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Research Progress on Magui Jiangcao Wenfei Yin in the Treatment of Rheumatoid Arthritis-Associated Interstitial Lung Disease

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Abstract: ***Rheumatoid arthritis (RA) is an autoimmune disease characterized pathologically by synovial and vascular inflammation. Its onset is often insidious and frequently involves multiple systems. Due to the abundant connective tissue and vascular structures in the lungs, RA most commonly affects the lungs and often secondary interstitial lung disease (ILD), which severely impacts patient prognosis. Currently, there is a lack of standardized clinical protocols for treating RA-associated ILD (RA-ILD), and in traditional Chinese medicine (TCM) practice, there is inconsistency between syndrome patterns and disease progression. This article reviews the progress in integrated Chinese and Western medicine diagnosis and treatment of RA-ILD, and explores the clinical efficacy and modern pharmacological research of Magui Jiangcao Wenfei Yin, aiming to provide a reference for future clinical management of this condition.***

Keywords: Rheumatoid arthritis, Interstitial lung disease, Magui Jiangcao Wenfei Yin, Integrated Chinese and Western medicine**.**

1. Introduction

Rheumatoid arthritis (RA) is an autoimmune inflammatory disease characterized clinically by morning stiffness, pain, swelling, and joint deformity. Its fundamental pathological feature is synovial inflammation. Beyond articular manifestations, RA can also involve the lungs, heart, kidneys, and other organs. Owing to the abundant connective tissue and vasculature in the lungs, pulmonary complications are the most common, with interstitial lung disease being a typical clinical presentation, termed rheumatoid arthritis-associated interstitial lung disease (RA-ILD). ILD is one of the most frequent systemic manifestations of connective tissue diseases [1].

Traditional Chinese medicine (TCM) demonstrates unique advantages in the management of RA-ILD. Based on theories such as “lung bi” (lung obstruction) and “phlegm-rheum” (phlegm-fluid retention), it emphasizes treatment principles of warming the lung to transform rheum and activating blood to unblock collaterals. Magui Jiangcao Wenfei Yin is a compound prescription composed of Magui Tongbi Granule and the classic formula Gancao Ganjiang Decoction. Magui Tongbi Granule originates from Mahuang Fuzi Xixin Decoction in the Treatise on Cold Damage (Shang Han Lun) and has effects of warming yang, dispersing cold, unblocking bi, and relieving pain. Gancao Ganjiang Decoction derives from the Essentials from the Golden Cabinet (Jin Gui Yao Lue) and is skilled in warming the lung, transforming rheum, and benefiting qi and harmonizing the middle. The combined use of these two formulas can not only relieve RA joint symptoms but also improve pulmonary interstitial lesions.

In recent years, clinical observations have shown that Magui Jiangcao Wenfei Yin has certain efficacy in improving pulmonary function parameters (e.g., DLCO, FVC) and alleviating symptoms such as cough and dyspnea in RA-ILD patients, with relatively few adverse reactions. However, most existing studies are small-sample observational trials lacking support from multi-center randomized controlled trials (RCTs), and the specific targets and molecular mechanisms remain to be further explored. Future research should integrate network pharmacology, metabolomics, and other technologies to elucidate the multi-component, multi-target network of this compound formula, and to verify its long-term efficacy and safety through high-quality clinical trials, thereby providing more reliable evidence for integrated Chinese and Western medicine treatment of RA-ILD.

2. Western Medicine Research on RA-ILD

2.1 Epidemiology of RA-ILD

The mortality rate of RA-ILD is significantly higher than that of general RA. The median survival time after diagnosis of RA-ILD is only 3–7 years, which is markedly shorter compared to RA patients without ILD and the general population [2]. It has been reported that the five-year mortality rate for RA-ILD ranges from 39% to 60% [3].

2.2 Pathological Mechanisms of RA-ILD

The etiology and pathogenesis of RA-ILD remain incompletely understood in modern medicine. Several risk factors for developing ILD in RA patients have been identified, including older age, male sex, smoking, and positivity for rheumatoid factor (RF) or anti-cyclic citrullinated peptide antibodies (ACPA). RA-ILD results from a combination of genetic, immunological, and environmental factors, with the core being autoimmune-mediated chronic inflammation and aberrant repair processes leading to pulmonary fibrosis.

