

Review

Meta-Analysis of the Clinical Efficacy of Thalidomide Combined With Traditional Chinese Medicine in the Treatment of Behcet's Disease

Kwun Kit Hung¹, Syu Yiu Michelle Ng¹, Sai Hei Fang¹ and Yan Ting Ip^{2,*}

¹ School of Stomatology, Jinan University, Guangzhou, China

² School of Public and Allied Health, Liverpool John Moores University, Liverpool, United Kingdom

* Correspondence: Yan Ting Ip, School of Public and Allied Health, Liverpool John Moores University, Liverpool, United Kingdom

Abstract: To systematically evaluate the clinical efficacy of thalidomide combined with traditional Chinese medicine (TCM), compared with monotherapy (either thalidomide or TCM monotherapy), in patients with Behçet's disease, and to perform a meta-analysis. Randomized controlled trials (RCTs) published from the inception of the databases to August 1, 2026, were systematically searched in the China National Knowledge Infrastructure (CNKI), Wanfang Data, VIP Database, PubMed, Web of Science, and Cochrane Library. Patients in the control groups received conventional thalidomide therapy, whereas those in the treatment groups received TCM in addition to conventional thalidomide therapy. A meta-analysis was performed to comprehensively evaluate the clinical efficacy of the two treatment approaches. A total of 10 studies were included in the meta-analysis. The pooled results showed that the clinical efficacy was significantly higher in the treatment group than in the control group (OR = 4.96, 95% CI: 2.78–8.83, $P < 0.00001$), with a statistically significant difference. Compared with conventional thalidomide therapy alone, thalidomide combined with TCM appears to be more effective in the treatment of Behçet's disease.

Keywords: behcet's disease; thalidomide; efficacy of traditional Chinese medicine; meta-analysis

1. Introduction

Behçet's disease (BD) is a chronic, relapsing, autoimmune inflammatory disorder, primarily characterized by vasculitis. Its typical clinical manifestations include recurrent oral aphthous ulcers, genital ulcers, uveitis, and skin lesions. In addition, BD can also involve multiple systems including the heart, large vessels, nervous system, gastrointestinal tract, and joints [1]. It has been reported that BD incidence is higher in the Mediterranean region, the Middle East, and the Far East (including Japan, Korea, and China) than in Western countries. The prevalence of BD in China has been estimated to be approximately 14 per 100,000 population. Consequently, the treatment of BD in China has been increasingly highlighted [1]. Current pharmacological treatments for BD include glucocorticoids, nonsteroidal anti-inflammatory drugs (NSAIDs), thalidomide, and colchicine [1].

Thalidomide is a first-line therapeutic drug for BD. It exerts immunomodulatory effects by inhibiting or activating various cytokines involved in immune responses and therefore plays an important role in managing BD [2]. Furthermore, several studies have also reported that thalidomide may provide greater therapeutic efficacy than colchicine [3], contributing to its widespread use in clinical practice. But the teratogenicity of thalidomide should not be neglected, as it may cause severe fetal malformations and adverse effects such as neuroaxonal degeneration with long-term use [1]. Therefore, thalidomide is contraindicated during pregnancy and should not be used in pregnant women.

Received: 10 July 2026

Revised: 17 August 2026

Accepted: 27 August 2026

Published: 31 August 2026



Copyright: © 2026 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

It has been reported that in recent years, research on traditional Chinese medicine (TCM) for immune-mediated disorders including Behçet's disease, systemic lupus erythematosus, and ankylosing spondylitis has achieved promising outcomes [4-5]. It has been suggested that Chinese herbal medicines can regulate qi-blood, nourish yin to dryness-suppressing, and harmonize yin-yang, thereby improving host autoimmune function and alleviating clinical symptoms [4]. With advances in medical practice, it has explored combination regimens of thalidomide plus TCM. Existing evidence demonstrates that TCM combined with thalidomide for Behçet's disease can markedly ameliorate clinical manifestations, enhance therapeutic effectiveness, reduce relapse rates, lower adverse events associated with high-dose pharmacotherapy, and offer convenient administration [6-7]. However, some studies hold the view that TCM therapies produce limited therapeutic benefits. Therefore, this study performed a systematic review and meta-analysis of clinical studies comparing thalidomide monotherapy versus thalidomide combined with TCM following the PRISMA framework. This work aims to compare the therapeutic effects of the two regimens and provide evidence-based data for clinical decision-making regarding treatment selection for BD.

