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Clinical application, potential pharmacological targets and quality marker prediction of a TCM formulation used (Shenling Baizhu San) in the treatment of respiratory diseases

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Shenling Baizhu San (SLBZS) is a formulation of traditional Chinese medicine (TCM) recorded in the Song Dynasty medical book *Taiping Huimin Heji Jufang* (AD 1078–1085). It comprises eleven herbs: Ginseng Radix Et Rhizoma, Atractylodis Macrocephalae Rhizoma, Poria, Dioscoreae Rhizoma, Nelumbinis Semen, Coicis Semen, Lablab Semen Album, Amomi Fructus, Platycodonis Radix, Glycyrrhizae Radix Et Rhizoma, and Jujubae Fructus. SLBZS has been employed for over 900 years in the treatment of pulmonary and gastrointestinal disorders because of its qualities that enhance spleen function, tonify the lungs, supplement qi, and mitigate diarrhoea. This study meticulously examined and synthesised the clinical relevance and pharmacological mechanisms of SLBZS, concentrating on respiratory diseases, in response to the increasing volume of clinical data about SLBZS. Meanwhile, according to the five principles of Q-marker determination, including quality transmission and traceability, metabolites specificity, formula compatibility environment, association between metabolites and effectiveness, metabolites measurability, the potential quality markers (Q-markers) that SLBZS in the treatment of respiratory diseases were predicted. This study will provide additional clinical research, clarify pharmacological mechanisms, and set quality control criteria for SLBZS in the treatment of respiratory diseases.

KEYWORDS

Shenling Baizhu San, respiratory diseases, clinical application, pharmacological mechanisms, quality markers

1 Introduction

Shenling Baizhu San (SLBZS) originated from the medicinal book *Taiping Huimin Heji Jufang* in the Northern Song Dynasty. As a formula of traditional Chinese medicine (TCM), it is composed of Renshen (Ginseng Radix Et Rhizoma), Baizhu (*Atractylodis Macrocephalae* Rhizoma), Fuling (*Poria*), Shanyao (*Dioscoreae* Rhizoma), Lianzi (*Nelumbinis* Semen), Yiyiren (*Coicis* Semen), Baibiandou (*Lablab* Semen Album), Sharen (*Amomi* Fructus), Jiegeng (*Platycodonis* Radix), Gancao (*Glycyrrhizae* Radix Et Rhizoma) and Dazao (*Jujubae* Fructus) (The Pharmacopoeia of the People’s Republic of China, 2020) (Table 1). SLBZS promotes useful qi and supports the spleen, alleviates dampness, and possesses anti-diarrhoeal properties. It is typically employed for diarrhoea resulting from spleen deficiency and dampness, as well as for lung qi deficit, phlegm dampness, cough, and asthma. The recipe incorporates Renshen, Baizhu, and Fuling to enhance qi and spleen function, eliminate moisture, and facilitate transportation. Shanyao and Lianzi enhance spleen and qi, possess astringent properties for the intestines, and serve as antidiarrheal agents; Baibiandou and Yiyiren effectively eliminate dampness and mitigate diarrhoea; Sharen works to eliminate dampness, promote qi circulation, and harmonise the stomach. SLBZS may serve as adjunctive medications for addressing gastrointestinal disorders, including ulcerative enteritis and persistent diarrhoea in clinical settings (Chen et al., 2022; Wang et al., 2022). Jiegeng facilitates lung qi circulation, alleviates obstructions, and regulates qi flow, rendering SLBZS effective in treating respiratory conditions such as chronic obstructive pulmonary disease (COPD) and bronchial asthma (Mao et al., 2021; Huang et al., 2023). The metabolites of SLBZS are intricate, particularly regarding the pharmacological mechanisms and quality marker metabolites in the treatment of respiratory disorders, which remain ambiguous and require more clarification.

The metabolites of TCM formulae are essential for clarifying their pharmacological effects. Previous research has comprehensively documented the aqueous extract of a specific TCM botanical medication in SLBZS, along with the metabolites

found in the serum (Wang et al., 2025; Wu et al., 2024; Han et al., 2025). Specific metabolites have exhibited beneficial effects on respiratory diseases (Li B. S. et al., 2021; Zhongyin et al., 2022; Xu et al., 2025). Nonetheless, there is inadequate evidence regarding the metabolites of SLBZS and the specific active metabolites that facilitate its therapeutic effects on respiratory illnesses. Quality markers (Q-markers) are active metabolites that signify the pharmacological properties, effectiveness, and quantifiability of TCM botanical drugs. This will act as a reference for the quality control of TCM botanical drugs and formulae, specifically focusing on metabolites with potential pharmacological effects, thereby becoming crucial for the development and application of TCM botanical drugs and formulae (Wu et al., 2024).

Recent years have seen the therapeutic efficacy of SLBZS validated by substantial foundational research and clinical trials, with the development of a broad array of qualitative and quantitative procedures for its chemical analysis and quality control. Nevertheless, these research findings have not been thoroughly synthesized. This research analyses the clinical application and pharmacological effects of SLBZS, utilizing the five principles of Q-marker to predict potential Q-markers of SLBZS in the treatment of respiratory illnesses. This study aims to improve the quality control standards of TCM botanical drugs and formulae, while providing insights and a basis for the ongoing development and implementation of SLBZS.

2 Methods of data acquisition

This study utilises primary literature obtained from the PubMed, Web of Science, and China National Knowledge Infrastructure (CNKI) databases. The search keywords are “Shenling Baizhu San”, “Respiratory System”, “Clinical Application”, “Pharmacological mechanism”, “metabolites”, “Ginseng Radix Et Rhizoma”, “*Atractylodis Macrocephalae* Rhizoma”, “*Poria*”, “*Dioscoreae* Rhizoma”, “*Nelumbinis* Semen”, “*Coicis* Semen”, “*Lablab* Semen Album”, “*Amomi* Fructus”, “*Platycodonis* Radix”, “*Glycyrrhizae* Radix Et Rhizoma”, “*Jujubae* Fructus” and their

TABLE 1 Botanical drugs of SLBZS.

Botanical name	English name	Local name	Part used	Fixed ratio
<i>Panax ginseng</i> C.A.Mey	Ginseng Radix Et Rhizoma	Renshen	Rhizome and Root	15
<i>Atractylodes macrocephala</i> Koidz	<i>Atractylodis Macrocephalae</i> Rhizoma	Baizhu	Rhizome	15
<i>Poria cocos</i> (Schw.) Wolf	<i>Poria</i>	Fuling	Sclerotia	15
<i>Dioscorea opposita</i> Thunb	<i>Dioscoreae</i> Rhizoma	Shanyao	Rhizome	15
<i>Nelumbo nucifera</i> Gaertn	<i>Nelumbinis</i> Semen	Lianzi	Seed	9
<i>Coix lacryma-jobi</i> L. var. <i>Mayuen</i> (Roman.) Stapf	<i>Coicis</i> Semen	Yiyiren	Seed	9
<i>Dolichos lablab</i> L	<i>Lablab</i> Semen Album	Baibiandou	Seed	12
<i>Amomum villosum</i> Lour	<i>Amomi</i> Fructus	Sharen	Fruit	6
<i>Platycodon grandiflorum</i> (Jacq.) ADC.	<i>Platycodonis</i> Radix	Jiegeng	Root	6
<i>Glycyrrhiza uralensis</i> Fisch	<i>Glycyrrhizae</i> Radix Et Rhizoma	Gancao	Rhizome and Root	10
<i>Ziziphus jujuba</i> Mall	<i>Jujubae</i> Fructus	Dazao	Fruit	7.5

combinations. The search ended on 31 January 2025, without any preceding time limitations established. The criteria for admission and disqualification were delineated as follows: 1) Clinical application of SLBZS or its modified variants in the treatment of respiratory disorders; 2) Pharmacological mechanisms associated with SLBZS or its modified variants in managing respiratory disorders; 3) Pharmacological mechanisms of the herbal metabolites found in SLBZS for respiratory disorder treatment; 4) Identification and quantitative assessment of metabolites in SLBZS. Reviews, meta-analyses, and case reports were excluded from the research. In the screening process, we initially reviewed titles and abstracts to find relevant studies that fit the inclusion criteria, followed by a thorough analysis of full-text publications, resulting in the inclusion of 64 papers.

3 Clinical application of SLBZS in respiratory diseases

3.1 Clinical application of SLBZS in COPD

COPD is a common respiratory disorder caused by alveolar or airway irregularities arising from continuous exposure to significant levels of toxic gases or particles. It is chiefly characterised by persistent airway obstruction, associated with elevated rates of disability and mortality (Wang et al., 2024a). A randomised controlled trial (Shi, 2024) assigned 104 patients with stable COPD to a control group and an observation group in a 1:1 ratio. The control group was administered tiotropium bromide powder inhalation, while the observation group received modified SLBZS alongside the control group's treatment. The findings indicated that modified SLBZS might markedly decrease the COPD assessment test (CAT) score and enhance pulmonary function metrics, including forced expiratory volume in one second (FEV1), forced vital capacity (FVC), and the FEV1/FVC ratio. A randomised controlled trial involving 78 COPD patients with lung-qi deficit (He, 2024) revealed that the combination of modified SLBZS significantly improved the overall effective treatment rate, FVC, FEV1, and FEV1/FVC in comparison to the administration of budesonide and formoterol inhalation powder alone. The effect was significantly superior to that of inhaling powder aerosol alone. A study by Zhang et al. (2023) demonstrated that the combination of SLBZS and salmeterol improved the overall efficacy of COPD treatment and improves FVC, FEV1, and FEV1/FVC ratios compared to salmeterol alone. Concurrently, it can improve arterial oxygen saturation (SaO₂), arterial partial pressure of oxygen (PaO₂), arterial partial pressure of carbon dioxide (PaCO₂), mucin 5AC (MUC5AC) in induced sputum, matrix metalloproteinase-9 (MMP-9), neutrophil elastase (NE), serum hypersensitive C-reactive protein (hs-CRP), interleukin-6 (IL-6), and plasma Brain Natriuretic Peptide (BNP) levels, exhibiting superiority compared to salmeterol alone.

3.2 Clinical application of SLBZS in asthma

Asthma is a common chronic respiratory disorder defined by dyspnoea, chest tightness, wheezing, and other symptoms. There are

approximately 300 million sufferers worldwide, with the incidence increasing each year (Li et al., 2020). Huang et al. (2023) found that SLBZS, when combined with salmeterol fluticasone aerosol, substantially mitigated clinical symptoms such as cough and expectoration, while also reducing diurnal peak expiratory flow (PEF), FEV1, FEV1/FVC, and other pulmonary function parameters in patients with chronic persistent bronchial asthma. It also elevated fractional exhaled nitric oxide (FeNO) levels, Asthma Control Test (ACT) scores, and other metrics, while significantly reducing the recurrence rate of bronchial asthma. A distinct randomised controlled trial (Gao, 2022) demonstrated that the combination of SLBZS and fluticasone propionate aerosol markedly reduces the duration and frequency of asthma attacks in children, while also improving clinical symptoms such as wheezing and cough, in comparison to fluticasone propionate aerosol alone. A separate study (Cui and Shang, 2019) demonstrated that modified SLBZS in conjunction with flixxdone might diminish the asthma Control Test (C-ACT) score and enhance FVC, FEV1, peak expiratory flow (PEF), FEV1/FVC, and other pulmonary ventilation function metrics in paediatric asthma patients.

3.3 Clinical application of SLBZS in allergic rhinitis

Allergic rhinitis is an allergic disorder of the nasal mucosa, predominantly induced by exposure to allergens in susceptible individuals. It manifests as nasal itching, sneezing, excessive nasal discharge, and nasal congestion, which can easily trigger asthma and sinusitis (Schaefer et al., 2023). Zhao et al. (2024) discovered that the combination of SLBZS and acupuncture alleviates clinical symptoms such as nasal itching, nasal congestion, dizziness, shortness of breath, rhinorrhea, and sneezing in patients with allergic rhinitis. Additionally, it enhances serum levels of interferon- γ (IFN- γ), Cluster of Differentiation 3⁺ (CD3⁺), Cluster of Differentiation 4⁺ (CD4⁺), and the CD4⁺/Cluster of Differentiation 8⁺ (CD8⁺) ratio, while diminishing interleukin-17 (IL-17) and CD8⁺ levels. A distinct randomised controlled trial (Ge and Jiang, 2022) demonstrated that the SLBZS combination, in contrast to standard treatment (loratadine tablets, cetirizine hydrochloride tablets and fluticasone nasal spray), significantly reduced serum concentrations of interleukin-4 (IL-4), interleukin-6 (IL-6), and immunoglobulin E (IgE), while augmenting levels of INF- γ and Soluble Programmed Death Ligand-1 (sPD-L1) in patients with rhinitis. Clinical symptoms that require alleviation encompass nasal congestion, rhinorrhea, nasal pruritus, sneezing, fatigue, dyspnoea, lethargy, and reduced vocal quality.

3.4 Others

SLBZS exhibits a favourable therapeutic impact on pneumonia and recurrent respiratory tract infections. A randomised controlled trial (Li, 2021) indicated that modified SLBZS combined with azithromycin significantly reduced serum concentrations of tumour necrosis factor- α (TNF- α), interleukin-8 (IL-8), IL-6, and CD8⁺, while enhancing levels of CD3⁺ and CD4⁺, thereby promoting

TABLE 2 Clinical application of SLBZS in respiratory diseases.

No.	Group	Medication (dosage of drug)	Number of people	Treatment effect	The medication time	Reference
1	Observation group	Modified SLBZS was applied on the basis of the control group	52	Total effective rate: 96.15% Prior treatment and after treatment: CAT (17.84 ± 3.28 and 13.32 ± 2.17) TCM syndrome score (15.15 ± 2.68 and 6.76 ± 1.31), FEV1/L (1.44 ± 0.28 and 1.92 ± 0.36), FVC/L (2.18 ± 0.35 and 2.65 ± 0.32), (FEV1/FVC)/% (66.06 ± 7.68 and 77.45 ± 6.31)	One dose per day, divided into two doses, for 3 months	Shi, (2024)
	Control group	Inhaled tiotropium bromide	52	Total effective rate: 88.46% Prior treatment and after treatment: CAT (18.97 ± 3.17 and 15.94 ± 2.48) TCM syndrome score (15.59 ± 2.15 and 8.07 ± 1.48), FEV1/L (1.47 ± 0.17 and 1.70 ± 0.31), FVC/L (2.21 ± 0.34 and 2.44 ± 0.36), (FEV1/FVC)/% (66.52 ± 7.15 and 69.67 ± 5.48)	One inhalation per time (18 μ g/inhalation), for 3 months	Shi, (2024)
2	Observation group	Modified SLBZS was applied on the basis of the control group	39	Total effective rate: 97.44% Prior treatment and after treatment: FEV1/L (1.19 ± 0.34 and 1.85 ± 0.67), FVC/L (2.13 ± 0.36 and 2.69 ± 0.53), (FEV1/FVC)/% (55.87 ± 5.06 and 68.77 ± 6.33)	One dose per day, divided into two doses, for 2 months	He, (2024)
	Control group	Budesonide formoterol aerosol for inhalation	39	Total effective rate: 79.49% Prior treatment and after treatment: FEV1/L (1.17 ± 0.32 and 1.42 ± 0.51), FVC/L (2.11 ± 0.39 and 2.32 ± 0.47), (FEV1/FVC)/% (55.45 ± 5.09 and 66.21 ± 5.83)	4.5 μ g twice a day, for 2 months	He, (2024)
3	Observation group	Modified SLBZS was applied on the basis of the control group	105	Total effective rate: 94.29% Prior treatment and after treatment: FEV1/L (1.32 ± 0.29 and 1.97 ± 0.36), FEV1/% (55.94 ± 12.70 and 69.46 ± 13.80), SaO2/% (81.60 ± 3.52 and 95.37 ± 4.04), PaO2/mmHg (55.96 ± 4.91 and 86.97 ± 5.88), PaCO2/mmHg (54.11 ± 3.61 and 41.82 ± 2.94), hs-CRP/(μ g/L) (13.44 ± 1.89 and 6.90 ± 1.31), IL-6/(ng/L) (4.29 ± 1.06 and 2.08 ± 0.61), BNP/(ng/L) (564.15 ± 39.22 and 354.75 ± 22.58), MUC5AC (195.19 ± 22.67 and 87.86 ± 8.24), MMP-9 (172.45 ± 19.22 and 74.44 ± 9.27), NE (1.91 ± 0.47 and 1.33 ± 0.28)	20g twice a day, for 3 months	Zhang et al. (2023)
	Control group	Salmeterol fluticasone inhalation aerosol	105	Total effective rate: 84.76% Prior treatment and after treatment: FEV1/L (1.36 ± 0.19 and 1.58 ± 0.29), FEV1/% (55.75 ± 12.42 and 63.74 ± 13.52), SaO2/% (81.74 ± 3.39 and 91.53 ± 3.75), PaO2/mmHg (55.74 ± 4.87 and 69.58 ± 5.36), PaCO2/mmHg (54.09 ± 3.48 and 46.25 ± 3.26), hs-CRP/(μ g/L) (13.27 ± 1.92 and 9.75 ± 1.62), IL-6/(ng/L) (4.31 ± 1.11 and 3.26 ± 0.84),	50 μ g twice a day, for 3 months	Zhang et al. (2023)

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TABLE 2 (Continued) Clinical application of SLBZS in respiratory diseases.

