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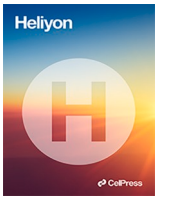

Review article

Global research status and trends of interactions between Traditional Chinese medicine and pulmonary fibrosis: A new dawn in treatment

Bokai Wei [a,1], Haozheng Li [b,c,1], Chengyu Wang [a,1], Jing Hu [a,*]

[a] School of Traditional Chinese Medicine, Shanghai University of Traditional Chinese Medicine, 1200# Cailun Rd., Shanghai, 201203, PR China
[b] Shanghai Institute of Infectious Disease and Biosecurity, Fudan University, 130# Dongan Road, Shanghai, 200032, PR China
[c] Department of Rehabilitation Medicine, Huanshan Hospital, Fudan University, 12# Wulumuqi Road, Shanghai, 200040, PR China

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ABSTRACT

Background: Pulmonary fibrosis (PF) remains a major sequela of COVID-19, yet its pharmacotherapy remains unsatisfactory. Recently, Traditional Chinese medicine (TCM) has garnered increasing recognition among patients and researchers because of its few side effects and efficacy. The objective of this study is to use bibliometric analysis to explore the current research landscape and emerging trajectories of TCM treating PF(TCM/PF) researches, and comprehensively evaluate publications with substantial citations within the domain of TCM/PF.

Materials and methods: TCM/PF publications from 1996 to June 15, 2023 were identified by a comprehensive search of the Web of Science Core Collection (WoSCC). The Bibliometrix of Origin, CiteSpace, Gephi, dycharts and VOSviewer were used for bibliometric analysis.

Results: A total of 358 papers were included. A rapid increase in the number of papers after 2013 was observed. China had the highest publication output and research contributions in this field. Beijing University of Traditional Chinese Medicine and Nanjing University of Traditional Chinese Medicineare leaders in productive research of this field. Nanjing University of Traditional Chinese Medicine had the highest citations (227). LI JIANSHENG from Henan University of Chinese Medicine was the most prolific author (8), with the highest number of citations (61), and TONG XIAO LIN from China Academy of Chinese Medical Sciences had the highest H-index (30). The leading journal publishing the most research (37) is Frontiers in Pharmacology and the Journal of Ethnopharmacology had the highest total citations (486). Burst analysis of keywords revealed three distinct phases of research. 1996 to 2013 marked the nascent stage of TCM/PF research; from 2014 to 2018, studies gradually focused on the underlying mechanisms governing TCM/PF. The most significant phase occurred from 2019 onward, where TCM/PF exhibited an explosive growth trend. This progression signifies a transition from foundational explorations to a comprehensive understanding of the mechanisms involved, ultimately leading to the current surge in research activities focused on TCM/PF. Notable research teams of this stage, led by LI JIAN SHENG and TONG XIAO LIN, have been at the forefront of advancing TCM/PF research. Their studies on Jinshui Huanxian formula and Qimai Feiluoping decoction have been pivotal in advancing the frontier of research in this domain. Furthermore, the monomeric compounds,

* Corresponding author.
E-mail addresses: willisb@163.com (B. Wei), lihaozheng3211@163.com (H. Li), thehamawangzi@163.com (C. Wang), shunjane666@163.com (J. Hu).
[1] These authors contributed equally to this work.

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including emodin, curcumin, salvianolic acid, baicalin, and oxymatrine, have sustained long-standing prominence.

Conclusions: This study gained insight into the research status, focal areas and evolving trends of global TCM/PF research. It also identified the most cited articles in TCM/PF and analyzed their characteristics, which may hold significant relevance for both clinical researchers and practitioners on future directions in this field.