2. Methods

2.1. Search Strategy

The Chinese databases were searched using the following Chinese keywords: "traditional Chinese medicine," "Chinese medicine," "Chinese herbal medicine," "Behçet's disease," "Huhuo disease," "Behçet disease," "thalidomide," and "Thalidomide." The English databases were searched using the keywords "Behçet's disease," "Traditional Chinese Medicine," and "thalidomide," in combination with relevant synonyms and related terms. A comprehensive literature search was conducted in the following electronic databases: PubMed, Cochrane Library, Web of Science, China National Knowledge Infrastructure (CNKI), Wanfang Data, and VIP Database. The search period extended from the inception of each database to August 1, 2026.

2.2. Inclusion and Exclusion Criteria

Inclusion criteria: (1) Randomized controlled trials (RCTs); (2) Patients with a confirmed diagnosis of Behçet's disease. All included studies were required to meet the diagnostic criteria established by the International Study Group/International Committee for Behçet's disease or other generally accepted diagnostic criteria; (3) The intervention group received thalidomide combined with traditional Chinese medicine. The control group received either thalidomide monotherapy or traditional Chinese medicine monotherapy; (4) The outcome measures included treatment rate, overall response rate, clinical efficacy, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and other relevant clinical outcomes.

Exclusion criteria: (1) Conference abstracts, reviews, studies with incomplete data, or unpublished studies; (2) Duplicate publications; (3) Studies for which the full text or essential information could not be obtained; (4) Studies published in languages other than Chinese or English; (5) Non-randomized controlled trials; (6) Animal experiments; (7) Studies in which Behçet's disease was mentioned in the title or abstract, but the specific diagnostic or inclusion criteria were not clearly stated in the main text; (8) Studies in which the control group received medications other than thalidomide, or the intervention group received traditional Chinese medicine alone or traditional Chinese medicine combined with medications other than thalidomide; (9) Studies in which Behçet's disease was mentioned in the title or abstract, but the treatment rate was not clearly reported in the main text.

2.3. Study Quality Evaluation

Three reviewers independently screened the literature according to the predefined inclusion and exclusion criteria. Data were extracted using a standardized, prespecified data extraction form, and the risk of bias was independently assessed. Duplicate records

were first removed, followed by screening of titles and abstracts and, subsequently, full-text articles. Any disagreements between reviewers were resolved through discussion or consultation with a third reviewer. The risk of bias in the included studies was assessed across relevant domains using the Cochrane risk-of-bias assessment tool in accordance with the Cochrane Handbook for Systematic Reviews of Interventions.

2.4. Statistical Analysis

Statistical analyses were performed in accordance with the Cochrane Handbook for Systematic Reviews of Interventions. For continuous outcomes, the weighted mean difference (WMD) was used as the effect measure. For dichotomous outcomes, odds ratios (ORs) were used as the effect measure. All effect estimates were reported with corresponding 95% confidence intervals (CIs) and point estimates.

Heterogeneity among the included studies was assessed initially. The statistical heterogeneity was quantitatively evaluated using the I^2 statistic. When substantial homogeneity was observed among the studies ($I^2 < 50\%$ or $P > 0.05$), a fixed-effect model was used for the meta-analysis. Otherwise, a random-effects model was applied.

3. Results

3.1. Literature Search Results

A total of 10 studies that met the predefined eligibility criteria were included in this meta-analysis [6-15]. All included studies were published in Chinese. The study selection process is presented in Figure 1.