No.	Group	Medication (dosage of drug)	Number of people	Treatment effect	The medication time	Reference
				BNP/(ng/L) (567.48 ± 38.46 and 389.42 ± 29.75), MUC5AC (198.16 ± 21.61 and 113.54 ± 12.16), MMP-9 (175.58 ± 19.65 and 93.02 ± 8.23), NE (1.93 ± 0.42 and 1.12 ± 0.22)		
4	Observation group	Modified SLBZS was applied on the basis of the control group	60	Prior treatment and after treatment: TCM syndrome score (13.67 ± 1.54 and 2.60 ± 0.52), FEV1/L (1.67 ± 0.38 and 2.87 ± 0.30), (FEV1/FVC)/% (53.15 ± 5.36 and 73.11 ± 5.19), PEF/L/s (2.25 ± 0.42 and 3.64 ± 0.44), FeNO (ppb) (44.01 ± 0.60 and 22.87 ± 0.59), ACT (12.98 ± 0.70 and 22.88 ± 0.57), MDA ($\mu\text{mol/L}$) (9.28 ± 1.16 and 4.35 ± 0.92), SOD (U/mL) (65.63 ± 10.77 and 89.53 ± 15.86), 8-iso-PG (pg/mL) (151.63 ± 24.37 and 62.86 ± 11.51), GSH-Px (U/mL) (144.55 ± 14.39 and 220.41 ± 18.19), VEGF (266.73 ± 23.38 and 164.91 ± 21.05), TGF- $\beta 1$ (503.03 ± 31.98 and 415.48 ± 36.79)	One dose per day, divided into two doses, for 12 weeks	Huang et al. (2023)
	Control group	Salmeterol and fluticasone aerosol	60	Prior treatment and after treatment: TCM syndrome score (13.72 ± 1.59 and 6.14 ± 0.71), FEV1/L (1.69 ± 0.35 and 2.31 ± 0.26), (FEV1/FVC)/% (52.87 ± 5.43 and 67.29 ± 5.72), PEF/L/s (2.27 ± 0.38 and 3.09 ± 0.56), FeNO (ppb) (43.95 ± 0.56 and 30.23 ± 0.87), ACT (12.88 ± 0.68 and 17.02 ± 0.66), MDA ($\mu\text{mol/L}$) (9.22 ± 1.21 and 6.21 ± 0.93), SOD (U/mL) (64.73 ± 11.02 and 82.22 ± 13.61), 8-iso-PG (pg/mL) (153.12 ± 23.79 and 84.32 ± 14.37), GSH-Px (U/mL) (145.20 ± 13.86 and 187.17 ± 17.39), VEGF (268.87 ± 23.92 and 210.69 ± 15.44), TGF- $\beta 1$ (498.73 ± 32.13 and 415.48 ± 36.79)	Twice a day, 1 inhalation each time, for 12 weeks	Huang et al. (2023)
5	Observation group	Modified SLBZS was applied on the basis of the control group	40	Total effective rate: 97.50% Prior treatment and after treatment: TCM syndrome score (14.11 ± 1.86 and 3.00 ± 1.03), duration of seizures (7.02 ± 1.78 and 4.20 ± 0.98), number of asthma exacerbations (4.78 ± 1.83 and 1.55 ± 0.31)	One dose per day, divided into two doses, for 30 days	Gao, (2022)
	Control group	Fluticasone propionate	40	Total effective rate: 75.00% Prior treatment and after treatment: TCM syndrome score (13.73 ± 2.02 and 5.79 ± 1.66), duration of seizures (7.46 ± 1.64 and 5.90 ± 0.86), number of asthma exacerbations (4.91 ± 1.91 and 2.72 ± 1.22)	50 μg once a day, for 30 days	Gao, (2022)

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TABLE 2 (Continued) Clinical application of SLBZS in respiratory diseases.

No.	Group	Medication (dosage of drug)	Number of people	Treatment effect	The medication time	Reference
6	Observation group	Modified SLBZS was applied on the basis of the control group	51	Total effective rate: 84.3% Prior treatment and after treatment: TCM syndrome score (22.84 ± 7.64 and 8.67 ± 6.41), C-ACT (15.35 ± 3.74 and 21.86 ± 4.42), PEF (3.22 ± 1.08 and 4.13 ± 1.22), FEV1/L (1.51 ± 0.50 and 1.92 ± 0.61), FVC/L (1.79 ± 0.60 and 2.59 ± 0.59), (FEV1/FVC)/% (75.71 ± 9.17 and 86.67 ± 6.17)	One dose per day, divided into two doses, for 1 month	Cui and Shang (2019)
	Control group	Fluticasone propionate was inhaled as an aerosol	51	Total effective rate: 72.5% Prior treatment and after treatment: TCM syndrome score (21.86 ± 8.62 and 11.70 ± 7.52), C-ACT (16.17 ± 3.30 and 21.65 ± 3.50), PEF (3.06 ± 1.21 and 3.67 ± 1.20), FEV1/L (1.53 ± 0.56 and 1.71 ± 0.47), FVC/L (1.72 ± 0.67 and 2.13 ± 0.44), (FEV1/FVC)/% (75.77 ± 9.79 and 81.13 ± 8.83)	125 µg once a day, for 1 month	Cui and Shang (2019)
7	Observation group	Acupuncture (Yintang, Yingxiang, Bitong, Fengchi, Shangxing, Hegu) was used on the basis of the control group	50	Total effective rate: 96% Prior treatment and after treatment: IFN-γ (10.12 ± 2.25 and 15.36 ± 4.32), IL-17 (465.32 ± 52.32 and 235.14 ± 35.52), CD3 ⁺ (%) (58.37 ± 3.29 and 69.89 ± 4.59), CD4 ⁺ (%) (33.16 ± 2.13 and 44.04 ± 3.47), CD8 ⁺ (%) (34.26 ± 3.86 and 26.21 ± 2.67), CD4 ⁺ /CD8 ⁺ (0.97 ± 0.32 and 1.68 ± 0.47)	Once a day for 30 days	Zhao et al. (2024)
	Control group	SLBZS	50	Total effective rate: 74% Prior treatment and after treatment: IFN-γ (10.21 ± 2.26 and 12.42 ± 4.11), IL-17 (465.62 ± 52.49 and 315.36 ± 38.65), CD3 ⁺ (%) (59.54 ± 3.86 and 65.36 ± 4.11), CD4 ⁺ (%) (34.14 ± 2.89 and 39.65 ± 3.21), CD8 ⁺ (%) (33.14 ± 3.54 and 29.23 ± 3.05), CD4 ⁺ /CD8 ⁺ (1.03 ± 0.35 and 1.36 ± 0.25)	One dose per day, divided into two doses, for 30 days	Zhao et al. (2024)
8	Observation group	Modified SLBZS was applied on the basis of the control group	50	Total effective rate: 68% Prior treatment and after treatment: IFN-γ (28.54 ± 3.57 and 58.76 ± 4.29), IL-4 (59.15 ± 3.26 and 42.76 ± 3.28), IL-6 (12.36 ± 1.28 and 5.93 ± 0.89), IgE(kU/L) (126.53 ± 8.27 and 47.92 ± 4.23), sPD-L1 (ng/mL) (1.72 ± 0.29 and 2.89 ± 0.11)	One dose per day, divided into two doses, for 1 month	Ge and Jiang (2022)
	Control group	Loratadine tablets, Cetirizine hydrochloride tablets, Fluticasone nasal spray	50	Total effective rate: 42% Prior treatment and after treatment: IFN-γ (29.76 ± 3.28 and 43.47 ± 4.33), IL-4 (59.83 ± 3.19 and 48.41 ± 3.27), IL-6 (12.45 ± 1.19 and 8.16 ± 0.82), IgE(kU/L) (124.82 ± 8.11 and 73.85 ± 4.51), sPD-L1 (ng/mL) (1.81 ± 0.33 and 2.28 ± 0.12)	0.5 mg (weight ≤30 kg)/time, 10 mg (Weight >30 kg)/time, once a day; 2.5 mg (≥3 years old and ≤6 years old)/time, 5–10 mg (>6 years old and ≤12 years old)/time, once a day; 100 µg/time, once a day, for 1 month	Ge and Jiang (2022)

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TABLE 2 (Continued) Clinical application of SLBZS in respiratory diseases.

No.	Group	Medication (dosage of drug)	Number of people	Treatment effect	The medication time	Reference
9	Observation group	Modified SLBZS was applied on the basis of the control group	48	Total effective rate: 95.83% Prior treatment and after treatment: TCM syndrome score (25.42 ± 3.35 and 4.19 ± 1.53), $CD4^+$ (29.50 ± 3.68 and 38.22 ± 4.89), $CD8^+$ (30.15 ± 4.25 and 24.11 ± 3.36), $CD3^+$ (51.23 ± 5.13 and 58.12 ± 4.56), $TNF-\alpha$ (ng/L) (29.15 ± 3.76 and 11.43 ± 3.22), IL-8 (ng/L) (27.01 ± 4.01 and 10.03 ± 2.64), IL-6 (ng/L) (21.26 ± 3.02 and 8.79 ± 2.59)	One dose per day, divided into two doses, for 4 weeks	Li, (2021)
	Control group	Azithromycin	45	Total effective rate: 80.00% Prior treatment and after treatment: TCM syndrome score (24.86 ± 4.01 and 8.63 ± 2.57), $CD4^+$ (30.04 ± 4.03 and 34.13 ± 5.02), $CD8^+$ (29.47 ± 3.97 and 26.09 ± 4.01), $CD3^+$ (50.36 ± 4.75 and 55.01 ± 5.12), $TNF-\alpha$ (ng/L) (28.77 ± 3.45 and 15.10 ± 4.09), IL-8 (ng/L) (26.65 ± 3.82 and 13.62 ± 3.25), IL-6 (ng/L) (20.74 ± 2.89 and 11.45 ± 3.13)	Azithromycin 10 mg/kg was given intravenously once a day for 5 days 10 mg/kg (azithromycin dry suspension), once a day, after 3 days of treatment, the drug was stopped for 4 days, and then the treatment was given for 3 cycles	Li, (2021)

lesion absorption and the alleviation of lung rales in paediatric patients with *Mycoplasma pneumoniae*. Furthermore, SLBZS combined with massage (Wang, 2024) can significantly improve expectoration, relieve cough, and decrease sputum volume in paediatric patients, while simultaneously lowering inflammatory markers such as IL-4 and $TNF-\alpha$ in sputum. A distinct study (Chen, 2018) revealed that SLBZS combined with pidotimod can reduce serum concentrations of IL-6, $TNF-\alpha$, procalcitonin (PCT), and cysteinyl leukotriene (Cysl-Ts) in patients with recurrent respiratory tract infections, while also mitigating clinical symptoms such as cough, tonsil hypertrophy, and lung rales.

In summary, SLBZS or modified SLBZS are commonly employed alongside drugs such as tiotropium bromide powder and salmeterol for the treatment of respiratory disorders, exhibiting considerable efficacy (Table 2). Nevertheless, the clinical examination of SLBZS has certain constraints. 1) Methodological constraints are present. Incorporating studies with limited sample sizes (e.g., 78 or 104 cases) may compromise the statistical validity of the findings and elevate the likelihood of a Type II error. 2) The description of the randomisation mechanism is absent. The randomisation grouping lacks a detailed description of the precise mechanism for random sequence generation and allocation concealment, potentially leading to selection bias. 3) Blinding was either defective or omitted. The study did not specify if a double-blind design was implemented, and both patients and assessors were cognisant that subgroups could introduce measurement bias. 4) The dosing specification lacks precision. This study indicates that several physicians may recommend differing dosages for the identical disease. Adequate scientific research on the correlation between dosage and effect are lacking, thereby compromising the efficacy and safety of treatment. 5) Functional testing were conducted individually. Lung function metrics, including FEV1 and FVC, were largely singular and, albeit being statistically significant, did not demonstrate a minimal

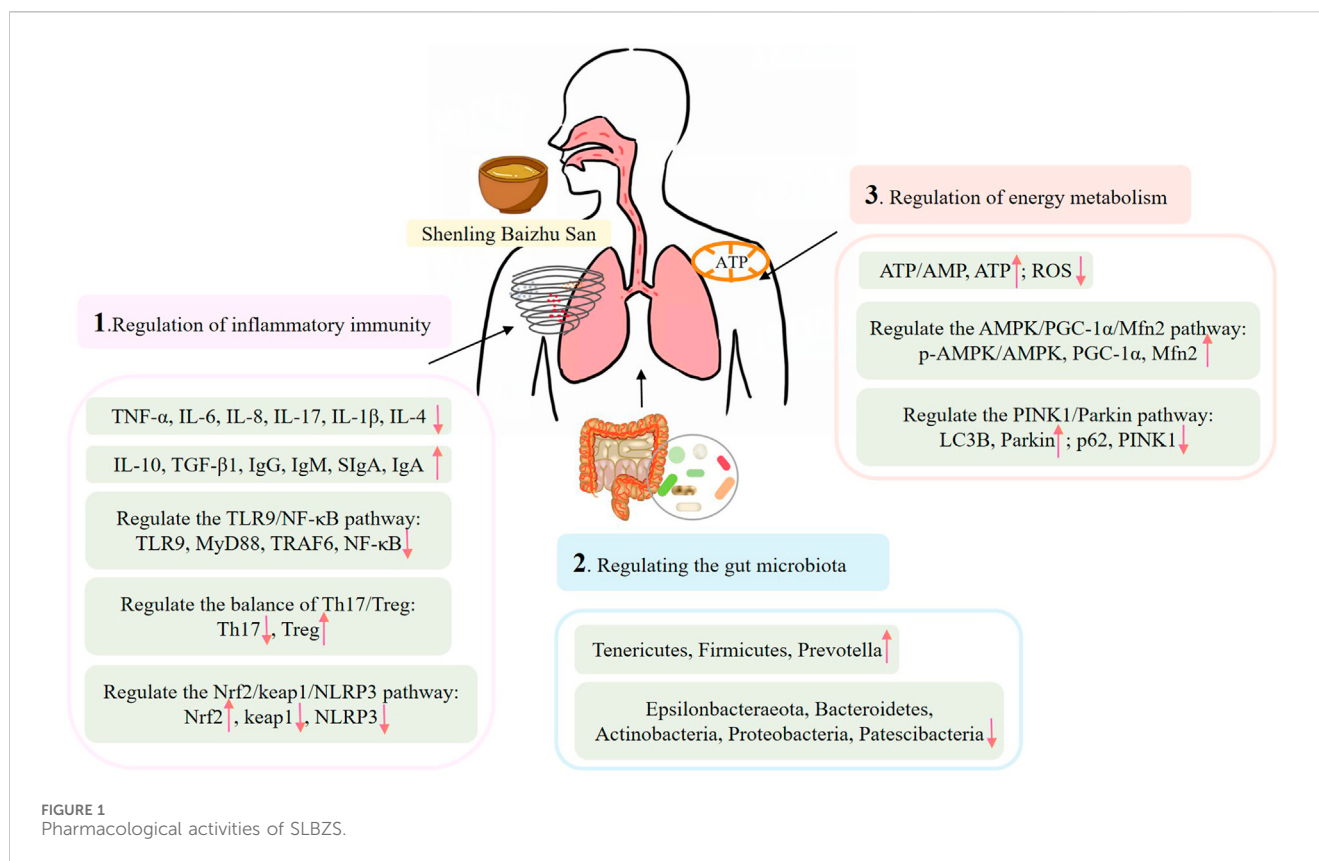
clinically relevant difference (MCID). 6) Insufficient follow-up. All trials had a follow-up duration of 6 months or less and did not provide evidence on the long-term efficacy and adverse effects, such as herbal liver and kidney damage, of SLBZS. Future investigations in clinical research on TCM will focus on enhancing experimental design, expanding sample inclusion, investigating dose-effect relationships, augmenting the assessment of functional indicators, and prolonging the follow-up period.

4 Pharmacological mechanisms of SLBZS in respiratory diseases

Pharmacological mechanisms suggest that SLBZS may therapeutically influence COPD, asthma, recurrent respiratory tract infections, pulmonary fibrosis, pneumonia, and other respiratory ailments by inhibiting inflammatory responses in lung tissue and airways, modulating immune function, enhancing gastrointestinal microbiota, and restoring mitochondrial energy metabolism (Figure 1).

4.1 Regulation of inflammatory immunity

Gao et al. (2024) found that SLBZS significantly reduced the levels of $TNF-\alpha$, IL-6, IL-8, and other inflammatory mediators in a COPD cell model induced by cigarette smoke extract (CSE), while also preventing cellular apoptosis. The process may pertain to the modulation of the Toll-like receptor (TLR) 9/nuclear factor kappa-B (NF- κ B) pathway. A study by Ouyang and Xu (2019) investigated the impact of SLBZS on airway inflammation in young asthmatic rats, revealing that SLBZS diminished the infiltration of inflammatory cells in the lung tissue. The underlying mechanism may involve a reduction in IL-17 levels and an



elevation in interleukin-10 (IL-10) and transforming growth factor- β 1 (TGF- β 1) levels. Li C. H. et al. (2024) established that SLBZS can reduce inflammatory infiltration in lung tissue, restore epithelial tissue shape, lower serum and alveolar lavage fluid concentrations of IL-17, and increase IL-10 levels. This may transpire via the regulation of the Th17/Treg equilibrium and the reestablishment of immunological function. Wang et al. (2020) found that SLBZS improves peak inspiratory flow (PIF), peak expiratory flow (PEF), and minute ventilation (MV) in rats with recurrent respiratory tract infection (RRTI), possibly associated with the modulation of serum immunoglobulin A (IgA), immunoglobulin G (IgG), immunoglobulin M (IgM), and other immune factors, along with a decrease in NF- κ B p65 expression in the trachea. Furthermore, it inhibited the levels of inflammatory factors such as TNF- α , interleukin-1 β (IL-1 β) and IL-4 in serum. Deng et al. (2024) developed a rat model of idiopathic pulmonary fibrosis through intratracheal administration of bleomycin, discovering that modified SLBZS markedly diminished inflammatory infiltration and collagen proliferation in the lung tissue of rats, as well as reduced the expression of IL-1 β and TNF- α in lung tissue. The proposed mechanism of action may involve the modulation of the Nrf2/Keap1/NLRP3 signalling pathway, thereby delaying the pathological progression of idiopathic pulmonary fibrosis in rats through the regulation of pyroptosis.