1. Introduction

Pulmonary fibrosis (PF) is usually regarded as a type of chronic interstitial lung disease. More precisely, PF represents a common pathological hallmark shared by various interstitial lung diseases, including idiopathic pulmonary fibrosis (IPF) [1,2]. It is characterized by the destruction of pulmonary alveolar structure, excessive migration and proliferation of fibroblasts, and excessive deposition of extracellular matrix (ECM). These pathological features lead to progressive dyspnea in patients, ultimately resulting in respiratory failure and death. Pirfenidone and nintedanib are therapeutic interventions approved by the U.S. FDA for clinical application in 2008 and 2014, respectively. However, they possess partial efficacy in halting the progression of PF and are associated with various side effects, including gastrointestinal reactions. Since the global COVID-19 pandemic began in late 2019, PF has emerged as one of the long-term or post-acute sequelae of COVID-19 [3]. It has garnered significant scrutiny from the medical community and researchers worldwide. Consequently, exploring the treatment of PF from various perspectives holds immense significance in contemporary medicine.

TCM is an important component of complementary and alternative medicine, distinguished by unique theories with over two thousand years of extensive clinical experience [4]. Although some controversy exist within mainstream medicine regarding TCM, particularly due to the philosophical nature of its theories and the unclear mechanisms of Chinese herbal medicine, TCM has garnered heightened interest in recent years due to its relatively good efficacy and fewer side effects. Data mining and statistical data analytic tools are required to analyze the interrelationship between TCM and PF and to find out the characteristic of Traditional Chinese medicine treating pulmonary fibrosis (TCM/PF). Bibliometric analysis has been recognized as an important method for the quantitative assessment of research status and development trends in a specific field, enabling researchers to gain a more systematic and rapid understanding of a given research area. Numerous research achievements of TCM have been presented in a more comprehensive manner through it, such as the interaction between TCM and gut microbiota [5], TCM nursing for insomnia [6], and the treatment of non-small cell lung cancer with triptolide [7]. In recent decades, a growing number of studies has focused on the relationship between TCM/PF. However, currently, there is no bibliometric analysis available between PF and TCM. After determining the search methods and reviewing the literature, we discovered that studies of TCM/PF have gradually emerged and evolved since 1992. Therefore, we