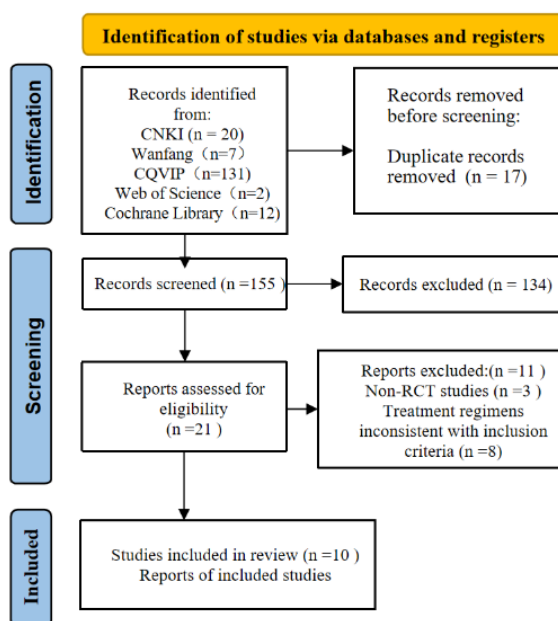


Figure 1. Prisma Flowchart of the Selection Process

3.2. Characteristics of the Included Studies

All 10 included studies provided detailed analyses of the intervention and control groups, and the baseline characteristics were comparable between the two groups [6-15]. All participants had a confirmed diagnosis of Behçet's disease. A total of 564 patients were included, comprising 283 patients in the intervention group and 281 patients in the control group. The sample sizes of the individual studies ranged from 17 to 40 participants. The main characteristics of the included studies are summarized in Table 1.

Table 1. Characteristics of the Included Studies.

Study ID	Sample size	Intervention		Treatment	Major outcomes*
		T/C	Intervention (T)	Intervention (C)	
Chen et al.(2018)	34/34		Shen's Decoction of Rehmannia Root, Scutellaria, Coptis and Smilax Glabra, Thalidomide	Thalidomide,50 mg/d	2 month A, B, C
Kong et al.(2023)	40/40		Thalidomide Tablets administered in two courses. Baise Buxie Granules	Thalidomide,100 mg/d	8 week A, B, C
Li et al. (2024)	31/31		Gancao Xiexin Decoction combined with thalidomide	Placebo plus thalidomide,50 mg/d-75mg/d	2 month A, D, E, F
Lin et al., (2011)	18/17		Thalidomide, Zhengqing Fengtongning Sustained-release Tablets	Thalidomide,100 mg/d	6 month A, B, E
Liu et al. (2015)	22/21		Oral thalidomide 75 mg/day plus Huiyan Zhuyu Decoction as tea substitute, 1 dose per day	Thalidomide,75 mg/d	3 month A, F
Ma et al. (2020)	25/25		thalidomide 50 mg/d, Wuwei Xiaodu Decoction, Lily Bulb and Rehmannia Decoction, Gancao Xiexin Decoction, Dosage	thalidomide tablets 50 mg/d	3 month A, B, C
Qu et al., (2016)	20/20		Oral thalidomide tablets, 50 mg/d, Yiqi Jiedu Quyu Formula, Decoct with water to 200 ml, divide into two doses to take in the morning and evening.	Oral thalidomide tablets, 50 mg/d	3 month A, B, D, E, F
Shen., (2011)	23/23		Glucosides of Paeony Capsules,600mg per dose, 2 times per day and oral thalidomide tablets, 50 mg per dose, twice daily	Total Glucosides of Paeony Capsules,600mg per dose, 2 times per day	6 month A, F
Zhang., (2014)	30/30		Self-formulated Indigo Powder for external use, once in the morning and once in the evening. Thalidomide, oral administration, once every night	Thalidomide,50 mg/d	8 weeks A, D, E, F
Zhang et al. (2018)	40/40		Oral thalidomide tablets, 2 tablets every night. Gancao Xiexin Decoction is added with water to 800 mL and decocted to approximately 250 mL, administered twice daily in the morning and evening.	Oral thalidomide tablets, 100mg/d	3 month A, F

*A: Clinical effects; B: Primary symptom response rate; C: Recurrence rate; D: Adverse effects; E: ESR, CRP; F: Comparison of healing time, clinical observation Indicators, remission period, seizure frequency, treatment Conditions, TCM syndrome efficacy, number of ulcers, serum inflammatory factors, immune function indexes, and erythrocyte sedimentation rate.