4.2 Regulating the gut microbiota

Feng et al. (2020) found that SLBZS may reduce bacterial load in the bronchoalveolar lavage fluid of mice with pneumonia. It can reduce the levels of IL-1 β , IL-6, TNF- α , interleukin-2 (IL-2), IL-8, interleukin-

12 (IL-12), and IFN- γ in lung tissue homogenate, increase the concentrations of IL-10 and other inflammatory mediators, and improve lung injury in mice. The process may relate to the augmentation of species diversity and abundance of gut bacteria. Wu et al. (2022) established a juvenile Balb/c mouse model demonstrating intestinal flora dysbiosis and pulmonary inflammation via the injection of antibiotics alongside lipopolysaccharide. SLBZS was found to increase IL-10 levels in the bronchoalveolar lavage fluid of this juvenile mouse model, while simultaneously reducing levels of IFN- γ , TNF- α , and serum IgM. The procedure may entail improving the Shannon index of intestinal microbiota, adjusting the levels of Bacteroidetes, Firmicutes, and Proteobacteria, and mitigating the immune and inflammatory reactions in the lungs of juvenile rats. Ouyang et al. (2020) conducted a study that established a mouse model of asthma typified by intestinal flora dysbiosis induced by antibiotics, sensitisation, and aerosol challenge. The study indicated that SLBZS could reduce inflammatory infiltration in the lung tissue of model mice, possibly by increasing the relative abundance of key bacteria such as *Pseudoprevotella*.

4.3 Regulation of energy metabolism

Inadequate skeletal muscle energy metabolism directly leads to respiratory failure in persons with COPD. Hu et al. (2020) established a mouse model of COPD with the application of cigarette smoke. SLBZS was discovered to protect mitochondrial energy metabolism in COPD mice by augmenting the expression of phosphorylated AMP-activated protein kinase (p-AMPK), peroxisome proliferator-activated receptor

gamma coactivator-1 α (PGC-1 α), and mitochondrial fusion protein 2 (Mfn2), thereby maintaining normal skeletal muscle function in these mice. A separate study (Zhou et al., 2020) demonstrated that SLBZS enhances mitochondrial functions, including reactive oxygen species levels, mitochondrial ATP production, and membrane potential, mitigates oxidative damage, and decreases early apoptosis of cells via the PTEN induced putative kinase 1 (PINK1)/Parkin pathway-mediated mitophagy in a COPD myoblast model.

While the aforementioned research indicate that the mechanism of action of SLBZS in treating respiratory disorders may involve the reduction of inflammatory responses, the modulation of gut flora, and the regulation of energy metabolism, other limitations persist. 1) Experimental models exhibit variations. Contemporary research predominantly relies on animal models (e.g., bleomycin-induced lung fibrosis, COPD resulting from cigarette smoke exposure); nonetheless, notable discrepancies exist in the immune microenvironment and disease progression between these models and human conditions. The regulation mechanism of Th17/Treg equilibrium in murine asthma models may not completely replicate the heterogeneity of human asthma. 2) Disintegration of route analyses. Numerous studies indicate that pathways including NF- κ B and NLRP3 are implicated in SLBZS; however, there is an absence of comprehensive study on the upstream and downstream elements of these pathways across the research. Is there cross-regulation between the TLR9/NF- κ B pathway (Gao et al., 2024) and the NLRP3 pathway (Deng et al., 2024)? This division may obscure the fundamental objectives of SLBZS. The absence of validation for protein phosphorylation and the lack of TLR9 knockdown rescue trials complicate the exclusion of off-target effects. 3) Lack of flora specificity. Alterations in gut flora abundance have been noted to correlate with enhancements in lung inflammation in studies (Feng et al., 2020; Wu et al., 2022); however, these studies predominantly rely on correlation analyses, necessitating further validation of causality through faecal transplantation experiments or controlled antibiotic clearance studies of flora. Conversely, current research has solely documented alterations at the phylum level (e.g., *Mycobacterium* anisopliae, *Mycobacterium* thickum); however, distinct strains within the same phylum may exhibit divergent immunomodulatory effects, necessitating future functional validation at the strain level. 4) Clinical significance. Energy metabolism research often utilises acute damage models to assess mitochondrial function; however, skeletal muscle depletion in COPD patients is a protracted process. The sustainability of SLBZS in regulating AMPK/PGC-1 α throughout the chronic progression of the disease requires more examination. Currently, research on energy metabolism has predominantly concentrated on skeletal muscle; however, the metabolic reprogramming of lung tissues, such as alveolar epithelial cells and fibroblasts, is equally vital in pulmonary fibrosis and asthma. Future studies should prioritise investigating whether SLBZS exerts a selective impact on mitochondria across various tissues.

5 Q-marker prediction analysis of SLBZS treatment for respiratory diseases

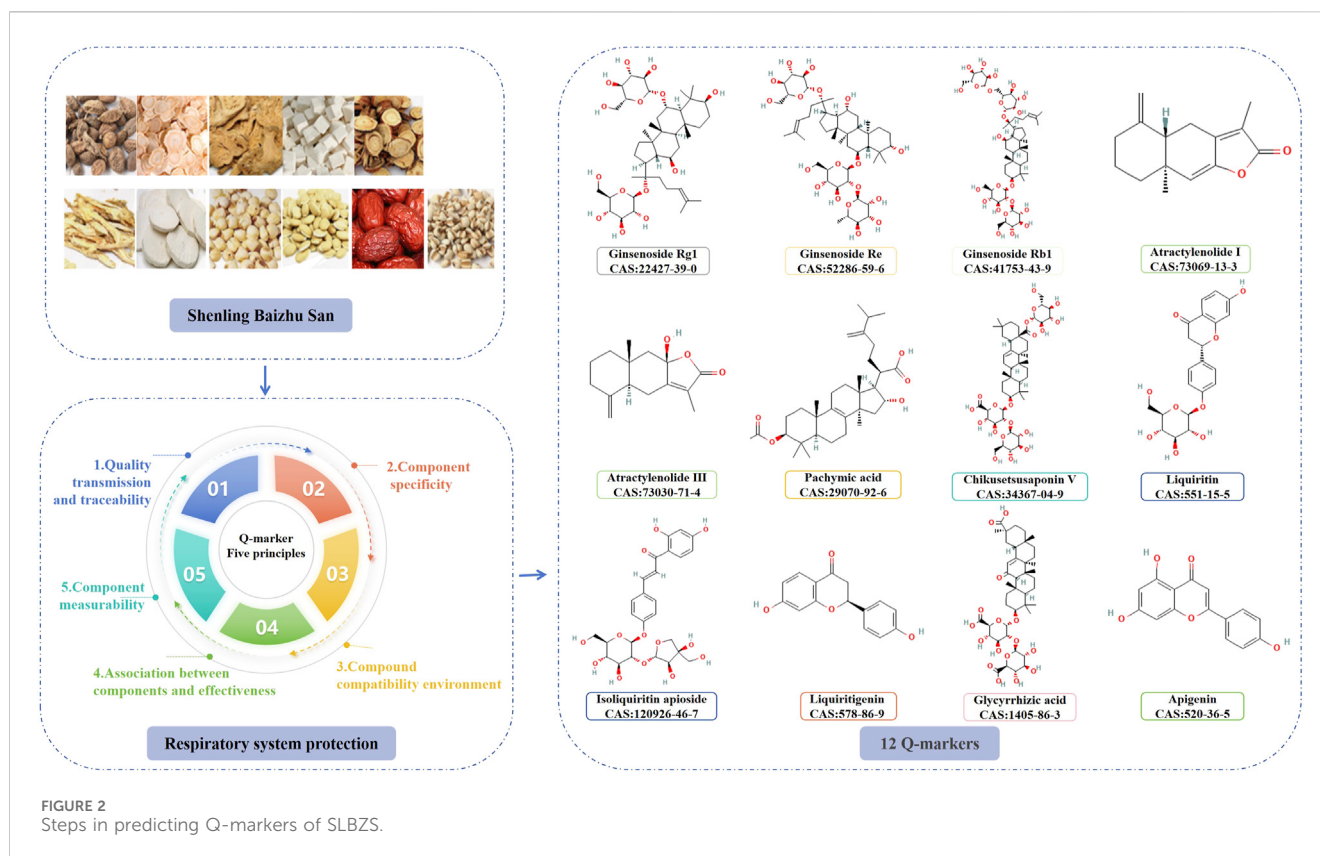
Substantial progress has been achieved in the clinical documentation and pharmacological investigation of SLBZS for

respiratory illnesses; however, the active components necessitate further elucidation. Liu Changxiao, a member of the Chinese Academy of Engineering, presented the Q-marker for TCM botanical medications, a novel concept designed to enhance quality control and improve the quality of TCM formulae. It includes five principles: quality transmission and traceability, metabolites specificity, formula compatibility environment, association between metabolites and effectiveness, metabolites measurability (Liu, 2021). The five concepts of Q-markers were utilised to forecast prospective Q-markers for SLBZS in the management of respiratory disorders (Figure 2).

5.1 Q-marker prediction based on quality transmission and traceability

The metabolites are the essential foundation for the efficacy of TCM formulae. Liquid chromatography, liquid chromatography-mass spectrometry, and more technologies can rapidly and accurately identify metabolites. In a study conducted by Ou et al. (2024), 83 metabolites were identified in the ethanol extract of SLBZS utilising UPLC-Q-TOF-MS/MS technology. These included 26 triterpenoid saponins, 15 flavonoid glycosides, eight flavonoids, seven triterpenoids, six alkaloids, five phospholipids, four fatty acids, four sesquiterpenoids, two fatty acid esters, two nucleotides, one nucleoside, one stilbene, one coumarin, and one phenanthrene. The metabolites of the aqueous extract of SLBZS were analysed using UPLC-Q-TOF-MS/MS technology, resulting in the identification of 104 metabolites, comprising 63 flavonoids, 14 organic acids, 13 terpenes, five coumarins, and nine other compounds (Li C. H. et al., 2024).

The blood constituents and metabolites of TCM botanical medications represent the primary active metabolites. Consequently, the examination of serum pharmacology is essential for finding quality markers in TCM botanical drugs. Gao et al. (2024) used UPLC-Q-TOF-MS/MS technology to analyze SLBZS serum and identified a total of 108 metabolites, including 30 prototype components and 78 metabolites. Among them, 30 prototype components mainly included one alkaloid compound from Yiyiren. Four flavonoid glycosides from Gancao; There were 18 triterpene saponins, including 13 from Gancao, four from Renshen, and one from Baibianidou. There were three triterpene acids, two from Fuling and one from Jiegeng. Two flavonoids from Gancao; one sesquiterpenoid from Baizhu; one phospholipid compound from Baibianidou. The metabolic pathways of 78 metabolites mainly included glucuronidation, sulfation, methylation, hydroxylation, and acetylation. Li L. et al. (2024) using UPLC-Q-TOF to analyse serum containing SLBZS, identifying 11 prototype components and 17 metabolites. The eleven prototype components comprised eight flavonoids, one phenolic acid, one terpenoid, and one coumarin. The metabolic pathways of 17 metabolites primarily encompassed phase I metabolism, including methylation, reduction, and double reduction, as well as phase II metabolism, comprising glucuronidation and sulfation. Moreover, Xu et al. (2021) employed UHPLC-MS/MS technology, identifying the presence of panaxadiol, ginsenoside Rg1, atractylenolide I, atractylenolide III, pachymic acid, neferine, nuciferine, diosgenin, platycodin D, and isoliquiritigenin in the



serum of rats administered SLBZS via gavage. The specifics of SLBZS in the bloodstream are presented in Table 3. Triterpene saponins, flavonoid glycosides, alkaloids, flavonoids, triterpenoids, and other metabolites are hypothesised to be the principal compounds by which SLBZS exerts its pharmacological effects.

5.2 Q-marker prediction based on metabolites specificity

Renshen is the desiccated root and rhizome of *Panax ginseng* C. A. Mey. It mostly consists of flavonoids, polysaccharides, saponins, and various other compounds. Ginsenosides are considered the principal active component among them (Ratan et al., 2020). The principal metabolites of Renshen include ginsenoside Rb1, ginsenoside Re, and ginsenoside Rg1 (Han et al., 2018).

Baizhu is the desiccated rhizome of *Atractylodes macrocephala* Koidz. It mostly comprises sesquiterpenes, triterpenes, polysaccharides, and other constituents (Zhu L. X. et al., 2018). Atractylenolide I and atractylenolide III serve as the distinctive metabolites of Baizhu (Xie et al., 2023).

Fuling is the desiccated sclerotia of *Poria cocos* (Schw.) Wolf, mostly consisting of triterpenoids, polysaccharides, sterols, diterpenoids, and other chemicals. Triterpenoids are widely regarded as the distinctive metabolites of Fuling (Zhu L. et al., 2018; Zhu et al., 2020).

Shanyao is the desiccated rhizome of *Dioscorea opposita* Thunb. The primary active constituents of Shanyao include phenolic acids, flavonoids, and polysaccharides. Batatasins and dioscin serve as the

distinctive metabolites of Shanyao (Liu et al., 2024; Chen et al., 2020).

Lianzi is the desiccated and mature seed of *Nelumbo nucifera* Gaertn. Lianzi primarily comprises alkaloids, polyphenols, triterpene saponins, and other constituents. Neferine and nuciferine serve as the distinctive metabolites of lotus seed (Pei, 2021).

Yiyiren is the desiccated and mature seed of *Coix lacryma-jobi* L. var. *Mayuen* (Roman.) Stapf, primarily composed of esters, fatty acids, polysaccharides, and phenols (Pan et al., 2023). Fatty acids and their lipids constitute the active components of Yiyiren, while Coixenolide serves as a distinctive metabolite of Yiyiren (Lu et al., 2022).

Baibianidou is the desiccated and fully developed seed of the leguminous species *Dolichos lablab* L. It mostly comprises polysaccharides, saponins, alkaloids, amino acids, and various other chemical constituents. Total saponins of white lentil and pekolic acid serve as distinctive metabolites of Baibianidou (Li, 2018; Han, 2021).

Jiegeng is the desiccated root of *Platycodon grandiflorum* (Jacq.) A. DC., mostly comprising saponins, flavonoids, phenolic acids, and various other chemical constituents. Platycodin serves as a distinctive metabolite of Jiegeng (Zhang et al., 2022).

Gancao refers to the desiccated roots and rhizome of *Glycyrrhiza uralensis* Fisch. Gancao primarily comprises triterpene saponins, flavonoids, coumarin, polysaccharides, and various other chemical constituents. Glycyrrhizic acid and celiose-glycyrrhizin serve as distinctive metabolites of Gancao (Cheng et al., 2021; Shang et al., 2022).

TABLE 3 The metabolites of SLBZS.