The main pathological features of RA-ILD include focal

proliferation of fibroblasts, extracellular matrix deposition, and alveolar sac-like dilation in lung tissues [4]. These changes cause distortion of the normal lung architecture and reduce the effective gas exchange area in distal regions, eventually leading to respiratory failure and death. RA, through autoantibodies (RF, anti-CCP antibodies, etc.), recognizes citrullinated peptides, activates the complement system, and recruits neutrophils, macrophages, and lymphocytes, promoting the release of inflammatory cytokines, triggering immune responses that transfer to the lungs and cause alveolar epithelial injury, resulting in ILD. Indeed, relevant studies have found that anti-CCP antibodies are associated with the occurrence of RA-ILD [5]. During this chronic inflammatory process, activated inflammatory cells release TGF-β, interleukins, and other factors through signaling pathways, ultimately leading to fibroblast activation and failure of repair mechanisms, culminating in pulmonary fibrosis. Additionally, studies on smoking history, sex, and MUC5B gene polymorphisms have provided insights into the potential genetic predisposition for fibrosis development in RA-ILD [6]. Some scholars reported that T cells stimulated by citrullinated HSP90β produced interferon-gamma (IFN-γ), suggesting a tendency toward a T-helper 1 (Th1) immune response, which is likely involved in the pathogenesis of RA-ILD [7].

2.3 Clinical Classification of RA-ILD

Based on radiological and histological findings, RA-ILD is typically classified into usual interstitial pneumonia (UIP), non-specific interstitial pneumonia (NSIP), and organizing pneumonia (OP). Radiologically, UIP is characterized predominantly by subpleural or basal honeycombing; histologically, it shows areas of dense fibrosis admixed with relatively normal parenchyma, with fibroblastic foci interspersed [8]. It is the most common and also the poorest-prognosis pattern of RA-ILD [9]. Compared with UIP, NSIP has a better prognosis, and its characteristic HRCT feature is ground-glass opacities with subpleural sparing [10]. OP is a non-specific inflammatory response of lung tissue to certain stimuli or injury, with pathological features of polypoid plugs within distal airways, composed mainly of fibroblasts, myofibroblasts, and loose connective tissue matrix [11].

3. Traditional Chinese Medicine Research on RA-ILD

There is no corresponding disease name for RA-ILD in TCM. Based on clinical manifestations such as dyspnea, cough, sputum production, and reduced pulmonary function, it is categorized under the scope of “lung bi” (lung obstruction) and “lung wei” (lung atrophy).

3.1 Etiology and Pathogenesis

The core pathogenesis of this disease is considered as “root deficiency with branch excess.” The root deficiency mainly involves deficiency of the lung, spleen, and kidney viscera, while the branch excess mainly manifests as intermingled phlegm and blood stasis. When lung qi is weak and defensive function is impaired, exogenous pathogenic factors (six excesses) can easily invade the lung. Spleen deficiency leads to failure in transporting and transforming body fluids, causing fluid retention and phlegm formation. Kidney qi deficiency results in failure to grasp qi, leading to dyspnea. Chronic illness damages the collaterals, and qi deficiency fails to promote blood circulation, causing blood stasis. Phlegm and stasis mutually obstruct the lung collaterals, depriving the lung of nourishment, and clinically manifesting as dyspnea, cough, and expectoration.

Professor Wang Guangyu holds that the pathogenesis of this disease should be investigated based on patients’ clinical characteristics. Exogenous pathogens invade the body through the skin and muscles; wind, cold, dampness, heat, and toxin obstruct the meridians and joints, causing pain and bi syndrome (joint obstruction). As the lung is the “canopy” (upper energizer) and connects with the defensive exterior, it governs qi and respiration. Repeated exogenous pathogen invasion or deficiency of healthy qi allows the pathogenic factors to linger, progressing from the exterior to the interior. Since the lung is associated with the skin and hair, it is first affected, leading to lung bi [12].

Professor Zhu Yuelan believes that the key pathogenesis lies in phlegm and stasis obstructing the collaterals. External pathogens invade the body when healthy qi is deficient and cannot expel them. Long-standing pathogenic retention blocks the flow of qi, blood, and body fluids, leading to qi stagnation and blood stasis, which obstruct the joints and meridians, causing pain. Prolonged bi syndrome results in improper distribution of fluids, which coalesce into phlegm; concurrently, blood stasis obstructs the water passages, causing qi congestion and fluid retention, further promoting phlegm production. Phlegm turbidity and blood stasis intertwine and become stubborn, making the disease protracted and difficult to cure. The lung is a delicate organ; if pathogenic factors linger and stagnate in the lung, obstructing the lung collaterals, lung qi cannot disperse and descend normally, causing lung bi. Over time, phlegm and stasis transform into heat, consuming qi and yin; the lung tissues lose nourishment, and the nature of the disease shifts from excess to deficiency, resulting in lung wei. Therefore, timely addition of herbs to resolve phlegm, remove stasis, unblock collaterals, and disperse nodules is crucial for addressing the pathogenesis [13].