3.3. Quality Assessment of the Included Studies

All 10 included studies reported randomization. Among them, five studies used a random number table for sequence generation [6-15]; one study used block randomization [12]; one study used computer-generated randomization [13]; one study claimed to adopt a double-blind design without providing sufficient implementation details [7]. The

remaining two studies did not provide sufficient details regarding the randomization methods and were therefore judged as having an "unclear risk of bias" [14-15].

None of the 10 studies provided sufficient information regarding allocation concealment or blinding; therefore, the risk of bias for these domains was judged as "unclear." No evidence of selective reporting bias was identified in any of the 10 studies [6-15]. However, the information provided was insufficient to adequately assess the risk of other potential sources of bias, and these domains were therefore also judged as "unclear." The quality assessment of all included studies is presented in Figure 2 and Figure 3.

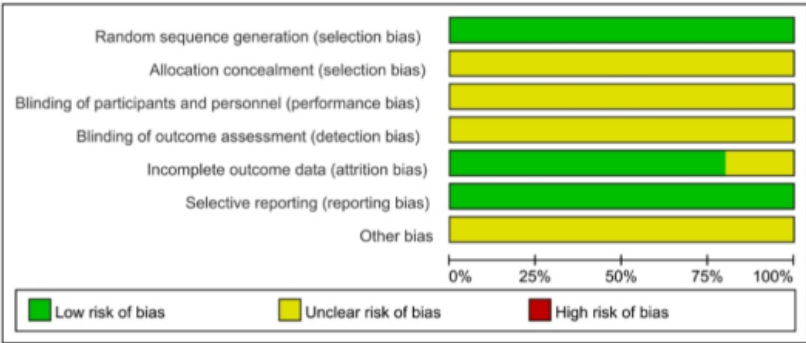


Figure 2. Quality Assessment Proportion Chart of Included Literature

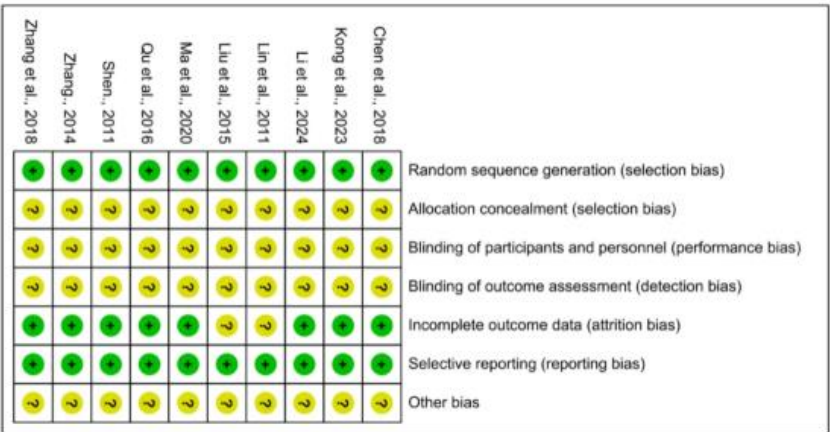


Figure 3. Summary Plot for Quality Assessment of Included Literature

3.4. Meta-Analysis Results

All 10 included studies evaluated clinical efficacy as an outcome measure [6-15]. Overall, there was no significant heterogeneity among the included studies ($P = 0.99$, $I^2 = 0\%$); therefore, a fixed-effect model was used for the meta-analysis. The results showed that the combination of thalidomide and traditional Chinese medicine was associated with significantly greater clinical efficacy than thalidomide alone ($OR = 4.96$, $95\% CI: 2.78-8.83$, $P < 0.00001$). The difference was statistically significant. The results are presented in Figure 4.