No.	Compounds	Formula	Method	Refs
1	1-Hexadecanoyl-sn-glycero-3-phospho-(1'-myo-inositol)	C ₂₅ H ₄₉ O ₁₂ P	Alcohol extraction, entering the blood	Gao et al. (2024)
2	(2E)-1-(2,4-Dihydroxyphenyl)-3-[4-[[2-O-[2-(1-piperidinyl)acetyl]-β-D-glucopyranosyl]oxy]phenyl]-2-propen-1-one	C ₂₈ H ₃₃ NO ₁₀	Alcohol extraction	Ou et al. (2024)
3	(2E)-3-[4-[[6-O-D-Apio-β-D-furanosyl-2-O-[2-(1-piperidinyl)acetyl]-β-D-glucopyranosyl]oxy]phenyl]-1-(2,4-dihydroxyphenyl)-2-propen-1-one	C ₃₃ H ₄₁ NO ₁₄	Alcohol extraction	Ou et al. (2024)
4	(2E)-3-[4-[[6-O-D-Apio-β-D-furanosyl-2-O-[2-(1-piperidinyl)acetyl]-β-D-glucopyranosyl]oxy]phenyl]-1-(2,4-dihydroxyphenyl)-2-propen-1-one Isomer	C ₃₃ H ₄₁ NO ₁₄	Alcohol extraction	Ou et al. (2024)
5	(2S)-2,3-Dihydro-7-hydroxy-2-[4-[[2-O-[2-(1-piperidinyl)acetyl]-β-D-glucopyranosyl]oxy]phenyl]-4H-1-benzopyran-4-one	C ₂₈ H ₃₃ NO ₁₀	Alcohol extraction	Ou et al. (2024)
6	1-(9Z,12Z-Octadecadienoyl)-glycero-3-phospho-(1'-myo-inositol)	C ₂₇ H ₄₉ O ₁₂ P	Alcohol extraction	Ou et al. (2024)
7	1-Linoleoyl-sn-glycero-3-phosphocholine	C ₂₆ H ₅₀ NO ₇ P	Alcohol extraction	Ou et al. (2024)
8	1-Linoleoyl-sn-glycero-3-phosphoethanolamine	C ₂₃ H ₄₄ NO ₇ P	Alcohol extraction	Ou et al. (2024)
9	1-O-Hexadecanoylhexitol	C ₂₂ H ₄₄ O ₇	Alcohol extraction	Ou et al. (2024)
10	1-Palmitoyl-sn-glycero-3-phosphoethanolamine	C ₂₁ H ₄₄ NO ₇ P	Alcohol extraction	Ou et al. (2024)
11	22-acetoxyl-glycyrrhizin	C ₄₄ H ₆₄ O ₁₈	Alcohol extraction	Ou et al. (2024)
12	22-beta-Acetoxyglycyrrhetaldehyde	C ₄₄ H ₆₄ O ₁₇	Alcohol extraction, entering the blood	Gao et al. (2024)
13	22-beta-Acetoxyglycyrrhetaldehyde Isomer	C ₄₄ H ₆₄ O ₁₇	Enter the bloodstream	Gao et al. (2024)
14	22-dehydroursaponin C	C ₄₂ H ₆₄ O ₁₅	Alcohol extraction, entering the blood	Gao et al. (2024)
15	22β-acetoxyl-glycyrrhizin	C ₄₄ H ₆₄ O ₁₈	Enter the bloodstream	Gao et al. (2024)
16	2'-hydroxyisowighteone glucoside	C ₂₅ H ₂₆ O ₆	Water extraction	Li et al. (2024a)
17	2-O-Acetyl-Platyonic acid A	C ₅₉ H ₉₂ O ₃	Alcohol extraction	Ou et al. (2024)
18	3-(4-Methoxyphenyl)-7-[[2-O-[2-(1-piperidinyl)acetyl]-β-D-glucopyranosyl]oxy]-4H-1-benzopyran-4-one	C ₂₉ H ₃₃ NO ₁₀	Alcohol extraction	Ou et al. (2024)
19	3,4-Didehydroglabridin	C ₂₀ H ₁₈ O ₄	Water extraction	Li et al. (2024b)
20	3,5-dihydroxybenzoic acid	C ₇ H ₆ O ₄	Water extraction	Li et al. (2024a)
21	5-hydroxymethylfurfural	C ₆ H ₆ O ₃	Water extraction	Li et al. (2024a)
22	6-Nitroveratric acid	C ₉ H ₉ NO ₆	Alcohol extraction	Ou et al. (2024)
23	6''-acetylviqiritin	C ₂₃ H ₂₃ O ₁₀	Water extraction	Li et al. (2024b)
24	6-Nitroveratric acid	C ₉ H ₉ NO ₆	Enter the bloodstream	Gao et al. (2024)
25	7-hydroxy-6,4'-dimethoxyisoflavone	C ₁₇ H ₁₄ O ₅	Water extraction	Li et al. (2024a)
26	7-O-methyl-lupinisoflavone	C ₂₁ H ₂₀ O ₆	Water extraction	Li et al. (2024b)
27	Adenosine	C ₁₀ H ₁₃ N ₅ O ₄	Water extraction	Li et al. (2024a)
28	Apigenin-7-O-glucoside	C ₂₁ H ₂₀ O ₁₀	Water extraction	Li et al. (2024b)
29	Apioglycyrrhizin	C ₂₆ H ₃₀ O ₁₃	Water extraction	Li et al. (2024a)
30	Araboglycyrrhizin	C ₄₁ H ₆₂ O ₁₄	Alcohol extraction, entering the blood	Gao et al. (2024)
31	Arginine	C ₆ H ₁₄ N ₄ O ₂	Water extraction	Li et al. (2024b)
32	Armepavine	C ₁₉ H ₂₃ NO ₃	Alcohol extraction	Ou et al. (2024)
33	Artemisinic acid	C ₁₅ H ₂₂ O ₂	Water extraction	Li et al. (2024a)
34	Atractylenolide III	C ₁₅ H ₂₀ O ₃		

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TABLE 3 (Continued) The metabolites of SLBZS.

No.	Compounds	Formula	Method	Refs
			Alcohol extraction, water extraction, and entry into the blood	Gao et al. (2024), Xu et al. (2021)
35	Atractylenolide I	C ₁₅ H ₁₈ O ₂	Alcohol extraction, water extraction, and entry into the blood	Xu et al. (2021)
36	Atractylenolidell Isomer	C ₁₅ H ₂₀ O ₂	Alcohol extraction	Ou et al. (2024)
37	Atractylon	C ₁₅ H ₂₀ O	Water extraction	Li et al. (2024b)
38	Azelaic acid	C ₉ H ₁₆ O ₄	Water extraction	Li et al. (2024a)
39	Batatasin I	C ₁₇ H ₁₆ O ₄	Alcohol extraction	Ou et al. (2024)
40	Batatasin III	C ₁₅ H ₁₆ O ₃	Alcohol extraction	Ou et al. (2024)
41	Betulinic acid	C ₃₀ H ₄₈ O ₃	Water extraction	Li et al. (2024b)
42	Biochanin A	C ₁₆ H ₁₆ O ₄	Water extraction	Li et al. (2024a)
43	Calycosin	C ₁₆ H ₁₂ O ₅	Water extraction	Li et al. (2024b)
44	cAMP Cyclic adenosine monophosphate	C ₁₀ H ₁₂ N ₅ O ₆ P	Alcohol extraction	Ou et al. (2024)
45	cAMP Isomer	C ₁₀ H ₁₂ N ₅ O ₆ P	Alcohol extraction	Ou et al. (2024)
46	Catechin	C ₁₅ H ₁₄ O ₆	Alcohol extraction, entering the blood	Ou et al. (2024)
47	Chikusetsusaponin V	C ₄₈ H ₇₆ O ₁₉	Alcohol extraction, entering the blood	Gao et al. (2024)
48	Chinensin	C ₁₇ H ₁₆ O ₆	Water extraction	Li et al. (2024a)
49	Chlorogenic acid A	C ₂₅ H ₂₄ O ₁₂	Water extraction	Li et al. (2024b)
50	Chlorogenic acid B	C ₂₅ H ₂₄ O ₁₂	Water extraction	Li et al. (2024a)
51	Corydine	C ₂₀ H ₂₃ NO ₄	Alcohol extraction	Ou et al. (2024)
52	Cynarin	C ₂₅ H ₂₄ O ₁₂	Water extraction	Li et al. (2024b)
53	Daidzein	C ₁₅ H ₁₀ O ₄	Water extraction, enters the blood	Li et al. (2024a)
54	Daidzin	C ₂₂ H ₂₂ O ₁₀	Water extraction	Li et al. (2024b)
55	Dehydrohispidol C	C ₂₁ H ₂₂ O ₅	Water extraction	Li et al. (2024a)
56	Dehydrohispidol D	C ₂₂ H ₂₄ O ₅	Water extraction	Li et al. (2024b)
57	Dehydropachymic acid	C ₃₃ H ₅₀ O ₅	Alcohol extraction	Ou et al. (2024)
58	Dehydrotumulosic acid	C ₃₁ H ₄₈ O ₄	Alcohol extraction, entering the blood	Gao et al. (2024)
59	Dihydroquercetin-7-O-rhamnoside	C ₂₁ H ₂₂ O ₁₁	Water extraction	Li et al. (2024a)
60	Diosgenin	C ₂₇ H ₄₂ O ₃	Enter the bloodstream	Xu et al. (2021)
61	Eleutherinolone	C ₂₂ H ₂₆ O ₉	Water extraction	Li et al. (2024b)
62	Epicatechin	C ₁₅ H ₁₄ O ₆	Alcohol extraction	Ou et al. (2024)
63	Ethyl palmitate	C ₁₈ H ₃₆ O ₂	Water extraction	Li et al. (2024a)
64	Formononetin	C ₂₂ H ₂₂ O ₉	Water extraction	Li et al. (2024b)
65	Formononetin	C ₁₆ H ₁₂ O ₄	Water extraction	Li et al. (2024a)
66	Fraxetin	C ₂₇ H ₃₀ O ₁₄	Water extraction	Li et al. (2024b)
67	Gancaonin E	C ₂₅ H ₂₈ O ₆	Alcohol extraction	Ou et al. (2024)
68	Gancaonin L	C ₂₀ H ₁₈ O ₆	Alcohol extraction	Ou et al. (2024)
69	Genistein	C ₁₆ H ₁₂ O ₅	Water extraction	Li et al. (2024a)

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TABLE 3 (Continued) The metabolites of SLBZS.

No.	Compounds	Formula	Method	Refs
70	Genkwanin	C ₁₆ H ₁₂ O ₅	Water extraction	Li et al. (2024b)
71	Ginsenoside Rb1	C ₅₄ H ₉₂ O ₂₃	Alcohol extraction, entering the blood	Gao et al. (2024)
72	Ginsenoside Re	C ₄₈ H ₈₂ O ₁₈	Alcohol extraction, entering the blood	Gao et al. (2024)
73	Ginsenoside Re Isomer	C ₄₈ H ₈₂ O ₁₈	Enter the bloodstream	Gao et al. (2024)
74	Ginsenoside Rf	C ₄₂ H ₇₂ O ₁₄	Alcohol extraction	Ou et al. (2024)
75	Ginsenoside Rg1	C ₄₂ H ₇₂ O ₁₄	Alcohol extraction, entering the blood	Gao et al. (2024), Xu et al. (2021)
76	Glabridin	C ₂₀ H ₂₀ O ₄	Water extraction	Li et al. (2024a)
77	Glabrolide	C ₂₂ H ₂₂ O ₆	Water extraction	Li et al. (2024b)
78	Glicophenone	C ₂₂ H ₂₂ O ₆	Water extraction	Li et al. (2024a)
79	Glisoliquiritigenin	C ₂₂ H ₂₂ O ₆	Water extraction	Li et al. (2024b)
80	Glycitin	C ₂₂ H ₂₂ O ₁₀	Enter the bloodstream	Li et al. (2024a)
81	Glycycoumarin	C ₂₁ H ₂₀ O ₆	Alcohol extraction, water extraction, and entry into the blood	Gao et al. (2024)
82	Glycyrol A	C ₂₀ H ₁₈ O ₆	Water extraction	Li et al. (2024b)
83	Glycyrol B	C ₂₀ H ₁₆ O ₆	Water extraction	Li et al. (2024a)
84	Glycyronin E	C ₂₅ H ₂₈ O ₆	Water extraction	Li et al. (2024b)
85	Glycyronin H	C ₂₅ H ₂₄ O ₆	Water extraction	Li et al. (2024a)
86	Glycyronin L	C ₂₀ H ₁₈ O ₆	Water extraction	Li et al. (2024b)
87	Glycyrrhetolide	C ₃₀ H ₄₄ O ₄	Water extraction	Li et al. (2024a)
88	Glycyrrhizic acid	C ₄₂ H ₆₂ O ₁₆	Alcohol extraction, entering the blood	Gao et al. (2024)
89	Glycyrrhizic acid G2	C ₄₂ H ₆₂ O ₁₇	Water extraction	Li et al. (2024b)
90	Glycyrrhizic acid Isomer	C ₄₂ H ₆₂ O ₁₆	Alcohol extraction, entering the blood	Gao et al. (2024)
91	Glyyunnansapogenin C	C ₃₀ H ₄₄ O ₄	Water extraction	Li et al. (2024a)
92	Glyyunnansapogenin E	C ₃₀ H ₄₆ O ₅	Water extraction, enters the blood	Li et al. (2024b)
93	Hedysarumscoparium coumestrol B	C ₁₆ H ₁₀ O ₆	Water extraction	Li et al. (2024a)
94	Hispidin A	C ₂₅ H ₂₆ O ₆	Water extraction	Li et al. (2024b)
95	Hispidin C	C ₂₁ H ₂₄ O ₅	Water extraction	Li et al. (2024a)
96	Hispidin D	C ₂₂ H ₂₆ O ₅	Water extraction	Li et al. (2024b)
97	Homoplantagin	C ₁₆ H ₁₄ O ₅	Water extraction	Li et al. (2024a)
98	Hordenine	C ₁₆ H ₁₂ O ₄	Water extraction	Li et al. (2024b)
99	Isoapioglycyrrhizin	C ₂₆ H ₃₀ O ₁₃	Water extraction	Li et al. (2024a)
100	Isococlaurine	C ₁₇ H ₁₉ NO ₃	Alcohol extraction	Ou et al. (2024)
101	Isoraxidin	C ₂₇ H ₃₀ O ₁₄	Water extraction	Li et al. (2024b)
102	Isoliquiritigenin	C ₁₅ H ₁₂ O ₄	Water extraction, enters the blood	Xu et al. (2021)
103	Isoliquiritin	C ₂₁ H ₂₂ O ₉	Alcohol extraction, water extraction, and entry into the blood	Gao et al. (2024)
104	Isoliquiritin apioside	C ₂₆ H ₃₀ O ₁₃		Gao et al. (2024)

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TABLE 3 (Continued) The metabolites of SLBZS.

No.	Compounds	Formula	Method	Refs
			Alcohol extraction, entering the blood	
105	Isolupalbigenin	C ₂₅ H ₂₆ O ₅	Water extraction	Li et al. (2024a)
106	Isorhamnetin-3-O-neohesperidoside	C ₂₈ H ₃₂ O ₁₆	Water extraction	Li et al. (2024b)
107	Isoschaftoside	C ₂₆ H ₂₈ O ₁₄	Water extraction, enters the blood	Li et al. (2024a)
108	Isovitexin	C ₂₁ H ₂₀ O ₁₂	Water extraction	Li et al. (2024b)
109	Kaempferol-3-O-robinobioside	C ₂₇ H ₃₀ O ₁₆	Water extraction	Li et al. (2024a)
110	Kaempferol-7-O-glucoside	C ₂₁ H ₂₀ O ₁₁	Water extraction	Li et al. (2024b)
111	Leucine	C ₆ H ₁₃ NO ₂	Water extraction	Li et al. (2024a)
112	Licocoumarone	C ₂₀ H ₂₀ O ₅	Water extraction, enters the blood	Li et al. (2024b)
113	Licoflavonol	C ₂₀ H ₁₈ O ₆	Alcohol extraction	Ou et al. (2024)
114	Licoisoflavone A	C ₂₀ H ₁₈ O ₆	Alcohol extraction	Ou et al. (2024)
115	Licorice chalcone B	C ₁₆ H ₁₄ O ₅	Water extraction	Li et al. (2024b)
116	Licorice chalcone C	C ₂₁ H ₂₂ O ₄	Water extraction	Li et al. (2024a)
117	Licorice chalcone D	C ₂₁ H ₂₂ O ₅	Water extraction	Li et al. (2024b)
118	Licorice chalcone E	C ₂₁ H ₂₂ O ₄	Water extraction	Li et al. (2024a)
119	Licorice flavonoid C	C ₂₀ H ₁₈ O ₅	Water extraction	Li et al. (2024b)
120	Licoricesaponin A3	C ₄₈ H ₇₂ O ₂₁	Alcohol extraction, entering the blood	Gao et al. (2024)
121	Licoricesaponin B2	C ₄₂ H ₆₄ O ₁₅	Alcohol extraction, entering the blood	Gao et al. (2024)
122	Licoricesaponin C2	C ₄₂ H ₆₂ O ₁₅	Alcohol extraction, entering the blood	Gao et al. (2024)
123	Licoricesaponin C2 Isomer	C ₄₂ H ₆₂ O ₁₅	Alcohol extraction	Ou et al. (2024)
124	Licoricesaponin E2	C ₄₂ H ₆₀ O ₁₆	Alcohol extraction, entering the blood	Gao et al. (2024)
125	Licoricesaponin G2	C ₄₂ H ₆₂ O ₁₇	Alcohol extraction, entering the blood	Gao et al. (2024)
126	Licoriphenone	C ₂₁ H ₂₄ O ₆	Water extraction, enters the blood	Li et al. (2024a)
127	Lignoceric acid	C ₂₄ H ₄₈ O ₂	Water extraction	Li et al. (2024b)
128	Linolenic acid	C ₁₈ H ₃₀ O ₂	Water extraction	Li et al. (2024a)
129	Liquiritigenin	C ₁₅ H ₁₂ O ₄	Alcohol extraction, water extraction, and entry into the blood	Gao et al. (2024), Li et al. (2024a)
130	Liquiritigenol	C ₂₁ H ₁₈ O ₆	Water extraction	Li et al. (2024b)
131	Liquiritin	C ₂₁ H ₂₂ O ₉	Alcohol extraction, water extraction, and entry into the blood	Gao et al. (2024); Li et al. (2024a)
132	Liquiritin apioside	C ₂₆ H ₃₀ O ₁₃	Enter the bloodstream	Gao et al. (2024)
133	Liquiritinapioside	C ₂₆ H ₃₀ O ₁₃	Alcohol extraction	Ou et al. (2024)
134	Lotusine	C ₁₉ H ₂₄ NO ₃ ⁺	Alcohol extraction	Ou et al. (2024)
135	Malic acid	C ₄ H ₆ O ₅	Water extraction	Li et al. (2024a)
136	Malonyl + Isoliquiritin apioside	C ₂₉ H ₃₂ O ₁₆	Alcohol extraction	Ou et al. (2024)
137	Malonyl + Liquiritinapioside	C ₂₉ H ₃₂ O ₁₆	Alcohol extraction	Ou et al. (2024)

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TABLE 3 (Continued) The metabolites of SLBZS.

