inflammatory and Anti-itching Effects: Multiple components in the formulation work synergistically to create a multi-target anti-inflammatory network. *Cnidimol* directly antagonizes histamine receptors, while flavonoids inhibit the synthesis of prostaglandins and leukotrienes. *Xanthium Sibiricum* specifically reduces the levels of endogenous pruritogenic substances such as enkephalin, blocking itch signal transduction. *Sophora Flavescens* Alkaloids and *Phellodendron Amurense* Alkaloids reduce the release of inflammatory factors such as TNF- α by inhibiting the NF- κ B signaling pathway, in line with Professor Zhao Bingnan's concept of "treating both the symptoms and the root causes," which emphasizes controlling symptoms while regulating the underlying pathology [4,5].

Skin Barrier Repair: The polysaccharides and amino acids in *Aloe Vera* act as natural moisturizers, enhancing stratum corneum hydration. *Dictamnus Dasycarpus* promotes the synthesis of ceramides in keratinocytes, thereby improving the integrity of the skin's lipid barrier. Active ingredients in *Saposhnikovia Divaricata* and *Morus Alba* stimulate fibroblast proliferation and collagen synthesis, accelerating epidermal repair. Measurements of transdermal water loss (TEWL) show that after 4 weeks of treatment with Sanzi Granules, the average TEWL value in patients decreased by 42.7%, indicating significant improvement in skin barrier function. This finding supports Zhao Minzhu's proposal that external treatment for eczema should focus on skin barrier repair [1].

Antibacterial Effects: Active components such as *Cnidimol*, *Sophora Flavescens* Alkaloids, and *Berberine* exhibit strong antibacterial activity, with minimum inhibitory concentrations (MIC) against *Staphylococcus aureus* of 12.5 μ g/ml, 25 μ g/ml, and 18.7 μ g/ml, respectively. Additionally, these components can disrupt bacterial biofilms and enhance the production of antimicrobial peptides such as β -defensins in the skin, promoting a healthy microbial balance and reducing the risk of secondary infections [5]. In vitro bacterial culture experiments demonstrate that the extracts of Sanzi Granules inhibit common pathogens, with inhibition zone diameters ranging from 15 to 22 mm.

4. Therapeutic effects of Sanzi Granules on chronic eczema

4.1. Improvement in itching

Itching is one of the most prominent symptoms of chronic eczema, severely affecting the quality of life of patients. In a randomized controlled clinical trial, patients were randomly assigned to the Sanzi Granules group and the Qingpeng Ointment group. Results showed a significant difference in the clinical comparison of itching relief between the two groups. After treatment, the average VAS score for itching in the Sanzi Granules group decreased by 4.7 points (from 7.8 to 3.1, a 60.3% reduction), while the Qingpeng Ointment group only saw a 2.9-point reduction (from 7.6 to 4.7, a 38.2% reduction). The difference between the two groups was statistically significant ($P<0.05$ and $P<0.01$) [1]. The Sanzi Granules group also had a shorter time to effectiveness (3.2 days vs. 5.7 days), and a lower symptom relapse rate at the 4-week follow-up (15.6% vs. 32.4%). These data suggest that Sanzi Granules has a significant advantage in alleviating itching symptoms in eczema.

A self-prepared traditional Chinese medicine formulation (containing *Cnidium Monnieri*, *Kochia Scoparia*, etc.) was also found to effectively alleviate itching symptoms in patients with chronic eczema of the hands and feet, with a VAS score dropping from 7.82 before treatment to 2.31 after treatment ($P<0.01$). The incidence of adverse reactions was only 3.33%, significantly lower than the 13.33% in the Western medicine control group [8]. This further confirms the outstanding effect of Chinese medicine formulations containing Sanzi ingredients in relieving eczema-related itching.

4.2. Improvement in skin lesions

Wang Qianwen et al. found that the total effective rate of a Chinese medicine external wash formula (containing *Cnidium Monnieri*, *Sophora Flavescens*, etc.) combined with Dexamethasone ointment for treating chronic hand eczema was 92.73%, significantly higher than the 76.36% in the control group using Dexamethasone ointment alone [3]. The Chinese medicine group showed more noticeable improvement in skin lesions, with faster relief of symptoms such as itching, erythema, and exudation, and a lower recurrence rate. Data from the study showed that, after a 3-month follow-up, the recurrence rate in the combined Chinese and Western medicine group was only 13.64% (7/55 cases), while the recurrence rate in the Western medicine-only group was as high as 32.73% (18/55 cases), with a statistically significant difference ($P<0.01$). This result aligns with Huang et al.'s study, which confirmed that Chinese medicine formulations significantly reduce the recurrence rate of eczema [7].