Professor Chao Enxiang classifies ILD within the category of lung wei. Based on clinical experience, he summarizes the basic pathogenesis as “lung heat leading to wilting,” a pattern of root deficiency with branch excess—deficiency of lung and kidney qi and yin as the root, and intermingled phlegm and stasis as the branch. His treatment principles are supplementing qi and nourishing yin, regulating and supplementing the liver and kidney, and activating blood to resolve stasis [14].

3.2 Clinical Staging

3.2.1 Lung Bi Stage (Active Stage)

Patients in the lung bi stage present with cough, wheezing, chest tightness, and progressively worsening dyspnea, often accompanied by fever and sputum production, with rapid disease progression. Imaging commonly shows ground-glass

opacities or consolidations. The lung is a delicate organ, opening to the nose and connecting with the skin; when six excess pathogenic factors invade the body, they first attack the lung. The main pathogenesis of lung bi is pathogenic factors impairing the lung, causing failure in dispersion and descending and obstruction of lung qi, predominantly excess patterns. As recorded in Differentiation of Syndromes (Bian Zheng Lu): "The development of lung bi from qi deficiency is unknown to all... when lung qi is injured, wind-cold-damp pathogens fill the lung orifices and cause bi." Treatment focuses on dispelling pathogenic factors while taking care to protect qi and yin.

Director Zhang Changxi believes that in the "lung bi" stage, the pathological core is pathogenic obstruction and phlegm coagulation, and treatment should emphasize dispelling pathogens, clearing the lung, and transforming phlegm [15]. Professor Wang Tan proposed the "two stages and seven syndromes" concept, with treatment principles of "warming the lung, supporting yang, removing bi, and unblocking collaterals." When pathogens are dominant, treatment focuses on dispelling them through warming lung to transform rheum, clearing and dispersing latent fire, and draining damp-heat; when pathogens are weak and bi is mild, supporting yang, unblocking bi, and dredging collaterals are emphasized [16].

3.2.2 Lung Wei Stage (Chronic/Persistent Stage)

The lung wei stage manifests as persistent dry cough or scanty sticky sputum, dyspnea and shortness of breath on exertion, fatigue, and other signs of healthy qi deficiency. Imaging commonly shows honeycomb lung, traction bronchiectasis, and other fibrotic changes. Lung wei is characterized by the lung tissues losing nourishment and becoming weak and useless. Prolonged illness consumes healthy qi, leading to deficiency of lung qi and yin, or deficient fire flares upward, scorching fluids into phlegm; the lung loses nourishment, and long-standing obstruction of lung collaterals impairs blood flow, eventually causing intermingled phlegm and stasis.

Professor Zhang Hongchun believes that lung wei is "atrophy of lung substance and atrophy of lung function," emphasizing equal importance on "supplementation" and "unblocking." On one hand, it requires supplementing qi and nourishing yin, and reinforcing lung and kidney to strengthen the root; on the other hand, it needs removing stasis, draining dampness, and unblocking collaterals to restore patency [17]. Professor Wang Guangyu, in the middle and especially late stages of disease progression, pays more attention to supporting healthy qi, focusing on supplementing lung and kidney and unblocking collaterals to resolve stasis, aiming to address both overall deficiency and limb obstruction [18].

4. Composition and Pharmacological Actions of Magui Jiangcao Wenfei Yin

Magui Jiangcao Wenfei Yin originated from the empirical formula of Professor Wang Yue, a renowned TCM practitioner in Jiangsu Province. It is composed of his empirical Magui Tongbi Granule combined with Gancao Ganjiang Decoction, comprising eight herbs including Ephedrae Herba (Mahuang), Cinnamomi Ramulus (Guizhi), Glycyrrhizae Radix et Rhizoma Praeparata cum Melle (Zhigancao), Zingiberis Rhizoma (Ganjiang), and Saposhnikoviae Radix (Fangfeng).

4.1 Main Components and Pharmacological Actions of Magui Tongbi Granule

Based on existing experiments and clinical applications, Magui Tongbi Granule shows significant efficacy in RA of the cold-dampness obstruction pattern [19].