No.	Compounds	Formula	Method	Refs
138	Mannide monooleate	C ₂₄ H ₄₄ O ₇	Alcohol extraction	Ou et al. (2024)
139	Medicarpin	C ₁₆ H ₁₄ O ₄	Water extraction	Li et al. (2024b)
140	Naringenin	C ₁₅ H ₁₂ O ₅	Water extraction	Li et al. (2024b)
141	Neferine	C ₃₈ H ₄₄ N ₂ O ₆	Alcohol extraction, entering the blood	Xu et al. (2021)
142	Neoisoliquiritin	C ₂₁ H ₂₂ O ₉	Alcohol extraction	Ou et al. (2024)
143	Nuciferine	C ₁₉ H ₂₁ NO ₂	Enter the bloodstream	Xu et al. (2021)
144	Oleanolic acid	C ₃₀ H ₄₈ O ₃	Alcohol extraction	Ou et al. (2024)
145	Orientin	C ₂₁ H ₂₀ O ₁₁	Water extraction, enters the blood	Li et al. (2024b)
146	Pachymic acid	C ₃₃ H ₅₂ O ₅	Alcohol extraction, entering the blood	Xu et al. (2021)
147	Pachymic acid B	C ₃₀ H ₄₄ O ₅	Water extraction	Li et al. (2024b)
148	Palmitic acid	C ₁₆ H ₃₂ O ₂	Alcohol extraction	Ou et al. (2024)
149	Panaxadiol	C ₃₀ H ₅₂ O ₃	Enter the bloodstream	Xu et al. (2021)
150	Phenylalanine	C ₉ H ₁₁ NO ₂	Water extraction	Li et al. (2024b)
151	P-hydroxycinnamic acid	C ₉ H ₈ O ₃	Water extraction	Li et al. (2024a)
152	Pinellic acid	C ₁₈ H ₃₄ O ₅	Alcohol extraction	Ou et al. (2024)
153	Platycodin A	C ₅₉ H ₉₄ O ₂₉	Alcohol extraction	Ou et al. (2024)
154	Platycodin C	C ₅₉ H ₉₄ O ₂₉	Alcohol extraction	Ou et al. (2024)
155	Platycodin D	C ₅₇ H ₉₂ O ₂₈	Alcohol extraction, entering the blood	Xu et al. (2021)
156	Platycodin D2	C ₆₃ H ₁₀₂ O ₃₃	Alcohol extraction	Ou et al. (2024)
157	Platycodin E	C ₆₂ H ₁₁₆ O ₄₃	Alcohol extraction	Ou et al. (2024)
158	Platycodins K	C ₅₉ H ₉₂ O ₃₀	Alcohol extraction	Ou et al. (2024)
159	Platycogenic acid A	C ₅₇ H ₉₀ O ₂₉	Alcohol extraction, entering the blood	Gao et al. (2024)
160	Polyporenic acid C	C ₃₁ H ₄₆ O ₄	Alcohol extraction	Ou et al. (2024)
161	Poricoic acid C	C ₃₁ H ₄₆ O ₄	Water extraction	Li et al. (2024b)
162	Protocatechuic acid	C ₇ H ₆ O ₄	Water extraction, enters the blood	Li et al. (2024a)
163	Quercitrin	C ₂₁ H ₂₀ O ₁₁	Alcohol extraction	Ou et al. (2024)
164	Rhamnose	C ₆ H ₁₄ O ₆	Water extraction	Li et al. (2024b)
165	Salicylic acid	C ₇ H ₆ O ₃	Water extraction	Li et al. (2024a)
166	Schaftoside	C ₂₇ H ₃₀ O ₁₅	Water extraction	Li et al. (2024b)
167	Schaftoside	C ₂₆ H ₂₈ O ₁₄	Water extraction	Li et al. (2024a)
168	Semiglycyrol B	C ₂₀ H ₁₆ O ₆	Water extraction	Li et al. (2024b)
169	Tetrahydroxymethoxychalcone	C ₁₆ H ₁₄ O ₆	Water extraction	Li et al. (2024a)
170	Tumulosic acid	C ₃₁ H ₅₀ O ₄	Alcohol extraction, entering the blood	Gao et al. (2024)
171	Tyrosine	C ₉ H ₁₁ NO ₃	Water extraction	Li et al. (2024b)
172	Uralensis saponin N	C ₂₄ H ₆₂ O ₁₇	Water extraction	Li et al. (2024a)
173	Uralol	C ₂₀ H ₁₈ O ₇	Water extraction	Li et al. (2024b)

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TABLE 3 (Continued) The metabolites of SLBZS.

No.	Compounds	Formula	Method	Refs
174	Uralsaponin B	C ₄₂ H ₆₂ O ₁₆	Alcohol extraction, entering the blood	Gao et al. (2024)
175	Ursolic Acid	C ₃₀ H ₄₈ O ₃	Alcohol extraction	Ou et al. (2024)
176	Vanillic acid	C ₈ H ₈ O ₄	Water extraction	Li et al. (2024b)
177	Vernolic acid	C ₁₈ H ₃₂ O ₃	Alcohol extraction	Ou et al. (2024)
178	Wighteone	C ₂₀ H ₁₈ O ₅	Water extraction	Li et al. (2024a)
179	Xenognosin B	C ₁₆ H ₁₂ O ₅	Water extraction	Li et al. (2024b)

Sharen is the desiccated and mature fruit of *Amomum villosum* Lour., *Amomum villosum* Lour. var. *xanthioides* T. L. Wu et Senjen, or *Amomum longiligulare* T. L. Wu, primarily comprising various chemical constituents, including volatile oil, which is typically regarded as the active component of amomum kernel, with bornyl acetate serving as a distinctive metabolite of Sharen (Feng et al., 2024).

Dazao is the desiccated and mature fruit of *Ziziphus jujuba* Mall. The composition mostly includes sugars, triterpenoids, phenolic acids, and other constituents, with ursolic acid and oleanolic acid serving as the distinctive metabolites of Dazao (Lu et al., 2021).

5.3 Q-marker prediction based on the formula compatibility environment

This TCM formula consists of Renshen, Baizhu, Fuling, Shanyao, Lianzi, Baibiandou, Sharen, Jiegeng, Gancao, and Dazao in the proportions of 15:15:15:15:9:9:12:6:6:10:7.5. Renshen has the ability to enhance qi levels in the body, particularly in the spleen and lungs. Baizhu exhibits properties of moisture desiccation, spleen energising, deficiency replenishment, and qi enhancement, whereas Fuling is distinguished by its capacity to alleviate water retention, promote moisture, and stimulate the spleen. The aforementioned three herbs are crucial in SLBZS. Shanyao enhances spleen and stomach function, while Lianzi also promotes spleen and stomach vitality, hence augmenting the effects of spleen and qi invigorating. Both Baibiandou and Yiyiren can enhance the efficacy of spleen fortification and dampness reduction. Sharen is capable of both dehumidifying and regulating the air machine. Jiegeng facilitates the enhancement of lung qi. Gancao nourishes qi, while Dazao nourishes the spleen and stomach, serving as adjunctive medications. The amalgamation of these TCM plant medications aims to enhance qi, stimulate the spleen, strengthen the lung, and promote the expulsion of moisture.

In clinical practice, individual TCM herbal remedies are often amalgamated with supplementary botanical medicines to generate a compound. The efficacy and potential pharmacodynamic qualities of TCM botanical drugs depend on the formulation or dosage of the plant. Consequently, it is imperative to forecast Q-markers associated with lung function preservation by integrating TCM within a composite context. A study (Zhang, 2019) demonstrated that the concentrations of ginsenosides Rg1, Re, Rf, Rb1, Rc, Rb2, and Rd elevated, whereas the concentration of atractone diminished

after the Renshen-Baizhu compatibility. Another study (Li et al., 2014) indicated a significant increase in the concentrations of ginsenosides Rg1, Re, Rf, Rd, and atractylenolide I in Renshen-Baizhu compatibility. The levels of ginsenosides Rb3 and F1 were significantly elevated in the Renshen-Shanyao compatibility study, whereas the concentrations of 16 ginsenosides, including Rg1, Re, Rf, Rb1, Rg2, Rc, Rb2, Rd, F2, Rg3, protopanaxriol, CK, Rh2, and the total sugar content, were markedly reduced (Zhao, 2015). Yue et al. (2018) analysed the constituents of volatile oil following the compatibility of Baizhu and Fuling, discovering the presence of new components, including 14 substances such as 5-methylfuran aldehyde, glycylene, terpene olefin, carpinene, and linolenic acid. A subsequent investigation (Wang et al., 2021) demonstrated a considerable rise in the concentrations of platycodin D, glycyrrhizic acid, and liquiritin when Jiegeng-Gancao was combined. The synergistic interaction between active components and certain herbs often accounts for the efficacy and therapeutic effects of TCM formulae. A single plant exhibits various pharmacological metabolites and mechanisms of action in a complex environment, resulting in unique therapeutic advantages.

5.4 Q-marker prediction based on the association between metabolites and effectiveness

The metabolites of a drug dictate its pharmacological impact and provide the essential element of Q-marker, which is vital for monitoring prescription quality. Studies suggest that the metabolites of SLBZS in treating respiratory disorders may be associated with the chemical components absorbed in the serum of Renshen, Baizhu, Fuling, Baibiandou, and Gancao. The mechanism of action of the active constituents of SLBZS is depicted in Table 4.

5.4.1 Renshen

Ginsenosides, particularly Rg1, Re, and Rb1, are the unique metabolites of Renshen and serve as the bioactive components of SLBZS, demonstrating considerable therapeutic effectiveness against acute lung injury, pneumonia, asthma, and various respiratory disorders. Ji et al. (2021) established a cellular model of acute lung injury by subjecting lung epithelial cells to lipopolysaccharide (LPS) exposure. They subsequently discovered that ginsenoside Rg1 may inhibit cell death by augmenting

TABLE 4 Mechanism of action of SLBZS active ingredients.

No.	Active ingredient	Model and dosage of administration	The medication time	Control drugs	Effect	Mechanism	Refs
1	Apigenin	Model of lung injury: mouse (20, 50 mg/kg), Primary Splenocytes	7 days		Anti-inflammatory, anti-oxidative stress	Downregulated MDA, IL-6 and TNF- α , upregulated SOD, GSH-PX, CAT, IL-2, CD4 ⁺ and CD8 ⁺	Liu et al. (2018)
2	Apigenin	Model of asthma: mouse (10, 20 mg/kg), HBE (20 μ M)	6 weeks; 16 h	Dexamethasone; selonsertib	Anti-inflammation, anti-apoptosis, anti-oxidative stress	Modulated ROS-ASK1-MAPK pathway, downregulated IL-5, IL-4, IL-13, IL-17, TNF- α , IFN- γ , T-bet, Gata3, ROR γ -t, p-ASK1/ASK1, p-JNK/JNK, p-p38/p38, p-ERK/ERK, cyto-chrome c, Bax, caspase-3, upregulated Foxp3, Bcl-2	Yu et al. (2023)
3	Apigenin	Model of COPD: WI-38 cells (10, 20, 40 μ M)	24 h	Resveratrol	Anti-oxidative stress, anti-aging	Modulated SIRT1-NAD ⁺ -CD38 Axis, downregulated SA- β -gal, ac-p53, p21, p16 and CD38, upregulated p-Rb, cyclin D1, SIRT1, NAD ⁺ , NAD ⁺ /NADH.	Li et al. (2021a)
4	Atractylolide I	Model of lung injury: mouse (5, 10, 20 mg/kg)	5 h	VGX-1027	Anti-inflammatory	Inhibition of TLR4/NF- κ B pathway, downregulate TNF- α , IL-6, IL-1 β , IL-13 and MIF, and upregulate IL-10	Zhang et al. (2015)
5	Atractylolide I	Model of recurrent respiratory tract infection: rat (3.33, 13.32 mg/kg)	6 weeks	Amoxicillin and clavulanate potassium	Anti-inflammatory, anti-oxidative stress	Inhibition of PI3K/Akt/mTOR pathway, downregulated IL-6, TNF- α , MDA, p-PI3K, p-Akt, p-mTOR, and upregulated SOD.	Wang et al. (2024c)
6	Atractylolide III	Model of lung injury: mouse (2, 8 mg/kg)	24 h		Anti-inflammatory, anti-apoptosis	Upregulation of Bcl-2, downregulation of IL-1 β , TNF- α , IL-6, Bax, caspase-3, VNN1 and FoxO1	Fu et al. (2021)
7	Atractylolide III	Model of silicosis: mouse (30 mg/kg)	28 days and 56 days		Activating autophagy, anti-apoptosis	Activation of EGFR-mTOR pathway, downregulated LC3-II/I, Beclin1, p62, caspase 9, caspase 3, Col-1 and α -SMA, and upregulated LAMP2, p-EGFR, p-PI3K and p-Akt	Tan et al. (2023)
8	Atractylolide III	Model of asthma: mouse (25 mg/kg); 16HBE (100 ng/ μ L)	10 days; 48 h		Anti-apoptosis	Inhibit the activation of NLRP3 inflammasome, restore Th1/Th2 balance, downregulate caspase-1, ASC, NLRP3, IL-4, IL-13, and upregulate IL-12, γ -IFN.	Zhu et al. (2020)
9	Atractylolide III	Model of asthma: mouse (0.1, 1, 10 mg/kg)	7 days	dexamethasone	Anti-inflammatory, anti-oxidative stress	Inhibition of STAT3, upregulation of IFN- γ , IL-10, IL-12, GSH, SOD, CAT, downregulation of IL-4, IL-5, IL-13, ROS, MDA, LDH.	Zhang et al. (2021)
10	Atractylolide III	Model of lung injury: rat (0.6, 1.2, 2.4 mg/kg)	28 days		Anti-oxidative stress	Activation of Nrf2/NQO1/HO-1 pathway, downregulate Caspase-3, Caspase-9, TGF- β , α -SMA, IL-6, iNOS, TNF- α , MDA, LDH, and upregulate IL-10,	Huai and Ding. (2020)

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TABLE 4 (Continued) Mechanism of action of SLBZS active ingredients.

No.	Active ingredient	Model and dosage of administration	The medication time	Control drugs	Effect	Mechanism	Refs
						SOD, GSH, Nrf2, NQO1 and HO-1	
11	Chikusetsusaponin V	Model of lung injury: mouse (5, 10, 20 mg/kg)	4 days		Anti-inflammatory	Inhibition of NF- κ B pathway, downregulation of TNF- α , IL-1 β , IL-6, p-p65, p-I- κ B, upregulation of LXR α	Su et al. (2019)
12	Ginsenoside Rb1	Model of lung injury: mouse (10, 20 mg/kg), RAW 264.7 cells (10, 20 μ g/mL)	24 days; 1 h		Anti-inflammatory	Inhibition of NF- κ B and MAPK pathways, downregulation of IL-1 β , IL-6, TNF- α , TLR2, p-p65, p-ERK, p-JNK.	Shaukat et al. (2019)
13	Ginsenoside Rb1	Model of asthma: mouse (10, 20 mg/kg)	3 days	Dexamethasone	Anti-inflammatory	Downregulated Th1/Th2, IL4, GATA3, upregulated IFN- γ , T-bet.	Chen et al. (2015)
14	Ginsenoside Re	Model of II/R lung injury: rat (8, 16 mg/kg)	5 days		Anti-inflammatory, anti-oxidative	Downregulated IL-6, TNF- α , IL-10, MDA, and upregulated SOD	Fang et al. (2014)
15	Ginsenosides Rg1	Model of lung injury: mouse (30 mg/kg), MLE-12 cells (25 μ g/mL)	24 h; 1 h		Activating autophagy, Anti-apoptosis	Downregulated p-p65, upregulated Nrf2	Ji et al. (2021)
16	Ginsenosides Rg1	Model of pulmonary inflammation: mouse (10, 20 mg/kg), A549 cells (12.5, 25, 50 μ M)			Anti-inflammatory, anti-endoplasmic reticulum stress	Downregulated TNF- α , IL-1 β , IL-6, p-p65, iNOS, CHOP, GRP78, IRE1 α and ATF6, upregulated SIRT1	Wang et al. (2019)
17	Ginsenosides Rg1	Model of lung injury: mouse (40, 200 mg/kg)	7 h		Anti-inflammatory, regulation of M2 macrophage infiltration, anti-apoptosis	Downregulation of NF- κ B, caspase-3, TNF- α , IL-1 β and IL-6	Bao et al. (2015)
18	Ginsenosides Rg1	Model of COPD: rat (5, 10, 20 mg/kg), HBE cells (40 μ M)	12 weeks; 48 h		Anti-Pulmonary Epithelial-Mesenchymal Transition	Inhibition of TGF- β 1/Smad pathway, downregulation of α -SMA, TGF- β 1, TGF- β R1, phospho-Smad2, phospho-Smad3, upregulation of E-cad	Guan et al. (2017)
19	Glycyrrhizic acid	Model of lung injury: rat (15 mg/kg)	3 months		Anti-inflammatory, anti-oxidative stress, anti-pulmonary fibrosis	Downregulated MDA, TNF- α , TGF- β , IL-1 β , MTC stain, α SMA, CD68, upregulated GSH, TAC.	Elsherbini et al. (2021)
20	Glycyrrhizic acid	Model of lung injury: mouse (200 mg/kg), RAW264.7 cells (100 μ g/mL)	25 h; 25 h		Anti-inflammatory, activates autophagy	Modulated PI3K/AKT/mTOR pathway, downregulated TNF- α , IL-1 β , HMGB1, P62, p-PI3K/PI3K, p-AKT/AKT, p-mTOR/mTOR, upregulated LC3-II/LC3-I, Beclin-1	Qu et al. (2019)
21	Glycyrrhizic acid	Model of lung injury: rat (25, 50 mg/kg)	24 h		Anti-inflammatory, anti-apoptosis, anti-oxidative stress	Inhibition of NF- κ B and MAPK pathways, downregulated TNF- α , IL-1 β , IL-6, NO, iNOS, MDA, 8-OHdG, NT, caspase-3, P-i- κ B- α , DNA binding activity of NF- κ B, p-JNK/JNK, p-p38/p38, Upregulated SOD, Bcl-2/Bax and I κ B- α	Zhao et al. (2016)

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TABLE 4 (Continued) Mechanism of action of SLBZS active ingredients.

