

The Mechanism of Action and Therapeutic Potential of Tanshinone in the Treatment of Acne

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Abstract. Acne, a common skin disorder, is prone to causing erythema and pigmentation. It has a high prevalence rate and is prone to recurrence. Traditional Chinese medicine (TCM) has a long history and rich experience in treating acne, with methods such as syndrome differentiation and treatment, acupuncture, TCM decoctions, and facial masks. The treatment approaches are unique and effective. This article, through analyzing the common combinations of TCM in the treatment of acne, found that the proportion of *Salvia miltiorrhiza* in the combinations of TCM preparations is significant. The research discovered that the active ingredients in *Salvia miltiorrhiza* have a remarkable effect on the treatment of acne. This article explores the inhibitory effect of tanshinone on androgen and the combined effect of *Salvia miltiorrhiza* and *Scutellaria baicalensis* in killing *Propionibacterium acnes*, and analyzes the mechanism of action of tanshinone in the treatment of acne. At the same time, it also investigates the research progress in improving the pigmentation caused by acne. However, in the treatment of acne, TCM mainly proves the effectiveness of treatment through practical means such as the review and summary of clinical results, with relatively few experimental explorations. Therefore, future research should focus on the exploration of the effective components and action mechanisms of TCM, as well as the investigation of new treatment methods.

Keywords: Acne, tanshinone, *scutellaria baicalensis*, androgen, *propionibacterium acnes*

1. Introduction

Acne, as one of the common diseases worldwide, has an incidence rate of approximately 9.4%, and it often occurs during adolescence with a high prevalence and a tendency to recur. Its clinical manifestations typically include comedones, papules, pustules or cysts. With the development of society, the pace of life has quickened and pressure has increased, leading to a rising incidence of acne. Currently, Western medicine often uses topical medications such as retinoids and antibiotics, oral medications such as antibiotics and hormones, as well as physical and chemical treatments (phototherapy, chemical peeling, etc.) in the treatment of acne.

Western medicine offers the advantages of convenience and quick effectiveness in treating acne. However, acne has a long course of disease and is prone to recurrence. Long-term use of Western drugs may cause side effects of varying degrees and lead to drug resistance. Compared with Western medicine, traditional Chinese medicine (TCM) has unique methods in treating acne, and it has fewer

side effects, is safer and more lasting than Western medicine. Therefore, it is accepted and chosen by a large number of patients. It is worth noting that Danshen, as a traditional Chinese medicine, has the effects of promoting blood circulation and removing blood stasis, relieving pain and dysmenorrhea, and clearing heat and detoxifying. It has long been widely used in the treatment of cardiovascular and cerebrovascular diseases, gynecological diseases and other conditions. In recent years, studies have found that the active components in *Salvia miltiorrhiza*, such as tanshinone I, tanshinone IIA, cryptotanshinone, etc, have significant anti-inflammatory, antibacterial and antioxidant effects, and show good therapeutic effects on acne. They are widely used in traditional Chinese medicine for the treatment of acne.

This article mainly analyzes the mechanism of treating acne from two aspects: the effect of tanshinone in reducing androgen and the killing of *Propionibacterium* acnes through the compatibility of *Scutellaria* and *Salvia miltiorrhiza*. It is of great significance for the selection of drugs and the exploration of new treatment methods.

2. Multilevel analysis of the pathogenesis of acne

The etiology of acne is complex. Modern medicine holds that acne is mainly related to excessive sebum secretion, elevated androgen levels, the colonization and proliferation of *Propionibacterium* acnes, and inflammatory responses [1].

TCM theory attributes the pathogenesis of acne to blood heat, damp-heat, wind pathogen invasion, blood stasis, and accumulated heat. Contemporary TCM perspectives suggest that its etiology is associated with functional disorders of the lung and stomach systems, specifically damp-heat in the lung and stomach, spleen deficiency, and liver qi stagnation [2]. Currently, TCM categorizes acne syndromes into the following primary types: wind-heat in the lung meridian, damp-heat in the spleen and stomach, disharmony of the Chong and Ren meridians, and phlegm-stasis coagulation [2-3].