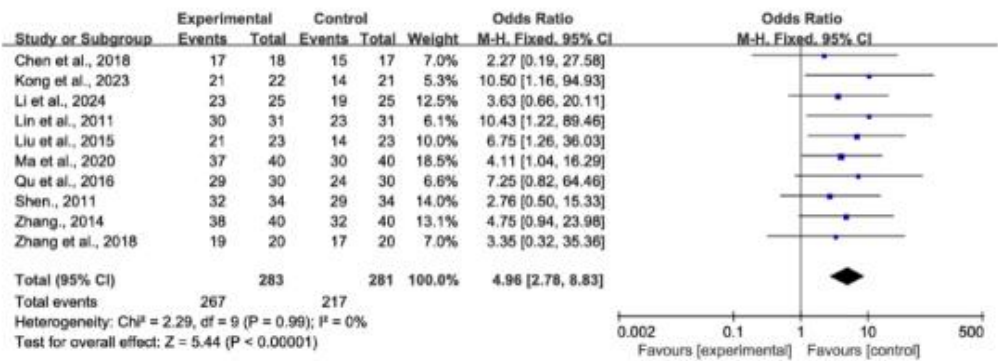


Figure 4. Forest Plot of Meta-Analysis for Odds Ratio (or) of Clinical Efficacy.

3.5. Sensitivity Analysis and Publication Bias Analysis of Clinical Efficacy

A sensitivity analysis was performed by sequentially excluding each study included in the meta-analysis. No significant changes were observed in the pooled results after the exclusion of any individual study, indicating that the results of this meta-analysis were relatively stable and robust.

To assess the risk of publication bias regarding clinical efficacy, an inverted funnel plot was constructed using the OR values on the horizontal axis and the standard error of the log-transformed OR [SE(log[OR])] values on the vertical axis. The funnel plot showed an apparent asymmetry between the left and right sides, suggesting a potential risk of publication bias for the clinical efficacy outcome. This potential risk of bias may be attributable to substantial differences in the inclusion criteria adopted by the included studies. The results are presented in Figure 5.

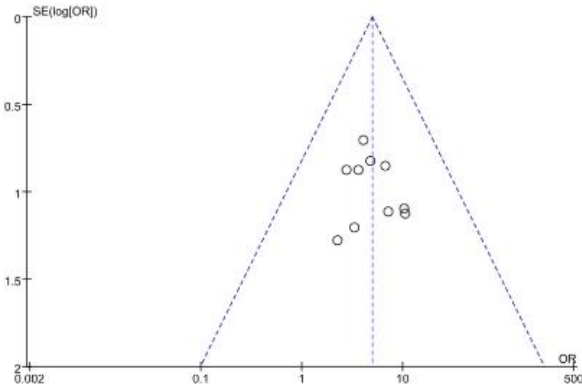


Figure 5. Funnel Plot of Clinical Efficacy

4. Discussion

Using the PRISMA framework, we identified and included 10 relevant randomized controlled trials (RCTs) from major Chinese- and English-language literature databases for this meta-analysis. The results demonstrated that, compared with thalidomide monotherapy, the combination of traditional Chinese medicine (TCM) and thalidomide significantly improved clinical efficacy in the treatment of Behçet's disease. These findings provide an evidence base for treatment selection and clinical decision-making in Behçet's disease and quantitative evidence supporting an integrative Chinese and Western medicine treatment strategy. They further suggest that TCM may have the potential to enhance therapeutic efficacy and reduce treatment-related toxicity by modulating immune dysregulation and alleviating inflammatory injury.

The main clinical manifestations of Behçet's disease include recurrent oral ulcers, genital ulcers, uveitis, and skin lesions, and the disease may also involve multiple organ

systems [16]. Previous studies have reported favorable clinical outcomes with the combination of TCM and thalidomide in patients with Behçet's disease [7,10,14]. For example, total glucosides of paeony (TGP) have been used in elderly patients with Behçet's disease aged >60 years and have demonstrated significant efficacy in alleviating mucosal lesions. Following treatment, the expression levels of TLR2 and TLR4 mRNA in the mucosal lesions of patients with Behçet's disease were significantly reduced compared with baseline levels [16]. In addition, treatment with tripterygium glycosides has been reported to reduce serum levels of IL-1 β , TNF- α , and IFN- γ , thereby reducing abnormally elevated proinflammatory cytokine levels [16].

Regarding the TCM interventions evaluated in the 10 studies included in the present meta-analysis, although some heterogeneity existed among the herbal prescriptions, the principal herbal components were generally concentrated on single herbs or compound formulations with immunomodulatory, anti-inflammatory, and vascular-protective properties. For example, some of the prescriptions included *Glycyrrhiza uralensis* (licorice) and *Rheum palmatum* (rhubarb). In terms of theory of traditional Chinese medicine and pharmacological mechanism, licorice has similar effects with glucocorticoids, and has the functions of anti-ulcer, anti-inflammatory and anti-allergic, and rhubarb has anti-infective, analgesic and anti-inflammatory effects. Processed rhubarb (*Rheum palmatum*) may be particularly effective in reducing inflammatory exudation and tissue necrosis in oral ulcers [16].