No.	Active ingredient	Model and dosage of administration	The medication time	Control drugs	Effect	Mechanism	Refs
22	Glycyrrhizic acid	Model of lung injury: mouse (10, 20, 40 mg/kg)	5 days	dexamethasone	Anti-inflammatory, immune regulation	Downregulated IL-4, IL-5 and IL-13, upregulated IFN- γ , Tregs and Foxp3	Ma et al. (2013)
23	Liquiritigenin	Model of lung injury: <i>S. aureus</i> strain 8325-4 (4, 8, 16, 32 mg/mL)	30 min		Anti-staphylococcus aureus	Inhibition of alpha-hemolysin	Dai et al. (2013)
24	Liquiritigenin	Model of pulmonary fibrosis: mouse (25, 50, 100 mg/kg), Primary mouse lung fibroblasts (3, 10, 30, 100 μ M)	14 days; 2 h		Anti-fibrosis, anti-oxidative stress	Activation of SIRT1/Nrf2 pathway, downregulated collagen I, α -SMA, GSH, SOD and ROS, upregulated MDA, CAT, HO-1, NQO-1 and SIRT1	Hua and Ren. (2024)
25	Liquiritin	Model of lung injury: Zebrafish (25, 50, 100 μ M), mouse (40, 80 mg/kg), RAW264.7 (100, 200,300 μ M)	0–80 h; 7 days; 2 h	dexamethasone	Anti-inflammatory	Inhibition of JNK/Nur77/c-Jun pathway, downregulation of TNF- α , IL-6, p-JNK, p-Nur77, p-c-Jun, upregulation of Nur77	Zhou et al. (2023)
26	Liquiritin	Model of lung injury: mouse (25, 50, 100 mg/kg), THP-1 cells (25, 50, 100 μ M)	12 h; 1 h		Anti-inflammatory	Inhibition of NF- κ B pathway, downregulated TNF- α , IL-6, IL-1 β , TRPV1, TRPA1, p-p65/p65, p-I- κ B α /I- κ B α	Liu et al. (2020)
27	Liquiritin	Model of lung injury mouse (20, 50 mg/kg), MLE-2 cells (50 μ M)	7 days; 3 h		Anti-inflammation, anti-iron death	Downregulated MDA, Fe+, TNF- α , IL-6, Hmgb1, Hif-1 α , HO-1, Ptgs2 and Acs14, upregulated GSH and Gpx4	Zhongyin et al. (2022)
28	Pachymaric acid	Model of pulmonary fibrosis: rat (10, 20, 40 mg/kg)	14 days		Inhibit endoplasmic reticulum stress, anti-oxidative stress, improve mitochondrial function	Downregulated Hyp, TGF- β 1, collagen I, α -SMA, fibronectin, MDA, ROS, GRP78, CHOP, Caspase 9 and ATF4, upregulated SOD, CAT and ATP.	Li et al. (2023)
29	Pachymaric acid	Model of lung injury: mouse (25, 50, 100 mg/kg)	28 days	Prednisone acetate tablets	Anti-inflammatory, anti-oxidative stress	Downregulated IL-6, TNF- α , HYD, MDA, NLRP3, ASC, IL-1 β , P20, TXNIP, upregulated IL-10, SOD, GSH-Px	Wang et al. (2023)
30	Pachymaric acid	Model of Pneumonia: rat (10, 20 mg/kg)	3 days		Anti-inflammatory, anti-apoptosis	Inhibition of NF- κ B and MAPK pathways, downregulated IL-6, IL-1 β , TNF- α , MCP-1, BAX, p-p65/p65, p-p38/p38, p-ERK1/2/ERK1/2, upregulated Bcl-2	Gui et al. (2021)

autophagy and Nrf2 expression. A study by Wang et al. (2019) indicates that ginsenoside Rg1 can alleviate inflammation and lung injury caused by sepsis. This protective effect may be attributed to the decrease of inflammatory factors TNF- α , IL-1 β , and IL-6 in lung tissue, together with the alleviation of endoplasmic reticulum stress. Furthermore, ginsenoside Rg1 can suppress lung epithelial-mesenchymal transition via modulating the infiltration of M2 macrophages in lung tissues (Bao et al., 2015; Guan et al., 2017). In a rat model of intestinal ischemia/reperfusion (I/R) lung injury, Fang et al. (2014) demonstrated that ginsenoside Re increased serum levels of TNF- α , IL-6, IL-10, superoxide dismutase (SOD), and malonaldehyde (MDA), showcasing its

antioxidative and anti-inflammatory effects. Shaukat et al. (2019) assessed the anti-inflammatory properties of ginsenoside Rb1 in mice with acute lung injury, discovering its regulation of NF- κ B and mitogen-activated protein kinase (MAPK) signalling pathways via TLR2, therefore preserving lung function in the subjects. Furthermore, ginsenoside Rb1 may exert an anti-asthmatic effect by modulating the Th1/Th2 balance (Chen et al., 2015).

5.4.2 Baizhu

Atractylolide I and atractylolide III are the principal metabolites of Baizhu. Research has shown that atractylolide I and atractylolide III provide advantageous effects on lung damage, asthma,

pulmonary fibrosis, and other ailments. In an *in vitro* investigation, Fu et al. (2021) demonstrated that atractonolide III could ameliorate lung injury caused by sepsis, potentially through the inhibition of Forkhead box protein O1 (FoxO1) and Vanin 1 (VNN1) protein expression, thereby decreasing lung tissue inflammation and suppressing cellular apoptosis. Atractylenolide III was demonstrated in a separate investigation to enhance autophagy failure, subsequently reducing apoptosis and alleviating lung fibrosis in silicotic mice (Tan et al., 2023). Atractylodes III can suppress the activation of the nucleotide-binding oligomerisation domain, NLRP3 inflammasome, restore Th1/Th2 balance in an asthma animal model, prevent death of bronchial epithelial cells, and demonstrate significant anti-asthma efficacy (Zhu et al., 2020). Moreover, research indicates that atractylenolide III can reduce oxidative stress in lung tissue and mitigate the symptoms of pulmonary fibrosis, asthma, and other conditions (Zhang et al., 2021; Huai and Ding, 2020). Atractylenolide I mitigates lung function impairment and reduces the inflammatory response in mice with acute lung injury via inhibiting TLR4 expression and NF- κ B activation (Zhang et al., 2015). Atractylenolide I can also modulate the Phosphoinositide 3-kinase (PI3K)/protein kinase B (Akt)/mammalian target of rapamycin (mTOR) signalling pathway to enhance lung function in a rat model of recurrent respiratory infections (Wang et al., 2024b).

5.4.3 Fuling

Pachymic acid shown an optimum protective effect on lung function in the study of anti-pulmonary fibrosis and anti-pneumonia. A study (Li et al., 2023) demonstrated that pachymic acid can mitigate the symptoms of pulmonary oedema and pulmonary fibrosis in rats, potentially via decreasing endoplasmic reticulum stress and enhancing mitochondrial activity. Pachymic acid may also mitigate lung fibrosis by diminishing inflammatory responses and oxidative stress (Wang et al., 2023). Pachymic acid may alleviate pneumonia symptoms in rats by reducing lung inflammation and avoiding cell death, potentially through the modulation of the NF- κ B and MAPK signalling pathways (Gui et al., 2021).

5.4.4 Baibiandou

Chikusetsusaponin V, derived from Baibiandou, has shown effectiveness in alleviating acute lung injury. Su et al. (2019) developed a mouse model of acute lung injury utilising lipopolysaccharide and found that chikusetsusaponin V ameliorated lung pathological damage by reducing the concentrations of TNF- α , IL-1 β , IL-6, and other inflammatory mediators in alveolar lavage fluid, while also inhibiting the activation of the NF- κ B signalling pathway.

5.4.5 Gancao

Glycyrrhizin, isorhamnetin, glycyrrhizin, and apigenin are the primary components of liquorice, demonstrating therapeutic effects against lung injury and pulmonary fibrosis. Liquiritin exhibits effective effectiveness in mitigating acute lung injury. Zhou et al. (2023) developed lung damage models utilising LPS in zebrafish and mice, revealing that Liquiritin markedly diminishes inflammation. This action may be ascribed to its suppression of the C-Jun N-terminal kinases (JNK)/Nur77/c-Jun signalling pathway. A

separate study (Liu et al., 2020) indicated that the anti-acute lung injury activity of liquiritin may be associated with transient receptor potential vanilloid-1 (TRPV1), transient receptor potential A1 (TRPA1) targets, and the NF- κ B signalling system. Research indicated that isoliquiritin apioside may safeguard the lungs by mitigating lung epithelial ferroptosis induced by hypoxia-inducible factor (Hif)-1 α -mediated ferroptosis in the context of acute lung injury resulting from ischemia/reperfusion (II/R) (Zhongyin et al., 2022). Liquiritigenin is an active component of Gancao. Research indicates that liquiritigenin safeguards lung cells by dose-dependently suppressing the manufacture of α -hemolysin by *Staphylococcus aureus* (Dai et al., 2013). Liquiritigenin may provide an anti-pulmonary fibrosis effect, potentially through the modulation of the Sirtuin 1 (SIRT1)/Nrf2 signalling pathway to influence myofibroblast development (Hua and Ren, 2024). The preventive influence of glycyrrhizic acid on pulmonary function merits our consideration. Research indicates that glycyrrhizic acid can mitigate oxidative stress, diminish inflammation, and avert pulmonary fibrosis to improve lung damage caused by sodium nitrite (Elsherbini et al., 2021). The enhancement of lung function by glycyrrhizic acid is associated with the suppression of autophagy (Qu et al., 2019), apoptosis (Zhao et al., 2016), and immunological modulation (Ma et al., 2013). Apigenin is a flavonoid constituent of Gancao. Research indicates that apigenin safeguards lung function by modulating inflammatory responses, oxidative stress levels (Liu et al., 2018), correcting immunological imbalances, and reducing cellular apoptosis (Yu et al., 2023). Moreover, apigenin can mitigate the senescence of lung fibroblasts via the SIRT1-NAD-CD38 axis (Li J. et al., 2021).

5.5 Q-marker prediction based on metabolites measurability

TCM formulations comprise many TCM botanical drugs in specific ratios, making it essential to identify the principal metabolites that mediate their pharmacological effects. Therefore, Q-markers must be measurable.

Liu et al. (2018) employed the HPLC method to quantitatively assess the constituents of SLBZS, revealing concentrations of 3.12–3.29 mg/g for ginsenoside Rg1, 1.78–1.99 mg/g for Rb1, 1.65–1.82 mg/g for ginsenoside Re, 1.07–1.22 mg/g for liquiritin, and 4.55–4.89 mg/g for glycyrrhizic acid, respectively. This technique is exceptionally sensitive and specific, suitable for the quality control of SLBZS. Furthermore, Wang et al. (2024c) developed a quick determination method for ginsenosides Rb1, Rg1, and Re utilising near-infrared hyperspectral imaging (NIR-HSI) technology, thereby enhancing and supplementing the quality control method of SLBZS. A study by Xu et al. (2021) assessed the pharmacokinetics of the active constituents of SLBZS in rat serum, revealing that the serum concentrations of shendiol, ginsenoside Rg1, atractylenolide I, atractylenolide III, pachymic acid, neferine, nuciferine, diosgenin, platycodin D, and isoglycyrrhizin exhibited significant correlations (0.44–397.50, 0.63–388.50, 0.44–400.50, 0.54–490, 0.31–279.00, 0.41–367.50, 0.38–355.50, 0.50–447.00, 0.42–382.50, 0.39–356.10 ng/mL), which may serve as a benchmark for the quality control of SLBZS. A separate study (Ren et al., 2020) employed high-performance liquid

chromatography with electrospray detection to quantify the concentrations of four components: liquiritinapioside, liquiritin, isoliquiritin apioside, and glycyrrhizic acid, yielding percentages of 0.26%–2.27%, 0.33%–5.07%, 0.14%–0.81%, and 0.77%–9.76%, respectively. Furthermore, quantitative analysis methods utilising HPLC for liquiritigenin, chikusetsusaponin V, and apigenin have been developed (Pei et al., 2019; Long et al., 2022; Yang et al., 2023).

In conclusion, according to the five principles established by Q-marker, the principal metabolites of SLBZS in the management of respiratory diseases include ginsenoside Rg1, ginsenoside Re, ginsenoside Rb1, atractylenolide I, atractonolide III, pachymic acid, Chikusetsusaponin V, liquiritin, isoliquiritin apioside, liquiritigenin, glycyrrhizic acid, and apigenin. Nonetheless, numerous issues persist in the study process concerning quality markers. 1) Constraints of metabolite detection methodologies. While UPLC-Q-TOF-MS/MS can swiftly identify numerous metabolites, its ability to differentiate isomers (e.g., ginsenoside Rg1 and Re) requires the integration of retention time or derivatisation techniques, and metabolites present in low concentrations may be overlooked due to inadequate ionisation efficiency. Moreover, certain blood-borne components may fail to achieve therapeutic quantities owing to limited protein binding or swift metabolism, whilst some undiscovered components may exert indirect effects via metabolism by gut flora. 2) Strengthen the hierarchical evaluation of data about component efficacy. The lung-protective action of ginsenoside Rg1 has only been confirmed in a murine model (Ji et al., 2021), and there is an absence of clinical randomised controlled trials to substantiate it. 3) Challenges in the practical implementation of quantifiable standards: HPLC-ELSD is appropriate for saponins lacking UV absorption (e.g., Chikusetsusaponin V) but exhibits lower sensitivity compared to LC-MS/MS; NIR-HSI is rapid yet necessitates a substantial sample size for calibration, potentially rendering it unsuitable for small batch production. The Q-marker prediction of SLBZS is hindered by the absence of *in vivo* target validation for most components through knockout experiments, inadequate data on pharmacokinetic interactions in compounding, and a deficiency of evidence-based medical research linking existing quality control criteria (e.g., glycyrrhizic acid) to clinical efficacy. This can be enhanced in the future by integrating web-based pharmacological prediction-experimental validation closed-loop studies with real-world data.

6 Conclusion

This study consolidated clinical records and established that SLBZS is useful in treating COPD, asthma, allergic rhinitis, *mycoplasma* pneumonia, recurrent respiratory tract infections, and other respiratory disorders. Pharmacological investigations concurrently demonstrate that SLBZS has advantages including the reduction of inflammation in lung tissue and airways, modulation of immunological responses, enhancement of gastrointestinal flora, and restoration of mitochondrial energy metabolism. This study aimed to elucidate the metabolites of SLBZS in the treatment of respiratory disorders by employing the five principles of Q-marker measurement to identify Q-markers relevant to SLBZS through five distinct criteria. In conclusion, twelve

constituents, including ginsenoside Rg1, ginsenoside Re, ginsenoside Rb1, atractylenolide I, atractonolide III, pachymic acid, Chikusetsusaponin V, liquiritin, isoliquiritin apioside, liquiritigenin, glycyrrhizic acid, and apigenin, may function as Q-markers for SLBZS in the treatment of respiratory disorders. The clinical implementation of this formula encounters several challenges, such as non-standard randomisation, a restricted sample size, dosage imprecision, and insufficient monitoring of adverse effects. The pharmacological mechanism exhibits challenges such as unclear chemical ingredients, insufficient animal and cellular models, and an absence of thorough exploration of the mechanism of action. Moreover, there are challenges such as the lack of standardised research methodology for predicting quality markers and insufficient exploration of the relationship between quality markers. All of these difficulties have hindered the execution and progression of this method. Future endeavours should concentrate on broadening therapeutic uses, clarifying pharmacological mechanisms, and finding quality indicators.

Author contributions

ZG: Writing – original draft, Writing – review and editing. TW: Writing – original draft, Writing – review and editing. LF: Conceptualization, Writing – original draft. QW: Conceptualization, Writing – original draft. YW: Conceptualization, Supervision, Writing – original draft. ZW: Conceptualization, Supervision, Writing – original draft. GL: Conceptualization, Writing – original draft. CO: Conceptualization, Writing – original draft. HZ: Conceptualization, Funding acquisition, Supervision, Writing – original draft. HY: Conceptualization, Funding acquisition, Supervision, Writing – original draft.