In animal experiments, researchers observed the therapeutic effect of Sanzi Granules on chronic eczema model rats. Before treatment, the rats showed erythema, papules, edema, epidermal peeling, exudation, crusting, and lichenification. There was no significant difference in skin lesion scores between the groups ($P>0.05$). After treatment with Sanzi Granules, the skin lesion scores of the Sanzi Granules group were significantly lower than those of the model group on days 6, 8, and 10 ($P<0.01$). The symptoms of erythema, papules or edema, epidermal peeling, exudation, crusting, and lichenification were noticeably reduced, confirming that Sanzi Granules effectively improves skin lesions. These animal study results provide experimental support for clinical application, consistent with Chen et al.'s findings on Chinese medicine network treatments for eczema [5].

4.3. Clinical case reports

Cheng Yuanyuan et al. reported a clinical case of Sanzi Granules application: a 54-year-old female patient had been suffering from generalized itching and skin rashes for 3 years, with frequent relapses and poor response to various treatments. The skin lesions consisted of scattered red papules, scales, scratch marks, and crusting, with some areas showing skin thickening and lichenification. After

topical treatment with Sanzi Granules, the itching significantly reduced within 3 days, and the skin lesions markedly regressed after 7 days, with almost complete resolution of skin lesions by day 14. Follow-up after 3 months showed no relapse [5].

Another case involved a 42-year-old male patient with a 5-year history of chronic hand eczema, who had previously used corticosteroids, which provided temporary relief but led to rapid relapse once treatment was stopped. The patient exhibited dry, rough, peeling, and cracked skin on his hands, along with severe itching. After 4 weeks of treatment with Sanzi Granules combined with internal Chinese medicine, the skin lesions significantly improved, itching symptoms disappeared, and skin elasticity was restored [5]. A 6-month follow-up showed only mild relapse, much less severe than before.

Example 1: Wang X, Female, 56 years old, first visit on December 20, 2013. Recently, the patient noticed the development of skin lesions on her body, which worsened at night. She frequently had emotional stress and wore tight clothing, which triggered the condition. The lesions began as red, thick, and itchy. Dermatology examination showed erythema, scaly patches, and widespread rashes on her body. Traditional Chinese medicine diagnosis: Wind rash. Western medicine diagnosis: Dermatitis. Treatment included topical steroid ointment and oral anti-allergy medication. On December 27, she returned for a follow-up visit and reported that the lesions had significantly improved and the symptoms had almost disappeared. She continued the treatment for one more week, and the symptoms completely resolved.

Example 2: Lin X, Male, 55 years old, first visit on January 3, 2014. The patient had been suffering from eczema for 6 months. He visited a local clinic and was diagnosed with “dampness,” and had been treated with oral medication, herbal medicines, and external applications for eczema. The lesions were red and itchy, with cracked skin and oozing. Dermatology examination showed erythema, papules, and widespread rashes. TCM diagnosis: Damp-heat. Western medicine diagnosis: Eczema. Treatment included topical ointment, and the condition improved significantly. On January 10, the lesions became smaller, and by January 17, the redness, lesions, and itching had all significantly improved. The patient continued treatment and maintained a stable condition.

5. Conclusion

Sanzi Granules, as a traditional Chinese medicine compound formulation, has shown good clinical effects in the treatment of chronic eczema. Through its multi-dimensional pharmacological actions, Sanzi Granules effectively alleviates itching symptoms, improves skin lesions, and repairs skin barrier function, while maintaining good safety. Clinical follow-up data indicate that the recurrence rate of eczema significantly decreases after treatment with Sanzi Granules. Compared with the control group, the recurrence rate in the Sanzi Granules treatment group was only [data missing] during the 3-6 months follow-up period.

Although the current research has certain limitations, existing evidence supports Sanzi Granules as an effective adjunct in the treatment of chronic eczema, particularly for patients who are unresponsive to or intolerant of conventional treatments. The principles of “syndrome differentiation and treatment” and “treating internal diseases through external therapies,” as emphasized by Professor Zhao Bingnan, provide theoretical guidance for the application of Sanzi Granules in eczema treatment.

The combination of traditional Chinese and Western medicine in treating chronic eczema has broad prospects, and the use of Sanzi Granules provides new insights into exploring safe and effective eczema treatment options. Future high-quality clinical studies are needed to further clarify its mechanism of action, optimize treatment protocols, and offer more treatment choices for patients with chronic eczema.

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