Ephedrae Herba (Mahuang): First recorded in Shennong's Classic of Materia Medica, Mahuang has primary effects of inducing sweating to release the exterior, ventilating the lung to relieve wheezing, promoting diuresis to reduce edema, and dispersing cold to unblock stagnation. Modern pharmacology shows that Mahuang's main chemical constituents include alkaloids, flavonoids, volatile oils, organic acids, amino acids, etc. Among them, ephedrine is the main analgesic component, and pseudoephedrine is an effective anti-inflammatory substance; its heat-clearing and analgesic effects are crucial in treating bi pain [20]. Professor Wang holds that Mahuang has vessel-unblocking and analgesic effects in the treatment of rheumatic bi, thus it is widely used in wind-cold-dampness bi [21].

Cinnamomi Ramulus (Guizhi): As the minister herb, Guizhi is pungent, sweet, and warm, belonging to the lung, heart, and bladder meridians. Its main effects include inducing sweating and relieving muscle tension, supporting yang and transforming qi, suppressing upward qi counterflow, and warming and unblocking meridians. Clinically, it is used for external wind-cold, joint bi pain, palpitations, phlegm-rheum, etc. Modern pharmacological studies indicate that the main chemical components of Guizhi are volatile oils (mainly cinnamaldehyde), organic acids, glycosides, tannins, steroids, coumarins, etc. [22]. Research shows that the volatile oil in Guizhi has significant anti-inflammatory effects, with cinnamaldehyde being the main active component, reducing inflammatory cytokine release via NF-κB pathway activation. Additionally, animal studies found that cinnamaldehyde effectively inhibits the upregulation of NF-κB target genes and the expression of COX-2 and iNOS in aged rats, exerting anti-inflammatory effects through multiple targets [23]. Furthermore, cinnamaldehyde has also been found to possess analgesic effects [24]. The combined use of Mahuang and Guizhi acts synergistically; studies show that their combination improves efficacy, produces synergistic effects, and reduces adverse reactions caused by Mahuang alkaloids [25].

Saposhnikoviae Radix (Fangfeng): Fangfeng has effects of dispelling wind and releasing the exterior, eliminating dampness and relieving pain, and calming wind to stop convulsions. It is commonly used for wind-cold colds, rubella itching, rheumatic bi pain, etc. Modern pharmacological studies show that active components in Fangfeng, including chromones, coumarins, and volatile oils, have analgesic and anti-inflammatory effects. Both the petroleum ether extract and n-butanol extract of Fangfeng exhibit anti-RA activity by effectively inhibiting the proliferation of RA fibroblast-like synoviocytes [26].

4.2 Classical Applications and Modern Research on

Gancao Ganjiang Decoction

Gancao Ganjiang Decoction is an important formula from the Treatise on Cold Damage and Miscellaneous Diseases. The original composition is Glycyrrhizae Radix et Rhizoma Praeparata (Zhigancao, 4 liang) and Zingiberis Rhizoma (Ganjiang, 2 liang), with a ratio of 2:1. The larger dosage of Zhigancao enhances the reinforcing effect while moderating the harsh and dry nature of Ganjiang to prevent yin injury. Ganjiang is warming but mobile, while Zhigancao is stationary but nourishing; together they provide dynamic and static balance, warming yang without dissipation. Gancao Ganjiang Decoction centers on "warming yang and supplementing deficiency," restoring middle energizer yang through the method of pungent and sweet generating yang, while also addressing upper energizer deficiency-cold. Although simple in composition, the formula has good clinical efficacy; many physicians believe it can "supplement the earth to generate metal," i.e., nourishing the lung by supplementing the spleen and stomach. It is a basic formula commonly used in modern clinical practice for lung wei, asthma, vertigo, frequent urination, and other conditions [27].

Glycyrrhizae Radix et Rhizoma Praeparata (Zhigancao): Its chemical constituents mainly include triterpenoid saponins, flavonoids, polysaccharides, coumarins, and alkaloids, with pharmacological effects including anti-inflammatory, immunomodulatory, and antioxidant activities [28].

Zingiberis Rhizoma (Ganjiang): Its main chemical constituents include 6-gingerol, α-zingiberene, geraniol, β-bisabolene, etc., with various pharmacological effects such as anti-inflammatory, antioxidant, and antitumor activities [29].