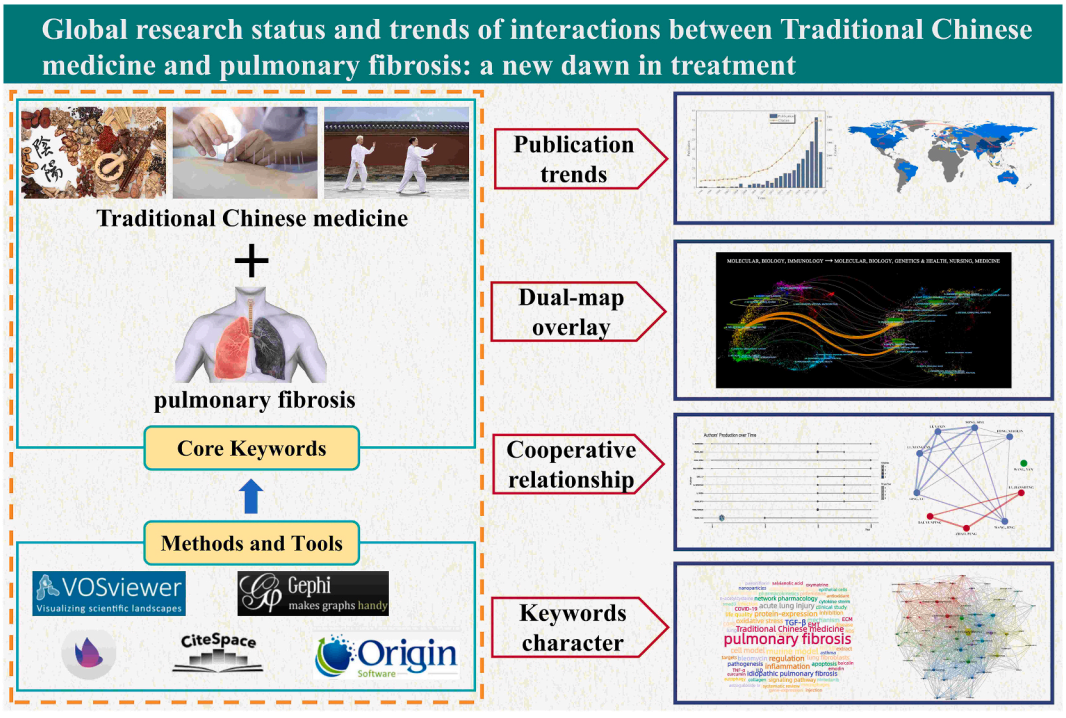

Fig. 1. Graphical abstract.

have selected studies published from January 1992 to June 2023 for bibliometric analysis, with an aim to provide valuable insights and serve as a reference point for further study of TCM/PF. The overall process, methodology, and findings of this study are depicted in Fig. 1.

2. Methods

2.1. Data source and search strategy

The Web of Science is globally acknowledged as a comprehensive and trusted citation database, with a substantial reach across various publishers. It offers better quality bibliometric information due to a lower incidence of duplicate records and a more comprehensive coverage of high-impact journals. To enhance the accessibility and inclusivity of data, this research has primarily concentrated on the WoSCC database.

Our search query was formulated as follows: TS = (Traditional Chinese medicine) OR TS=(moxibustion) OR TS=(acupuncture) OR TS=(chinese herb) OR TS=(herbal medicine) OR TS=(decoction) OR TS=(chinese medicine compounds) OR TS=(chinese herbal compounds) OR TS=(formula) OR TS=(chinese patient medicine) OR TS=(capsules) OR TS=(powder) OR TS=(granules) OR TS=(herbal medicine) OR TS=(decoction) TS=(granules) OR TS=(chinese medicine pills) OR TS=(cream formula) OR TS=(daoyin) OR TS=(wuqinxi) OR TS=(tai ji) OR TS=(tai chi) AND TS=(pulmonary fibrosis) OR TS=(radiation-induced pulmonary fibrosis) OR TS=(pneumosilicosis) OR TS=(anthracosis) OR TS=(aluminum pneumoconiosis) OR TS=(coalworker pneumoconiosis) OR TS=(graphite pneumoconiosis) OR TS=(cement pneumoconiosis) OR TS=(silicosis fibrosis) OR TS=(paraquat poisoning) OR TS=(cystic pulmonary fibrosis) OR TS=(interstitial lung disease) OR TS=(idiopathic pulmonary fibrosis) OR TS=(idiopathic nonspecific interstitial pneumonia) OR TS=(respiratory bronchiolitis-interstitial lung disease) OR TS=(desquamative interstitial pneumonia) OR TS=(cryptogenic organising pneumonia) OR TS=(idiopathic pleuroparenchymal fibroelastosis) OR TS=(unclassifiable idiopathic interstitial pneumonia) OR TS=(arthritis-interstitial lung disease) OR TS=(systemic sclerosis-interstitial lung disease).

This search strategy was conducted on June 20, 2023, encompassing literature published between January 1, 1992, and June 15, 2023, and covering the citation indexes SSCI and SCIE. The search yielded a total of 1221 relevant entries. These measures were implemented to ensure a robust and inclusive approach to data collection, ultimately upholding the scientific integrity and validity of the research.

2.2. Inclusion criteria

Articles and reviews with the subject matter limited to TCM/PF were included. The focus was determined based on the title and abstract of each work. Conference abstracts, letters, news pieces, and previously published editorial material were excluded. Furthermore, we restricted the extent of our investigation to publications in the English language. Following these selection criteria, a total of 358 studies (Fig. 2) were included in our investigation.