TCM, guided by TCM theory, exhibits significant advantages in its multi-component and multi-target characteristics. It demonstrates diverse mechanisms of action, including anti-inflammatory, antibacterial, and immunomodulatory effects, which align with the multifaceted pathogenesis of acne. Consequently, TCM presents promising application prospects and therapeutic potential in the treatment of acne. Inflammatory response is an important link in promoting the development of acne. Macrophages play a key role in the generation, development and regression of acne inflammation. TCM has been proven to have certain advantages in improving the role of macrophages in mediating acne inflammation [4].

Contemporary medical research indicates that the pathogenesis of acne is closely associated with androgens. In males, the production of androgens is primarily facilitated by the Leydig cells within the testes. In females, reproductive organs such as the ovaries and uterus serve as receptors for androgen expression, thereby establishing androgens as critically significant steroid hormones in the female physiology. Dehydroepiandrosterone (DHEA) and its sulfated form, DHEA sulfate, are transported via the androgen receptor protein (ARP) through the circulatory system into sebaceous gland cells, where they serve as precursors for the synthesis of testosterone (T), the primary androgen in humans. Approximately 1% to 2% of the free testosterone (T) in serum exhibits biological activity. This testosterone is converted into dihydrotestosterone (DHT) by the enzyme 5 α -reductase. DHT selectively binds to ARs in facial sebaceous glands, leading to hyperactive sebum secretion. The subsequent accumulation of lipids results in follicular occlusion, thereby promoting the formation of acne [5].

3. The mechanistic role of tanshinone in the treatment of acne vulgaris

In recent years, TCM has achieved a more comprehensive understanding of the pathogenesis of acne. Building upon the traditional theoretical framework of wind-heat, blood-heat, and lung-heat, TCM has expanded its perspective to include novel pathogenic factors such as damp-heat, blood stasis, kidney deficiency, and phlegm accumulation. Based on the core pathogenesis of acne induced by "heat," "dampness," "toxin," and "stasis," or the formation of acne due to prolonged consumption of spicy and greasy foods leading to damp-heat stagnation and upward steaming to the face, TCM predominantly employs formulas that clear heat, detoxify, cool the blood, and activate blood circulation for the treatment of acne [3]. For instance, formulations such as Loquat Lung-Clearing Decoction, Ephedra and Cinnamon with Four Substances Decoction, and Capillaris Decoction are commonly employed [6-8]. Through an analysis of the compatibility of the aforementioned prescriptions, it has been observed that *Salvia miltiorrhiza* (Danshen) is consistently included as a key herbal component, with a significantly higher dosage compared to other medicinal herbs. This leads to the inference that *Salvia miltiorrhiza* plays a substantial role and demonstrates therapeutic efficacy in the treatment of acne.

Salvia miltiorrhiza, commonly referred to as "Danshen," derives its name from its characteristic red root bark and purple flesh, which resembles the shape of ginseng. This herb exhibits a slightly cold nature and a bitter taste, and is renowned for its efficacy in promoting blood circulation, resolving stasis, and alleviating inflammation. In the treatment of acne, the active compound tanshinone is identified as the principal therapeutic constituent of *Salvia miltiorrhiza*. Tanshinones are lipophilic components extracted from the roots of *Salvia miltiorrhiza*, comprising over ten monomeric compounds including Tanshinone I and Tanshinone IIA. Ju Qiang employed semi-quantitative RT-PCR technology to demonstrate that tanshinone significantly downregulates the expression of AR mRNA in sebaceous gland cells (SZ95), reduces protein expression, and inhibits the binding of DHT to AR, thereby diminishing sebum secretion and mitigating acne formation [9].

Gao Lihong et al. conducted an experiment involving 30 male Wistar rats, which were randomly divided into three equal groups [10]. The first group received intragastric administration of tanshinone (400mg/Kg), while the second group served as the normal control group receiving 400mg/Kg physiological saline. The third group was administered diosgenin (400mg/Kg) intragastrically. All three groups initiated the treatment following the human chorionic gonadotropin stimulation test, with daily administration continuing for four consecutive weeks. Following the completion of the gavage procedure, the animals were euthanized by decapitation, and the testes were precisely excised. The tissues underwent fixation, embedding, sectioning, and staining processes. Utilizing the localization and qualitative analysis method, five microscopic fields were examined under light microscopy for each section. The average of the observation results from each section was calculated. Through the assessment of staining intensity and distribution, immunohistochemical scoring of Steroidogenic Factor-1 (SF-1) in Leydig cells was performed across experimental groups. The findings indicate that, compared to the normal control group, tanshinone may exert its anti-androgenic effects by suppressing SF-1 expression in Leydig cells, thereby reducing testosterone (T) secretion in the testicular interstitium. In addition, the seminal vesicle and prostate weight assay demonstrates that tanshinone exerts anti-androgenic effects through its antagonistic mechanism against testosterone propionate.