Moreover, several studies have shown the positive effects of TCM in the treatment of other immune-mediated diseases. Studies have shown that TCM may exert significant therapeutic effects in systemic lupus erythematosus (SLE), with potential mechanisms involving multitarget regulation of immune-cell function, systemic suppression of inflammatory signaling pathways, reduction of renal injury, and protection of multiple organs [17]. A study on animals also showed that astragalus polysaccharides can exert therapeutic effects by correcting dysbiosis of the gut microbiota and reducing systemic inflammatory responses. Furthermore, astragalus polysaccharides improved the cognitive dysfunction of SLE mice by protecting the blood-brain barrier and relieving oxidative damage in brain tissue [17].

The present study has several limitations. First, the number of high-quality RCTs evaluating the combination of TCM and thalidomide for Behçet's disease remains limited worldwide. Most available studies were conducted at single centers and predominantly involved East Asian populations, with a lack of large-scale, multinational, and multiethnic data. Consequently, only 10 studies were ultimately included, with a relatively small overall sample size of just over 500 patients. Furthermore, some studies had methodological deficiencies in random sequence generation, allocation concealment, and implementation of double blinding, which may have introduced selection and measurement biases and thereby affected the robustness of the pooled estimates. Second, considerable differences existed among the studies in terms of TCM prescriptions, dosages, treatment durations, and thalidomide regimens, resulting in substantial clinical heterogeneity. Third, most of the original studies had relatively short follow-up periods, generally ranging from 8 to 24 weeks, and lacked adequate assessment of long-term relapse rates, cumulative disease damage, and long-term safety. Therefore, the present findings are more applicable to the evaluation of short-term efficacy, whereas the long-term benefit-risk profile should be interpreted with caution.

Future research should focus on the following aspects: (1) conducting multicenter, large-sample, randomized, double-blind, placebo-controlled clinical trials and adhering strictly to the CONSORT statement for reporting to improve the level of evidence; (2) extending the follow-up period to at least 1–2 years and systematically collecting key endpoints, including relapse rates, reduction or discontinuation of glucocorticoids or immunosuppressive agents, and progression of organ involvement; (3) adopting standardized TCM preparations, such as extracts with fixed proportions or granule formulations, to reduce heterogeneity among prescriptions and conducting dose-response studies; and (4) incorporating biomarker-based subgroup analyses, including

cytokine profiles, TLR expression, and the proportions of T-cell subsets, to identify patient characteristics associated with greater benefit from combination therapy. These approaches may enable a more comprehensive and accurate evaluation of the efficacy and safety of TCM combined with thalidomide for Behçet's disease and further elucidate the distinctive therapeutic potential and clinical value of TCM in this refractory autoimmune disease.