2.3. Data extraction

Our data review and filtering process proceeded as follows: (1) Three research team members independently reviewed the literature, excluding any publications inconsistent with the research theme. Disputed papers were eliminated via team consensus. (2) Corrections and unifications were made on selected literature, institutions, and countries to mitigate biases stemming from variations in author names, institutions, or countries. (3) Keyword standardization was implemented to rectify inadvertent repetitions in keyword co-occurrence diagrams caused by non-standard keyword forms, inconsistencies in wording, or plurality by standardizing keywords.

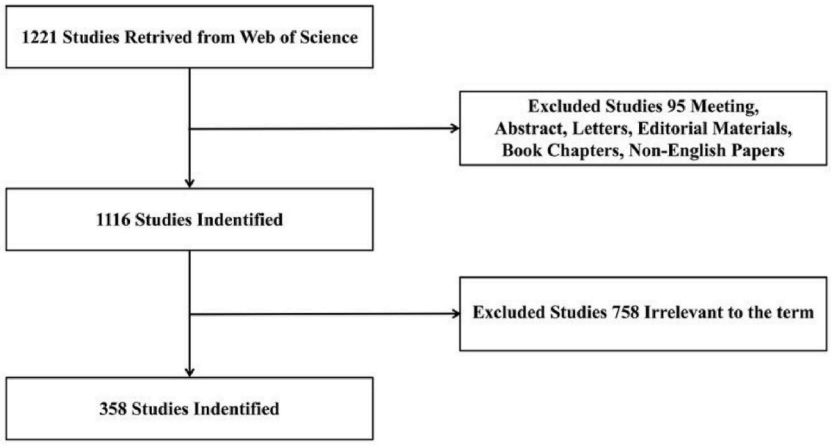

Fig. 2. Flowchart of study inclusion criteria.

The bibliometric tools used in this study included Origin 2023, VOSviewer, CiteSpace 5.7 R2, and Gephi.

3. Results

3.1. Annual publication trends and classification in TCM/PF

The temporal evolution of publications and citations can reflect the pace and trends of research in the field. Of the 358 publications analyzed (Fig. 3A), articles constituted 279 (76 %), while 79 were reviews (24 %). The articles were further divided into five research types: TCM formula (37.4 %), monomeric compound (30.4 %), single herb (8.4 %), TCM exercise (0.8 %) and acupuncture (0.5 %). Fig. 3B illustrates the annual increase in publications and citations in this field. From 1996 to 2004, a gradual rise was observed in annual publications, with increased attention from 2005. From 2013 onward, the number of published papers portrayed a consistent ascent. Notably, 2022 witnessed an exponential growth, and considering the data inclusion only up to the first half of 2023, we anticipate that the total number of articles published in 2023 will surpass 2022. Simultaneously, the overall growth of citation counts is consistent with the number of publications, foretelling a significant increase in citation numbers in 2023, indicating the scholarly interest and attention garnered by this field of research.

3.2. Analysis of journals

Table 1 shows the analysis of the top ten journals according to their publications. "Frontiers in Pharmacology" published the highest number of papers (n = 37), followed by "Journal of Ethnopharmacology" (n = 32), and "Evidence-Based Complementary and Alternative Medicine" (n = 25). Given the quantity of publications and their respective impact factors, "Frontiers in Pharmacology" and "Journal of Ethnopharmacology" likely represent the most influential journals in this research field. Moreover, it's notable that a majority of these journals are Open Access, suggesting a high degree of academic openness in this field.

We also enumerated the citation counts for these top ten journals (Table 2). "Journal of Ethnopharmacology" leads with 486