4. Synergistic research on the compatibility of *Scutellaria baicalensis* and *Salvia miltiorrhiza*

TCM emphasizes the principle of herbal compatibility, which maximizes the therapeutic efficacy of medicinal substances through rational combination. Formulations such as Wuwei Xiaodu Decoction, Zishen Xiegan Decoction, and Qingre Chushi Xiaocuo Decoction exemplify the synergistic combination of *Scutellaria baicalensis* (Huangqin) and *Salvia miltiorrhiza* (Danshen). Research has demonstrated that both *Salvia miltiorrhiza* and *Scutellaria baicalensis* exhibit significant inhibitory effects against *Propionibacterium acnes*.

TCM facial masks are extensively utilized in the treatment of acne. These masks are formulated by blending various TCM powders into a paste, characterized by their natural composition and non-irritating properties, which effectively minimize allergic reactions. They not only enhance cutaneous blood circulation and facilitate the absorption of active pharmaceutical ingredients but also effectively remove sebum and particulate matter from skin pores. Consequently, TCM facial masks have gained significant popularity among acne patients.

Song Weiqiang et al. conducted a study to analyze the antimicrobial activity of a *Scutellaria baicalensis*-*Salvia miltiorrhiza* facial mask formulation [11]. The researchers employed the two-fold serial microdilution method to determine the minimum inhibitory concentration (MIC) and minimum bactericidal concentration (MBC) of the formulation against *Propionibacterium acnes* and *Staphylococcus aureus*. The experimental results demonstrate that the *Scutellaria baicalensis*-*Salvia miltiorrhiza* compound mask formulation exhibits potent bactericidal efficacy against *Propionibacterium acnes* and *Staphylococcus aureus* within a 10-12 hour timeframe. This synergistic combination further substantiates the therapeutic potential of tanshinone in antimicrobial and anti-inflammatory applications.

5. Clinical application and combined therapy exploration of *Salvia miltiorrhiza* in acne treatment

Clinical studies have substantiated the extensive application of *Salvia miltiorrhiza* in acne treatment. Bao Benxia et al. observed the efficacy of TCM facial masks combined with modified Pipaqingfei Decoction in treating acne [6]. Ma Xiaohong et al. employed Mahui Siwu Decoction in conjunction with TCM facial masks to treat 45 cases of common acne [7]. While Zhang Cuiyue et al. demonstrated significant therapeutic outcomes by using modified Yinchenhao Decoction combined with TCM facial masks in 31 cases of acne associated with gastrointestinal damp-heat syndrome [8]. These clinical applications collectively underscore the remarkable efficacy and clinical value of *Salvia miltiorrhiza*.

The Chinese Acne Treatment Guidelines (2024 Revised Edition) classify acne into three degrees and four grades based on the nature of skin lesions. The classification is as follows: Mild (Grade I): Comedones; Moderate (Grade II): Inflammatory papules; Moderate (Grade III): Comedones, papules, and pustules; Severe (Grade IV): Cysts and nodules. Currently, moderate to severe acne is commonly treated with combination therapies, including oral Chinese herbal medicine combined with Chinese herbal facial masks, fire needle therapy combined with oral Chinese herbal medicine, and integrated traditional Chinese and Western medicine therapies [12].