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Conflict of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

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References

- Bao, S., Zou, Y., Wang, B., Li, Y., Zhu, J., Luo, Y., et al. (2015). Ginsenoside Rg1 improves lipopolysaccharide-induced acute lung injury by inhibiting inflammatory responses and modulating infiltration of M2 macrophages. *Int. Immunopharmacol.* 28 (1), 429–434. doi:10.1016/j.intimp.2015.06.022
- Chen, D. (2018). To investigate the effect of Shenling baizhu powder combined with pidotimod on children with recurrent respiratory tract infection and its influence on the improvement of inflammatory factors and immune indicators. *Anti-Infection Pharm.* 15 (09), 1519–1521. doi:10.13493/j.issn.1672-7878.2018.09-017
- Chen, J., Shen, B., and Jiang, Z. (2022). Traditional Chinese medicine prescription Shenling BaiZhu powder to treat ulcerative colitis: clinical evidence and potential mechanisms. *Front. Pharmacol.* 13, 978558. doi:10.3389/fphar.2022.978558
- Chen, M. Y., Liu, W., Chou, G. X., and Wang, Y. L. (2020). Research progress on chemical constituents and pharmacological activities of *Dioscorea opposita* thunb. *Acta Chin. Med. Pharmacol.* 48 (02), 62–66. Available online at: <https://link.cnki.net/doi/10.19664/j.cnki.1002-2392.200035>.
- Chen, T., Xiao, L., Zhu, L., Ma, S., Yan, T., and Ji, H. (2015). Anti-asthmatic effects of ginsenoside Rb1 in a mouse model of allergic asthma through relegating Th1/Th2. *Inflammation* 38 (5), 1814–1822. doi:10.1007/s10753-015-0159-4
- Cheng, M., Zhang, J., Yang, L., Shen, S., Li, P., Yao, S., et al. (2021). Recent advances in chemical analysis of licorice (Gan-Cao). *FitoTerapia* 149, 104803. doi:10.1016/j.fitote.2020.104803
- Cui, H. Q., and Shang, L. L. (2019). Clinical observation on treatment of bronchial asthma in children with flutide combined with shenling baizhu powder. *Clin. J. Traditional Chin. Med.* 31 (02), 309–312. doi:10.16448/j.cjctm.2019.0092
- Dai, X. H., Li, H. E., Lu, C. J., Wang, J. F., Dong, J., Wei, J. Y., et al. (2013). Liquiritigenin prevents *Staphylococcus aureus*-mediated lung cell injury via inhibiting the production of α -hemolysin. *J. Asian Nat. Prod. Res.* 15 (4), 390–399. doi:10.1080/10286020.2013.771344
- Deng, X. M., Huang, F., Shang, C., Liu, Y., Duan, X. Q., Wu, X. Z., et al. (2024). Experimental study of modified Shenlingbaizhu powder regulating Nrf2/keap1/NLRP3 signaling pathway to improve idiopathic pulmonary fibrosis. *Lishizhen Med. Materia Medica Res.* 35 (09), 2081–2085.
- Elsherbini, A. M., Maysarah, N. M., El-Sherbiny, M., Al-Gayyar, M. M., and Elsherbiny, N. M. (2021). Glycyrrhizic acid ameliorates sodium nitrite-induced lung and salivary gland toxicity: impact on oxidative stress, inflammation and fibrosis. *Hum. and Exp. Toxicol.* 40 (4), 707–721. doi:10.1177/0960327120964555
- Fang, F., Qiu, L., Liao, J. H., Kuang, X. C., Zou, L. H., Jiao, Y., et al. (2014). Anti-inflammatory and antioxidant effect of ginsenoside re on the lung injury induced by intestinal ischemia reperfusion in rats. *Cent. South Pharm.* 12 (06), 521–524. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tuBS4Ucce5tA2i8_DOUYcjPXH7AfW10ONFqjtmF17wp8fXVi-yxPNctmifctSR9TQJgIVPIABxTo66rginOU95LJfKb_TDK-XTbKCN-A-BbEXWdpRdZOQU&uniplatform=NZKPT&language=CHS.
- Feng, J., Dai, W., Zhang, C., Chen, H., Chen, Z., Chen, Y., et al. (2020). Shen-ling-Bai-zhu-san ameliorates inflammation and lung injury by increasing the gut microbiota in the murine model of *Streptococcus pneumoniae*-induced pneumonia. *BMC complementary Med. Ther.* 20 (1), 159. doi:10.1186/s12906-020-02958-9
- Feng, L., Wang, Z., Lei, Z., Zhang, X., Zhai, B., Sun, J., et al. (2024). Amomum villosum Lour.: an insight into ethnopharmacological, phytochemical, and pharmacological overview. *J. Ethnopharmacol.* 335, 118615. doi:10.1016/j.jep.2024.118615
- Fu, J. D., Gao, C. H., Li, S. W., Tian, Y., Li, S. C., Wei, Y. E., et al. (2021). Atractylenolide III alleviates sepsis-mediated lung injury via inhibition of FoxO1 and VNN1 protein. *Acta cir. bras.* 36 (8), e360802. doi:10.1590/ACB360802
- Gao, G. L. (2022). Effect of Shenling baizhu powder combined with fluticasone propionate aerosol on children with asthma of lung-spleen qi deficiency in remission stage. *Clin. Med.* 42 (08), 115–117. doi:10.19528/j.issn.1003-3548.2022.08.045
- Gao, Z., Wang, J., Lu, G., Wu, Q., Wang, S., Wu, X., et al. (2024). Exploration the mechanism of Shenling Baizhu San in the treatment of chronic obstructive pulmonary disease based on UPLC-Q-TOF-MS/MS, network pharmacology and *in vitro* experimental verification. *J. Ethnopharmacol.* 324, 117728. doi:10.1016/j.jep.2024.117728
- Ge, L. L., and Jiang, B. X. (2022). Effect of modified shenling baizhu powder in the Adjuvant Treatment of allergic rhinitis in children with lung spleen qi deficiency syndrome. *Chin. Foreign Med. Res.* 20 (10), 36–40. doi:10.14033/j.cnki.cfmr.2022.10.010
- Guan, S., Xu, W., Han, F., Gu, W., Song, L., Ye, W., et al. (2017). Ginsenoside Rg1 attenuates cigarette smoke-induced pulmonary epithelial-mesenchymal transition via inhibition of the TGF- β /smad pathway. *BioMed Res. Int.* 2017, 7171404. doi:10.1155/2017/7171404
- Gui, Y., Sun, L., Liu, R., and Luo, J. (2021). Pachymic acid inhibits inflammation and cell apoptosis in lipopolysaccharide (LPS)-induced rat model with pneumonia by regulating NF- κ B and MAPK pathways. *Allergologia Immunopathol.* 49 (5), 87–93. doi:10.15586/aei.v49i5.468
- Han, J. (2021). Content determination and component analysis of total saponins in *Lablab Semen albums*. *J. Anhui Agric. Sci.* 49 (08), 195–198. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tsSb0T6-efnwq8ZgGZi7xaavykPGI-lk-O1yQh4JzRVaPRtkU5WphUWgQmTP0bt_rUgLCMhgdq3mburHrClWCiU7FMwt_J-jcsMIIn9IaY0wndL88e1gzV-5f1T1eak2FMawZK3vqJS6A==&uniplatform=NZKPT&language=CHS.
- Han, S. Y., Bae, M. G., and Choi, Y. H. (2018). Stereoselective and simultaneous analysis of ginsenosides from ginseng berry extract in rat plasma by UPLC-MS/MS: application to a pharmacokinetic study of ginseng berry extract. *Mol. Basel, Switz.* 23 (7), 1835. doi:10.3390/molecules23071835
- Han, X., Sun, C., Ding, H., Deng, S., Li, M., Lou, J., et al. (2025). Integration of transcriptomics and metabolomics reveals the mechanism of *Glycyrrhizae Radix Et Rhizoma* extract inhibiting CCL5 in the treatment of acute pharyngitis. *Phytomedicine Int. J. phytotherapy Phytopharm.* 137, 156360. doi:10.1016/j.phyto.2024.156360
- He, L. P. (2024). Shenling baizhu powder combined with western medicine in the treatment of chronic obstructive pulmonary disease with lung and spleen qi deficiency Type. *Chin. Med. Mod. Distance Educ. China* 22 (24), 159–161.
- Hu, T., Zhou, X. Y., Xue, D., and Zhou, L. H. (2020). Study on the protective effect and mechanism of the method of strengthening the spleen to benefit the lung on the mitochondrial energy metabolism of skeletal muscle of mice with chronic obstructive pulmonary disease. *Tianjin J. Traditional Chin. Med.* 37 (11), 1294–1298.
- Hua, Q., and Ren, L. (2024). The SIRT1/Nrf2 signaling pathway mediates the anti-pulmonary fibrosis effect of liquiritigenin. *Chin. Med.* 19 (1), 12. doi:10.1186/s13020-024-00886-1
- Huai, B., and Ding, J. (2020). Atractylenolide III attenuates bleomycin-induced experimental pulmonary fibrosis and oxidative stress in rat model via Nrf2/NQO1/HO-1 pathway activation. *Immunopharmacol. Immunotoxicol.* 42 (5), 436–444. doi:10.1080/08923973.2020.1806871
- Huang, S. R., Yang, H. F., Ding, H. B., and Li, X. Y. (2023). Effect of Shenling Baizhu powder combined with salmeterol and fluticasone in the treatment of chronic bronchial asthma on the balance of body oxidation and antioxidant. *Shaanxi J. Traditional Chin. Med.* 44 (06), 730–733+737. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tsNipVM8N6U2RQHGHj3F8JY-j-YIE9efNvrXVrHEOHPsuJPUlamkjNvA4FT1_vLptbXUKrvKGVUmGLLG9tingM_DG16EqBgF2MeqErKXwmjYhUHVV2JZsqXYT5r-tW50=&uniplatform=NZKPT&language=CHS.
- Ji, Q., Sun, Z., Yang, Z., Zhang, W., Ren, Y., Chen, W., et al. (2021). Protective effect of ginsenoside Rg1 on LPS-induced apoptosis of lung epithelial cells. *Mol. Immunol.* 136, 168–174. doi:10.1016/j.molimm.2018.11.003
- Li, B. S., Zhu, R. Z., Lim, S. H., Seo, J. H., and Choi, B. M. (2021a). Apigenin alleviates oxidative stress-induced cellular senescence via modulation of the SIRT1-NAD [formula: see text]-CD38 Axis. *Am. J. Chin. Med.* 49 (5), 1235–1250. doi:10.1142/S0192415X21500592
- Li, C. H., Fu, Q. Q., and Zhao, K. Z. (2024a). Study on the therapeutic effect of shenling baizhu san on Alleviating bronchial asthma in mice by regulating Th17/treg balance. *Hubei J. Traditional Chin. Med.* 46 (11), 3–6.
- Li, H. Y. (2018). *Study on the anti-diarrheal ingredients and quality standard standardization of white lentil*. Hunan University of Chinese Medicine. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tulOBPSMuGepGbkjRaXixVy1CjcmTwKNHIV6m2k8UP7-OxKyKgedvGhkVIU5Eo9_zRFPL7kC0hA8RZOycpk8EAaFs28rQOKpWRqV8WT6uQ9G1Y_XSHyvE1xw-vQej0RezFYw-qE6jgQ==&uniplatform=NZKPT&language=CHS.
- Li, J., Lu, K., Sun, F., Tan, S., Zhang, X., Sheng, W., et al. (2021b). Panaxydol attenuates ferroptosis against LPS-induced acute lung injury in mice by Keap1-Nrf2/HO-1 pathway. *J. Transl. Med.* 19 (1), 96. doi:10.1186/s12967-021-02745-1
- Li, L., Jin, R. J., and Ji, L. (2023). Pachymic acid ameliorates bleomycin-induced pulmonary fibrosis through inhibiting endoplasmic reticulum stress in rats. *Environ. Toxicol.* 39, 5382, 5390. doi:10.1002/tox.23824
- Li, L., Zhang, Y. L., Chen, M. Q., Bai, S. S., Wang, Z. J., Fang, H. H., et al. (2024b). Analysis on chemical composition and constituents absorb in the blood of shenling

baizhu san by UPLC-Q-TOF-MS/MS. *Traditional Chin. Drug Res. Clin. Pharmacol.* 35 (04), 553–562. doi:10.19378/j.issn.1003-9783.2024.04.013

Li, M. X., Sun, L., Meng, Z. Q., Ding, G., Wang, Z. Z., and Xiao, W. (2014). Content changes of chemical constituents in ginseng radix and Atractylodis Macrocephalae rhizoma before and after compatibility. *Chin. Traditional Herb. Drugs* 45 (24), 3549–3552. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXCSstbk-tu11L0QjY7vW-YRk7GpSNFFS_MCB59cG2okY5V-ZYNNNpcn9hk0u7hbz13eP4YaoEz-2chBq4pgWOx96Tug1zSej9VJCLBk6g_OB6EjNbEZH7s_zFRQvBHueEHFa75gBOu1fLYGY855BQ==&uniplatform=NZKPT&language=CHS.

Li, W., Gao, R., Xin, T., and Gao, P. (2020). Different expression levels of interleukin-35 in asthma phenotypes. *Respir. Res.* 21 (1), 89. doi:10.1186/s12931-020-01356-6

Li, Y. H. (2021). Effect of Shenling baizhu powder combined with azithromycin in the treatment of children with mycoplasma pneumoniae pneumonia. *Henan Med. Res.* 30 (16), 3004–3006.

Liu, C. J., and Zhu, Q. (2018). Study on HPLC characteristic fingerprint of shenlingbaizhu powder and simultaneous determination of its five indicative components. *China Pharm.* 27 (15), 12–16. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXCSstbk-tuV5dnSJdetzDWbpVqmbhpVvUkRopGYDXzndZgiR9YmT_U5RKb-3ffZ0v2wE685wRUSKOUp7JlVrlZQDP_KH0mDoiGskpVkwCEB90GzF08ZbztNAPn9QwP05zdDhykzQmb8JZ_TlHg==&uniplatform=NZKPT&language=CHS.

Liu, C. X. (2021). Five-year review on development of quality markers of traditional Chinese medicine. *Chin. Traditional Herb. Drugs* 52 (09), 2511–2518. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXCSstbk-tvF0BDaUGIio3A1x1P27210VWl-HjMhBLmZAJ_ksr_JfLy3KMbtsoXKA8M83wYUA06B8rwjQzpxlTtjdFwts0Ejgy2EsXyhpqP-LNECK17zhQDuID8RKR1EaMkCKH1rLe3rvLhjCshTAA==&uniplatform=NZKPT&language=CHS.

Liu, H., Li, X., Xu, H., Wang, X., Gong, Z., Xu, Y., et al. (2024). Rapid identification and determination of chemical components of huai yam based on UPLC-Q-Exactive-MS and fragmentation patterns. *Nat. Prod. Res.*, 1–7. doi:10.1080/14786419.2024.2337117

Liu, Y., Li, Z., Xue, X., Wang, Y., Zhang, Y., and Wang, J. (2018). Apigenin reverses lung injury and immunotoxicity in paraquat-treated mice. *Int. Immunopharmacol.* 65, 531–538. doi:10.1016/j.intimp.2018.10.046

Liu, Z., Wang, P., Lu, S., Guo, R., Gao, W., Tong, H., et al. (2020). Liquiritin, a novel inhibitor of TRPV1 and TRPA1, protects against LPS-induced acute lung injury. *Cell calcium* 88, 102198. doi:10.1016/j.ceca.2020.102198

Long, J., Zhou, C. Y., Tian, L., Tu, X., Hu, X. L., and Shi, J. Q. (2022). Determination of 13 components in panacis japonici rhizoma and its tota saponins by UPLC-Q/TOF-MS. *J. Hubei Minzu Univ. Ed.* 39 (03), 56–61. Available online at: <https://link.cnki.net/doi/10.13501/j.cnki.42-1590/r.2022.03.014>.

Lu, G. Y., Xing, X. Y., Wang, J. Y., Wang, Y., Ma, K., and Wang, S. J. (2022). Research progress of Shenling Baizhu San and predictive analysis on its quality markers. *China J. Chin. Materia Medica* 47 (19), 5171–5181. doi:10.19540/j.cnki.cjcm.20220421.201

Lu, Y., Bao, T., Mo, J., Ni, J., and Chen, W. (2021). Research advances in bioactive components and health benefits of jujube (*Ziziphus jujuba* Mill.) fruit. *J. Zhejiang Univ. Sci. B* 22 (6), 431–449. doi:10.1631/jzus.B2000594

Ma, C., Ma, Z., Liao, X. L., Liu, J., Fu, Q., and Ma, S. (2013). Immunoregulatory effects of glycyrrhizic acid exerts anti-asthmatic effects via modulation of Th1/Th2 cytokines and enhancement of CD4(+)/CD25(+)Foxp3+ regulatory T cells in ovalbumin-sensitized mice. *J. Ethnopharmacol.* 148 (3), 755–762. doi:10.1016/j.jep.2013.04.021

Mao, Y., Hu, G., Meng, Q., Li, X., Sun, X., Zhou, J., et al. (2021). Efficacy of Shenling Baizhu San on stable chronic obstructive pulmonary disease patients: a systematic review and meta-analysis. *J. Ethnopharmacol.* 272, 113927. doi:10.1016/j.jep.2021.113927

Ou, C. X., Liu, Y. Y., Gao, Z., Wang, J. Y., Wu, Q. L., Zhao, H. J., et al. (2024). Effects of Platycodonis radix on the chemical constituents in shenling baizhu san by UPLC-Q-TOF-MS/MS. *Res. Pract. Chin. Med.* 38 (05), 46–54. Available online at: <https://link.cnki.net/doi/10.13728/j.1673-6427.2024.05.008>.

Ouyang, X. R., Liang, Y. N., Lin, X. L., and Xu, H. (2020). Effect of shen ling baizhu powder on airway inflammation and regulation of GutMicrobiota in asthmatic mice. *Traditional Chin. Drug Res. Clin. Pharmacol.* 31 (11), 1282–1288. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXCSstbk-tvEdzf7HRsVcxsgW63xXoblnYAxoJG3BcsrQDwCl8cLX_SWMWwLx_jqxsFqVq1VlUmUJCgTgWcY-76xwVTthkhj4szY4h6tYTgZbjGZwMOJHPbIqTw85xxKvBSAZvqCjEM=&uniplatform=NZKPT&language=CHS.