Zhang Qianyun et al. found that the combination of Zhigancao and Ganjiang exhibits synergistic effects. Using UPLC-LTQ-Orbitrap-MS technology to study the compatibility changes, they found that after combination, the dissolution of licochalcone, glabrone, and sanggenon increased, which may be the result of the synergistic interaction [30]. Another study using network pharmacology analysis of Gancao Ganjiang Decoction suggested that inflammation and immune regulation may be important mechanisms for its therapeutic efficacy [31].

4.3 Synergistic Effects of Combined Medication

Mahuang and Guizhi synergistically ventilate lung qi; Ganjiang and Zhigancao work together to warm the lung, transform rheum, and strengthen the spleen and harmonize the middle; Fangfeng dispels wind, disperses cold, removes dampness, and also relieves pain. All herbs combined achieve the effects of dispelling wind and dispersing cold, warming the lung and transforming rheum, and unblocking collaterals to remove bi.

Studies have found that Mahuang–Guizhi compatibility shows obvious antagonistic toxicity, with marked toxicity reduction and efficacy enhancement; Guizhi significantly reduces the cumulative toxicity caused by ephedrine [32]. Moreover, the anti-inflammatory effect of the combination is more pronounced in vivo than that of either herb alone. Guizhi–Zhigancao compatibility enhances the effect of warming meridians and unblocking vessels, consistent with TCM synergy theory [33]. Xia Jinjin et al. [34], using network pharmacology analysis, identified 115 common targets for Mahuang–Zhigancao, with key active components possibly including quercetin and kaempferol. Their analysis indicated that these key active components possess anti-inflammatory, antioxidant, and other pharmacological activities.

Magui Jiangcao Wenfei Yin integrates the "dispelling wind and removing dampness" action of Magui Tongbi Granule and the "warming lung and transforming rheum" action of Gancao Ganjiang Decoction. This aligns with the TCM understanding of RA-ILD as "root deficiency with branch excess and phlegm-stasis obstructing collaterals," and its multi-target therapeutic advantages are supported by modern pharmacological mechanisms. This research provides an important scientific basis for TCM treatment of RA-ILD and opens new avenues for developing integrated Chinese-Western medicine therapeutic approaches.

5. Exploration of the Mechanisms of Action of Magui Jiangcao Wenfei Yin

5.1 Anti-inflammatory and Immunomodulatory Effects

As analyzed above, Mahuang, Guizhou, Zhigancao, Ganjiang, etc., all possess anti-inflammatory and immunomodulatory effects, and their combined efficacy is significantly enhanced. These herbs together synergistically inhibit inflammatory responses, regulate imbalanced immune functions, and alleviate pulmonary inflammatory injury through multiple targets and pathways.

Zhu Fenglin et al. [35] demonstrated through animal experiments that Magui Tongbi Granule, an important component of Magui Jiangcao Wenfei Yin, inhibits LPS-induced PGE2 expression in RAW264.7 cells. This result, together with its inhibitory effects on histamine- induced capillary permeability increase and carrageenan- induced rat paw edema, suggests that the anti-inflammatory mechanism of this formula may be related to the inhibition of PGE2 expression. Wang Dong et al., using network pharmacology analysis, found that the important mechanisms of Gancao–Ganjiang compatibility involve anti-inflammatory and immunomodulatory activities.

5.2 Inhibition of Pulmonary Fibrosis

Pulmonary fibrosis is a complex pathological process. Magui Jiangcao Wenfei Yin may intervene through inhibiting pro-fibrotic factors, suppressing fibroblast activation and proliferation, and counteracting oxidative stress:

5.2.1 Inhibition of Pro-fibrotic Factor TGF-β1

TGF-β1 is a crucial pro-fibrotic factor in the progression of pulmonary fibrosis [36]. In animal studies, Mahuang polysaccharide was found to reduce airway and lung tissue inflammation by regulating inflammatory factors and the TGF-β1/Smad2 signaling pathway [37]. Li Wei et al. [38] demonstrated through experiments that glycyrrhizic acid, one of the main active components in Gancao Ganjiang Decoction,

can significantly reduce lung tissue inflammation and later-stage fibrosis in bleomycin-induced IPF mice, a process possibly related to glycyrrhizic acid regulating monocyte–macrophage phenotypic skewing and modulating TGF-β1 expression.

5.2.2 Inhibition of Fibroblast Activation and Proliferation

Cai Fenglin et al. [39] verified through cell experiments that isoliquiritigenin can inhibit TGF-β1-induced fibrosis progression in A549 cells. Furthermore, the overall anti-inflammatory effect of the formula reduces inflammatory cytokines (e.g., TNF-α, IL-1β, IL-13) that stimulate fibroblasts, thereby reducing fibrogenesis.