In a clinical study conducted by Shi Xiao et al., 97 patients with moderate acne were randomized into two treatment groups: isotretinoin monotherapy group and isotretinoin combined with Runzao Decoction group [12]. The combination therapy demonstrated superior efficacy after 8-12 weeks of treatment and exhibited a lower recurrence rate at the 6-month follow-up. Similarly, Wu Youqing et al. conducted a randomized controlled trial involving 60 patients, comparing conventional therapy

(isotretinoin combined with clarithromycin) with a combination of TCM (Wuwei Xiaodu Decoction) and fire needle therapy [13]. The results indicated that the combination therapy group achieved significantly better outcomes in terms of both skin lesion improvement and psychological assessment scores after 4 weeks of treatment. A study conducted by Cui Tailun et al. involving 60 patients with conglobate acne demonstrated that the combination therapy of isotretinoin with Qinggan Qucuo Formula resulted in significantly greater improvement in skin lesions and fewer adverse reactions compared to the monotherapy group after an 8-week treatment period [14].

Based on the comprehensive analysis of the aforementioned clinical outcomes, it has been substantiated that the combined therapeutic approach, integrating TCM formulations with adjunctive treatments such as fire needle therapy or fruit acid peeling, demonstrates superior efficacy compared to monotherapy. Consequently, the implementation of combination therapy proves to be more effective in the treatment of acne vulgaris.

6. Post-acne hyperpigmentation: advances in therapeutic interventions

Acne, as a chronic inflammatory dermatological condition, is characterized by a recurrent course and often leaves erythema and hyperpigmentation on the skin, with severe cases potentially leading to scar formation [15]. Consequently, many patients experience issues such as appearance-related anxiety and psychological distress, which significantly impact their quality of life and occupational functioning. Consequently, an increasing number of acne patients are seeking treatments for post-acne hyperpigmentation. In contemporary Western medicine, prevalent therapeutic modalities include intense pulsed light (IPL) therapy, laser treatment, and chemical peels. However, these approaches may be cost-prohibitive and are often associated with adverse effects such as localized burning sensations and erythema. TCM offers distinctive therapeutic interventions for post-acne erythema and hyperpigmentation, including oral administration of herbal decoctions, topical application of herbal facial masks, and fire needle therapy. Xu Chang et al. conducted a study based on data regarding the treatment of post-acne erythema and pigmentation with TCM [16]. Kou Shu further analyzed the efficacy of TCM in addressing post-acne erythema and pigmentation, revealing that external application of TCM frequently employs herbs such as *Angelica dahurica*, *Bletilla striata*, *Poria cocos*, and *Typhonium giganteum* for these conditions [17]. With the continuous advancement of research on TCM in treating acne, significant progress has been made in addressing related issues such as pigmentation and erythema. This has led to the development of comprehensive strategies including internal TCM treatment, external TCM application, acupuncture therapy, and integrated TCM-Western medicine approaches [15]. Furthermore, modern technologies have been employed to enhance drug efficacy, such as utilizing corneosomes (CS) as carriers for Tanshinone IIA (CTS), which improves drug compatibility and prevents adverse effects [18]. Additionally, 3D printing technology has been utilized to develop 3D-printed mesh hydrogels containing cryptotanshinone for localized delivery in acne treatment [19]. These advancements provide patients with safer and more effective therapeutic options.

7. Conclusion

This study, through an analysis of the clinical application and therapeutic outcomes of *Salvia miltiorrhiza* in acne treatment, as well as the clinical efficacy of the *Salvia miltiorrhiza*-*Scutellaria baicalensis* combination, demonstrates that *Salvia miltiorrhiza* exerts its anti-acne effects by reducing androgen levels, while the *Salvia miltiorrhiza*-*Scutellaria baicalensis* combination exhibits potent bactericidal activity against *Propionibacterium acnes*. The study has demonstrated the

significant therapeutic potential of *Salvia miltiorrhiza* in acne treatment. However, current research predominantly relies on clinical application analysis, which is constrained by insufficient sample sizes, limited mechanistic exploration, and a lack of experimental investigations. Notably, the synergistic pharmacokinetics between tanshinone and baicalin remain unquantified. Future research necessitates the validation of findings through expanded clinical trials and multi-omics analysis. By leveraging modern technologies to further innovate treatment modalities, such as the tanshinone IIA nano-delivery system (enhancing bioavailability via chitosan carriers), the 3D-printed mesh-like hydrogel of cryptotanshinone, or the intelligent compatibility of traditional Chinese and Western medicine (e.g., combining baicalin to optimize anti-inflammatory and antibacterial dual pathways), there is potential to overcome therapeutic efficacy bottlenecks. These advancements warrant in-depth exploration to promote the modernization of TCM.

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