Ouyang, X. R., and Xu, H. (2019). Inhibitory effect of Shenling baizhu powder on AirwayInflammation in young asthmatic rats. *Traditional Chin. Drug Res. Clin. Pharmacol.* 30 (07), 812–815. doi:10.19378/j.issn.1003-9783.2019.07.010

Pan, X., Shen, Q., Zhang, C., Zhang, X., Li, Y., Chang, Z., et al. (2023). Coicis Semen for the treatment of malignant tumors of the female reproductive system: a review of traditional Chinese medicinal uses, phytochemistry, pharmacokinetics, and pharmacodynamics. *Front. Pharmacol.* 14, 1129874. doi:10.3389/fphar.2023.1129874

Pei, H. T. (2021). Chemical constituents of different parts from *Nelumbo nucifera*, and sedative effect of Nelumbinis Semen. Available online at: <https://link.cnki.net/doi/10.27162/d.cnki.gjlin.2021.004693>.

Pei, Y. Q., Shi, H. P., Yan, H., Huang, S. L., Dong, W., and Wang, G. Q. (2019). Quality evaluation of Glycyrrhizae Radix et Rhizoma Praeparata Cum Melle based on HPLC fingerprint and multi-component quantitative analysis by QAMS. *Chin. Traditional Herb. Drugs* 50 (18), 4293–4304. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXCSstbk-tu7H8sEkMqFK7NmQ0d5Eh30qLCCqmwI8H281hnRbMAJPW-I33v_eVAQIdSAgRg8vobqAO7N8fQd-4A0TJ3AEEq0kdfequATwQQC2iCg92ru2eEnXVsVrVHqtPjMOf3vDWgM=&uniplatform=NZKPT&language=CHS.

Qu, L., Chen, C., He, W., Chen, Y., Li, Y., Wen, Y., et al. (2019). Glycyrrhizic acid ameliorates LPS-induced acute lung injury by regulating autophagy through the PI3K/AKT/mTOR pathway. *Am. J. Transl. Res.* 11 (4), 2042–2055. PMID: 31105816; PMCID: PMC6511780.

Ratan, Z. A., Haidere, M. F., Hong, Y. H., Park, S. H., Lee, J. O., Lee, J., et al. (2020). Pharmacological potential of ginseng and its major component ginsenosides. *J. ginseng Res.* 45 (2), 199–210. doi:10.1016/j.jgr.2020.02.004

Ren, X., Hu, C., and Zhang, L. Z. (2020). Determination of four active components in radix glycyrrhizae by HPLC-CAD. *Anhui Med. Pharm. J.* 24 (07), 1304–1308. Available online at: <https://kns.cnki.net/kcms2/article/abstract?v=9CXCSstbk-tuFU7G7xTw9T6Lkmmpp6uDg059FbnrCS3qCldJnLHOzz4wU66PD7bQAcsdx216C-vBghVG72DZHj9BGWotbbbAypRhUs0BkSPWYNsBzv7i5syDjllUUG7gXD4p7Dxbo=&uniplatform=NZKPT&language=CHS>.

Schaefer, M., Zimmermann, K., and Enck, P. (2023). A randomized controlled trial of effects of open-label placebo compared to double-blind placebo and treatment-as-usual on symptoms of allergic rhinitis. *Sci. Rep.* 13 (1), 8372. doi:10.1038/s41598-023-34790-9

Shang, Z., Liu, C., Qiao, X., and Ye, M. (2022). Chemical analysis of the Chinese herbal medicine licorice (Gan-Cao): an update review. *J. Ethnopharmacol.* 299, 115686. doi:10.1016/j.jep.2022.115686

Shaukat, A., Guo, Y. F., Jiang, K., Zhao, G., Wu, H., Zhang, T., et al. (2019). Ginsenoside Rb1 ameliorates Staphylococcus aureus-induced Acute Lung Injury through attenuating NF- κ B and MAPK activation. *Microb. Pathog.* 132, 302–312. doi:10.1016/j.micpath.2019.05.003

Shi, C. S. (2024). To observe the effect of Shenlingbaizhu powder combined with tiotropium bromide in the treatment of chronic obstructive pulmonary disease in remission stage and its influence on pulmonary function. *Med. Forum* 28 (07), 145–148. Available online at: <https://link.cnki.net/doi/10.19435/j.1672-1721.2024.07.046>.

Su, K., Zhang, G., Zhang, X., and Jiang, W. (2019). Chikusetsusaponin V attenuates lipopolysaccharide-induced acute lung injury in mice by modulation of the NF- κ B and LXR α . *Int. Immunopharmacol.* 70, 174–179. doi:10.1016/j.intimp.2019.02.023

Tan, S., Yang, S., Kang, H., Zhou, K., Wang, H., Zhang, Y., et al. (2023). Atractylenolide III ameliorated autophagy dysfunction via epidermal growth factor receptor-mammalian target of rapamycin signals and alleviated silicosis fibrosis in mice. *Laboratory investigation; a J. Tech. methods pathology* 103 (2), 100024. doi:10.1016/j.labinv.2022.100024

Wang, C., Yu, J., Guo, Y., Jiang, M., Zhong, K., and Wang, X. (2025). Separation and purification of ginsenosides and flavonoids in from the leaves and stems of Panax quinquefolium by high-speed countercurrent chromatography and online-storage inner-recycling countercurrent chromatography. *J. Sep. Sci.* 48 (2), e70073. doi:10.1002/jssc.70073

Wang, C. C., Zhang, Y. L., Geng, W. J., Gui, S. Y., Peng, D. Y., and Wang, J. T. (2021). Study on Herbal Drug Pair of Platycodonis Radix and Glycyrrhizae Radix et Rhizomain Classical Prescription Jiegeng Tang. *Mod. Chin. Med.* 23 (05), 826–831. Available online at: <https://link.cnki.net/doi/10.13313/j.issn.1673-4890.20200227001>.

Wang, H., Hou, Y. N., Yang, M., Feng, Y., Zhang, Y. L., Smith, C. M., et al. (2022). Herbal formula shenling baizhu san for chronic diarrhea in adults: a systematic review and meta-analysis. *Integr. cancer Ther.* 21, 15347354221081214. doi:10.1177/15347354221081214

Wang, Q. L., Yang, L., Peng, Y., Gao, M., Yang, M. S., Xing, W., et al. (2019). Ginsenoside Rg1 regulates SIRT1 to ameliorate sepsis-induced lung inflammation and injury via inhibiting endoplasmic reticulum stress and inflammation. *Mediat. Inflamm.* 2019, 6453296. doi:10.1155/2019/6453296

Wang, S., Tan, W., Zhang, L., and Jiang, H. (2023). Pachymic acid protects against bleomycin-induced pulmonary fibrosis by suppressing fibrotic, inflammatory, and oxidative stress pathways in mice. *Appl. Biochem. Biotechnol.* 196, 3344, 3355. doi:10.1007/s12010-023-04686-5

Wang, X. L., Li, W., Zhu, S., Shi, X. C., and Chen, W. (2024c). Effect of atractylenolide I on lung injury in rats with RecurrentRespiratory tract infection of lung and spleen qi deficiency byRegulating the PI3K/Akt/mTOR signaling pathway. *Traditional Chin. Drug Res. Clin. Pharmacol.* 35 (02), 216–223. doi:10.19378/j.issn.1003-9783.2024.02.008

Wang, Y., Wang, S., Bai, R., Li, X., Yuan, Y., Nan, T., et al. (2024a). Prediction performance and reliability evaluation of three ginsenosides in Panax ginseng using hyperspectral imaging combined with a novel ensemble chemometric model. *Food Chem.* 430, 136917. doi:10.1016/j.foodchem.2023.136917

- Wang, Y., Zhang, N., Liu, F., Zhou, J., Teng, G., and Huang, H. (2024b). A new perspective for improving COPD: ginsenoside Rg3 links SIRT1 to inhibit mitochondrial autophagy. *Discov. Med.* 36 (191), 2386–2398. doi:10.2479/Discov.Med.202436191.220
- Wang, Y. J., Wei, D. D., Wang, H. J., Cao, J. X., and Li, J. Y. (2020). Effects of shenling baizhu powder on immune function in rats with recurrent respiratory tract infections of qi-deficiency of lung and spleen. *Inf. Traditional Chin. Med.* 37 (05), 33–37. doi:10.19656/j.cnki.1002-2406.200126
- Wang, Y. L. (2024). Effect of Shenlingbaizhu powder combined with massage on cough in children. *Guangming J. Chin. Med.* 39 (01), 95–97. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tso74SrWlaBsJmQLDbiThy-QkNZ2aPco2OUPm-qyRvRce_HlQqEaLkfydFAyTlJnmBfABHlcfK7UPCauTQtdzMnTlJEDgnLzKselv1dHiVzm15wrxqoSKW81AEV91AOJo=&uniplatform=NZKPT&language=CHS.
- Wu, Q., Ou, C., Wang, J., Wu, X., Gao, Z., Zhao, Y., et al. (2024). Jiawei Kongsheng Zhenzhong Pill: marker compounds, absorption into the serum (rat), and Q-markers identified by UPLC-Q-TOF-MS/MS. *Front. Pharmacol.* 15, 1328632. doi:10.3389/fphar.2024.1328632
- Wu, T., Hou, W., Li, S., Liu, C., and Zhang, Y. (2024). Integrated analysis and separation of 5-lipoxygenase inhibitors from triterpenes of *Poria cocos* using bioaffinity ultrafiltration UPLC-Q-Exactive, molecular docking and target-based multiple complex networks. *Fitoterapia* 175, 105856. doi:10.1016/j.fitote.2024.105856
- Wu, Y. L., Liu, X. P., Jia, Y. X., Wang, X. R., Wu, Y., Li, Y. Y., et al. (2022). Effect of shenling baizhu powder on pulmonary inflammatory response in juvenile mice with intestinal dysbiosis. *Chin. J. Inf. Traditional Chin. Med.* 29 (11), 79–85. doi:10.19879/j.cnki.1005-5304.202111648
- Xie, Z., Lin, M., He, X., Dong, Y., Chen, Y., Li, B., et al. (2023). Chemical constitution, pharmacological effects and the underlying mechanism of atractylenolides: a review. *Mol. Basel, Switz.* 28 (10), 3987. doi:10.3390/molecules28103987
- Xu, C., Xu, H., Dai, X., Gui, S., and Chen, J. (2025). Effects and mechanism of combination of *Platycodon grandiflorum* polysaccharides and *Platycodon* saponins in the treatment of chronic obstructive pulmonary disease rats through the gut-lung axis. *J. Ethnopharmacol.* 341, 119305. doi:10.1016/j.jep.2024.119305
- Xu, X., Wang, W., Chen, Y., Zhang, Q., Li, B., Zhong, Y., et al. (2021). Simultaneous determination of ten bioactive components from shenling baizhu san in rat plasma by UHPLC-MS/MS: application to a comparative pharmacokinetic study in normal and two models of ulcerative colitis rats. *Evidence-based complementary Altern. Med.* 2021, 3518241. doi:10.1155/2021/3518241
- Yang, Y., Jiang, Z. M., Ni, L., Wang, J. H., Yang, Z. R., Liu, S. Q., et al. (2023). Content determination of vanillic Acid, Ferulic acid and apigenin in *kalimeris indica* by HPLC. *China Pharm.* 32 (21), 83–86. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tvqG4IVSqdD8hUtYYcGiniPP_HzG0kl8jlsQCIYFRilvLgk3zrNsWqgJWtsx9ExMeXRY69qTm9fNaITcdX6QL3mu5m8SdtxDFQ8S4DPGao9XMRfPmz627AToe_Rylj5ZQ=&uniplatform=NZKPT&language=CHS.
- Yu, H., Huang, X., Zhu, H. H., Wang, N., Xie, C., Zhou, Y. L., et al. (2023). Apigenin ameliorates non-eosinophilic inflammation, dysregulated immune homeostasis and mitochondria-mediated airway epithelial cell apoptosis in chronic obese asthma via the ROS-ASK1-MAPK pathway. *Phytomedicine Int. J. phytotherapy Phytopharm.* 111, 154646. doi:10.1016/j.phymed.2023.154646
- Yue, M. Y., Yu, H. Y., Zhou, Q. M., and Pan, Y. (2018). GC-MS in analysis of chemical composition of volatile oil in different ratio of *Atractylodes Macrocephalae* rhizoma and *Poria*. *Chin. J. Exp. Traditional Med. Formulae* 24 (11), 61–66. Available online at: <https://link.cnki.net/doi/10.13422/j.cnki.syfx.20181108>.
- Zhang, J. L., Huang, W. M., and Zeng, Q. Y. (2015). Atractylenolide I protects mice from lipopolysaccharide-induced acute lung injury. *Eur. J. Pharmacol.* 765, 94–99. doi:10.1016/j.ejphar.2015.08.022
- Zhang, L., Yi, H., Jiang, D., and Li, Z. (2021). Protective effects of Atractylenolide III on inflammation and oxidative stress in ovalbumin-induced asthma mice and its possible mechanisms. *General physiology biophysics* 40 (2), 137–146. doi:10.4149/gpb.2020046
- Zhang, L. F., Duan, B., Liu, F., Tian, X. Z., and Zhang, Y. F. (2023). Effect and mechanism of shenling baizhu powder in treatment of stable phase of chronic obstructive pulmonary disease. *Liaoning J. Traditional Chin. Med.* 50 (12), 109–112. doi:10.13192/j.issn.1000-1719.2023.12.031
- Zhang, S., Chai, X., Hou, G., Zhao, F., and Meng, Q. (2022). *Platycodon grandiflorum* (Jacq.) A. DC.: a review of phytochemistry, pharmacology, toxicology and traditional use. *Phytomedicine Int. J. phytotherapy Phytopharm.* 106, 154422. doi:10.1016/j.phymed.2022.154422
- Zhang, S. Y. (2019). Study on the compatibility mechanism of Ginseng Radix combined with *Atractylodes Macrocephalae* Rhizoma in the treatment of chronic atrophic gastritis. Chengdu University of Traditional Chinese Medicine. Available online at: <https://link.cnki.net/doi/10.26988/d.cnki.gcdzu.2019.000298>.
- Zhao, H., Zhao, M., Wang, Y., Li, F., and Zhang, Z. (2016). Glycyrrhizic acid prevents sepsis-induced acute lung injury and mortality in rats. *J. Histochem. Cytochem. official J. Histochem. Soc.* 64 (2), 125–137. doi:10.1369/0022155415610168
- Zhao, L. (2015). Research on quality evaluation and effectiveness of the compatibility of ginseng and other 4 Chinese medicines. Jilin Agricultural University. Available online at: https://kns.cnki.net/kcms2/article/abstract?v=9CXcStbk-tvUBB2rg1qw81olbVpyb13C8rrNPSaKyHDR583Ok_B7lJzg3Ql8m1B3peldEt9GkcEBwQxKG94Y44cPgJHKBw4JLwvTl0RIOEO7WnATKsEeFxQ2OFGzqJHWIVQDKoBBvJn0qkY6wsdE8Q==&uniplatform=NZKPT&language=CHS.
- Zhao, L. P., Yan, C. D., Li, Y. L., Zhang, Y., and Yue, Y. G. (2024). Clinical efficacy of shenling baizhu powder combined with Acupuncture and moxibustion on allergic rhinitis with Qi Deficiency in lungs and spleen syndrome and effect on Serum IFN- γ and IL-17 levels. *World J. Integr. Traditional West. Med.* 19 (11), 2203–2207. doi:10.13935/j.cnki.sjzx.241116
- Zhongyin, Z., Wei, W., Juan, X., and Guohua, F. (2022). Isoliquiritin apioside relieves intestinal ischemia/reperfusion-induced acute lung injury by blocking Hif-1 α -mediated ferroptosis. *Int. Immunopharmacol.* 108, 108852. doi:10.1016/j.intimp.2022.108852
- Zhou, H., Yang, T., Lu, Z., He, X., Quan, J., Liu, S., et al. (2023). Liquiritin exhibits anti-acute lung injury activities through suppressing the JNK/Nur77/c-Jun pathway. *Chin. Med.* 18 (1), 35. doi:10.1186/s13020-023-00739-3
- Zhou, X. Y., Song, Y. H., Xue, D., Zhang, L. H., and Hu, T. (2020). Protective mechanism of Shenling Baizhu powder on the injured cells of COPD skeletal muscle based on mitochondrial autophagy. *J. Guangdong Pharm. Univ.* 36 (03), 369–374. Available online at: <https://link.cnki.net/doi/10.16809/j.cnki.2096-3653.2020021803>.
- Zhu, B., Zhang, Q. L., Hua, J. W., Cheng, W. L., and Qin, L. P. (2018). The traditional uses, phytochemistry, and pharmacology of *Atractylodes macrocephala* Koidz.: a review. *J. Ethnopharmacol.* 226, 143–167. doi:10.1016/j.jep.2018.08.023
- Zhu, C., Zhang, L., Liu, Z., Li, C., Bai, Y., and Wang, L. (2020). Atractylenolide III reduces NLRP3 inflammasome activation and Th1/Th2 imbalances in both *in vitro* and *in vivo* models of asthma. *Clin. Exp. Pharmacol. and physiology* 47 (8), 1360–1367. doi:10.1111/1440-1681.13306
- Zhu, L., Xu, J., Zhang, S., Wang, R., Huang, Q., Chen, H., et al. (2018b). Qualitatively and quantitatively comparing secondary metabolites in three medicinal parts derived from *Poria cocos* (Schw.) Wolf using UHPLC-QTOF-MS/MS-based chemical profiling. *J. Pharm. Biomed. analysis* 150, 278–286. doi:10.1016/j.jpba.2017.11.066
- Zhu, L. X., Xu, J., Wang, R. J., Li, H. X., Tan, Y. Z., Chen, H. B., et al. (2018a). Correlation between quality and geographical origins of *Poria cocos* revealed by qualitative fingerprint profiling and quantitative determination of triterpenoid acids. *Mol. Basel, Switz.* 23 (9), 2200. doi:10.3390/molecules23092200