5.2.3 Anti-oxidative Stress

Liquiritin and 6-gingerol have been shown to possess anti-fibrotic effects, with mechanisms related to inhibition of inflammation and oxidative stress [40].

5.3 Improvement of Pulmonary Function

Numerous studies indicate that Mahuang components (methylephedrine, ephedrine, pseudoephedrine) can dilate bronchi by directly stimulating pulmonary β2-adrenergic receptors, causing bronchodilation and rapidly relieving bronchospasm, thereby improving ventilation [41].

Anti-inflammatory effects reduce airway mucosal congestion, edema, and inflammatory cell infiltration, lower airway hyperreactivity, and thus improve ventilation resistance.

As mentioned above, inhibiting fibrosis itself preserves lung elasticity and protects alveolar structure, thereby maintaining or improving lung compliance and diffusing capacity.

5.4 Comparison with Conventional Western Medicine Treatment

Currently, there is no unified guideline for the treatment of RA-ILD in Western medicine. Clinical management requires immunosuppressive therapy to control irreversible joint damage, often including conventional synthetic DMARDs, biological DMARDs, etc. [42]. According to the 2023 American College of Rheumatology/American College of Chest Physicians guidelines for RA-ILD treatment, mycophenolate mofetil, azathioprine, and rituximab are recommended as first-line therapy, with cyclophosphamide and short-term glucocorticoids as additional options [43]. A major drawback is that almost all antirheumatic drugs and glucocorticoids have immunosuppressive effects, increasing the risk of infections [44].

In TCM treatment, based on the core pathogenesis of RA-ILD as root deficiency with branch excess, treatment should focus on “warming yang and transforming rheum, and treating the lung, kidney, and spleen together.” In Magui Jiangcao Wenfei Yin, Ganjiang warms the lung and transforms rheum, Guizhi unblocks yang and relieves bi, Mahuang ventilates the lung and relieves wheezing, and Zhigancao harmonizes the various herbs. The combined use of these herbs provides multi-target synergistic action, toxicity reduction, enhanced efficacy, and better safety.

However, the two approaches are not mutually exclusive. According to existing research, compared with Western medicine alone, integrated Chinese and Western medicine treatment for RA-ILD shows better efficacy and safety [45]. Combination therapy can effectively improve the overall clinical response rate and significantly improve pulmonary function parameters such as FVC and DLCO [46].

6. Discussion and Prospects

TCM recognizes RA-ILD as a five-body bi caused by exogenous pathogenic invasion that, over time, affects the internal viscera, mainly involving the lung, spleen, and kidney. The main pathological factors are dampness, phlegm, stasis, and toxin, closely related to dysregulation of the lung, spleen, liver, and kidney. Treatment centers on supplementing deficiency and reducing excess, with syndrome-based differentiation and integrated Chinese-Western medicine approaches, which can effectively improve patients’ quality of life. Magui Jiangcao Wenfei Yin, with its principle of warming the lung and transforming rheum, dispelling wind, dispersing cold, and unblocking collaterals, aligns with the core pathogenesis of RA-ILD and represents an important formula in integrated therapy.

The advantages of TCM treatment lie in significant efficacy in relieving clinical symptoms and improving pulmonary function parameters, with fewer adverse reactions. However, there are some limitations in clinical practice: First, there is a lack of standardized syndrome differentiation and classification with no unified criteria. Second, treatment regimens rely on individual experience, and formula selection lacks standardized references. Third, research on single herbs is more abundant than research on compound formulas. Fourth, the systemic mechanisms of multi-component, multi-target, multi-pathway integrated regulation of pulmonary fibrosis still need further elucidation.

For future improvements, it is desirable to establish objective indicators by integrating modern physicochemical parameters with TCM syndrome elements to develop unified syndrome differentiation and diagnostic criteria for RA-ILD. This would not only improve efficacy but also promote the deeper application of TCM theories in modern medicine. Further research should deepen the pharmacodynamic and pharmacological studies of the complete Magui Jiangcao Wenfei Yin formula, as well as its specific molecular mechanisms of anti-fibrotic and immunomodulatory actions. Future studies should also combine large-sample clinical trials to define the pattern evolution rules and employ in-depth molecular mechanistic analyses to perfect the “disease–syndrome–formula” scientific association framework, providing references for optimizing integrated diagnostic and therapeutic strategies for RA-ILD.

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