References

1. National Health Commission of the People's Republic of China, *Behçet's disease/Behçet's syndrome (2025 edition)*, *Chinese Practical Journal of Rural Doctor*, vol. 33, no. 3, 2025.
2. H. and Y. C. Wang, "Clinical observation of Baise Buxie Granules combined with thalidomide in the treatment of Behçet's disease," *China's Naturopathy*, vol. 31, no. 20, pp. 95–98, 2023, doi: 10.19621/j.cnki.11-3555/r.2023.20.17.
3. D. Hu and Y. X. Lü, "Clinical observation of thalidomide in the treatment of 36 patients with Behçet's disease," *Modern Medicine & Health*, vol. 27, no. 14, pp. 2169–2170, 2011.
4. Y. C. Ma and Q. Zhou, "Effects of Guizhi Shaoyao Zhimu Decoction combined with thunder fire moxibustion in patients with ankylosing spondylitis," *Henan Medical Research*, vol. 35, no. 11, pp. 3802–3808, 202.
5. J. X. Chen, "Traditional Chinese medicine therapies for different subtypes of lupus erythematosus," *Shanxi Market Herald*, 2023.
6. L. L. Liu, H. W. Shao, and M. L. Gao, "Clinical observation on 23 cases of oral ulcer in Behçet's disease treated by integrated traditional Chinese and Western medicine," *Chinese Journal of Ethnomedicine and Ethnopharmacy*, vol. 24, no. 21, pp. 68–70, 2015.
7. Z. X. Lin, Y. Q. Jiang, Y. C. Dai, L. S. Dai, Z. X. Chen, and H. Y. Sun, "Therapeutic effect of low-dose thalidomide combined with traditional Chinese medicine in the treatment of Behçet's disease," *Practical Pharmacy and Clinical Remedies*, vol. 14, no. 1, pp. 57–61, 2011, doi: 10.14053/j.cnki.ppcr.2011.01.013
8. W. W. Chen, X. Su, and P. A. Shen, "Clinical observation of Shen's Shengdi Qinlian Tufuling Decoction combined with thalidomide in the treatment of Behçet's disease," *Shanghai Journal of Traditional Chinese Medicine*, vol. 52, no. 3, pp. 34–38, 2018, doi: 10.16305/j.1007-1334.2018.03.013.
9. H. and Y. C. Wang, "Clinical observation of Baise Buxie Granules combined with thalidomide in the treatment of Behçet's disease," *China's Naturopathy*, vol. 31, no. 20, pp. 95–98, 2023, doi: 10.19621/j.cnki.11-3555/r.2023.20.17.
10. D. Li, Y. Chen, Y. X. Zhao, Q. S. Wang, and S. L. Ma, "Clinical efficacy study of modified Gancao Xiexin Decoction in the treatment of Behçet's disease (BD)," *Database of Chinese Sci-Tech Periodicals - Medicine*, 2024, advance online publication.
11. Y. L. Zhang, Q. Li, F. Z. Wang, W. G. Zhang, C. Y. Zhou, and J. J. Li, "Analysis of efficacy and safety of Xiexin Decoction combined with low-dose thalidomide in Behçet's disease patients with oral mucosal lesions," *Journal of Hunan University of Chinese Medicine*, vol. 38, no. 10, pp. 1179–1183, 2018, doi: 10.3969/j.issn.1674-070X.2018.10.020.
12. H. R. Qu, S. J. Xi, Z. Y. Cao, and Y. W. Zheng, "Clinical observation of Yiqi Jiedu Quyu Decoction combined with thalidomide in the treatment of Behçet's disease," *Shanghai Journal of Traditional Chinese Medicine*, vol. 50, no. 5, pp. 84–85, 2016, doi: 10.16305/j.1007-1334.2016.05.016.
13. Z. Y. Zhang, "Clinical research on treating Behçet's syndrome with self-designed Qingdai San," *Clinical Journal of Chinese Medicine*, vol. 6, no. 35, pp. 121–123, 2014.
14. D. Shen, "Observation on therapeutic effect of total glucosides of paeony combined with thalidomide in 23 cases of Behçet's disease," *China Modern Doctor*, vol. 49, no. 13, p. 36, 2011.
15. H. X. Ma, X. H. Liang, and X. F. Ge, "Clinical observation on thalidomide combined with traditional Chinese medicine in the treatment of Behçet's disease," *Chinese Medicine Modern Distance Education of China*, vol. 18, no. 19, pp. 126–129, 2020, doi: 10.3969/j.issn.1672-2779.2020.19.050.
16. K. L. Liu and L. Y. Zhang, "Research progress on traditional Chinese medicine in the treatment of Behçet's disease," *CJGMCM (Guangming Journal of Chinese Medicine)*, vol. 38, no. 16, pp. 3256–3259, 2023, doi: 10.3969/j.issn.1003-8914.2023.16.055.
17. X. Y. Xu, S. M. Liang, R. Li, R. Luo, G. M. Zheng, and X. F. Pang, "Research progress in traditional Chinese medicine for systemic lupus erythematosus," *Journal of Practical Traditional Chinese Internal Medicine*, 2026, advance online publication.

Disclaimer/Publisher's Note: The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of Publisher and/or the editor(s). Publisher and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.