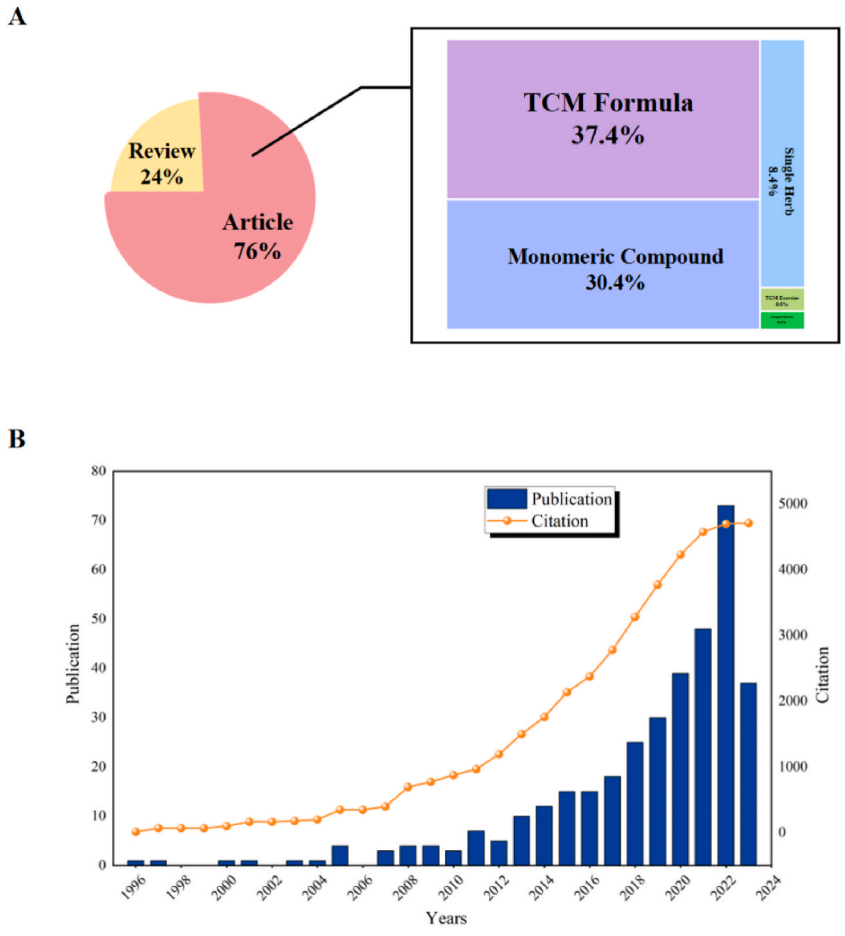

Fig. 3. Annual publication trends and classification in TCM/PF (A) Classifications of publication in TCM/PF. **(B)** Annual scientific production and cumulative scientific production of publications in TCM/PF.

Table 1
The top 10 productive journals in the TCM/PF.

Rank	Journal	Publications	Citation	Open Access	Impact Factor (2022)	Categories	Quartile
1	FRONTIERS IN PHARMACOLOGY	37	16	YES	5.6	PHARMACOLOGY & PHARMACY	Q1
2	JOURNAL OF ETHNOPHARMACOLOGY	33	273	Optional	5.4	CHEMISTRY, MEDICINAL	Q1
						INTEGRATIVE COMPLEMENTARY MEDICINE	Q1
						PHARMACOLOGY & PHARMACY	Q1
						PLANT SCIENCES	Q1
3	EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE	25	115	YES	/	INTEGRATIVE & COMPLEMENTARY MEDICINE	Q3
4	MEDICINE	16	711	YES	1.6	MEDICINE, GENERAL & INTERNAL	Q3
5	BIOMEDICINE & PHARMACOTHERAPY	14	120	YES	7.5	MEDICINE, RESEARCH & EXPERIMENTAL	Q1
						PHARMACOLOGY & PHARMACY	Q1
6	PHYTOMEDICINE	11	32	Optional	7.9	CHEMISTRY, MEDICINAL	Q1
						INTEGRATIVE COMPLEMENTARY MEDICINE	Q1
						PHARMACOLOGY & PHARMACY	Q1
						PLANT SCIENCES	Q1
7	CHINESE MEDICINE	10	165	YES	4.9	INTEGRATIVE & COMPLEMENTARY MEDICINE	Q1
						PHARMACOLOGY & PHARMACY	Q1
8	SCIENTIFIC REPORTS	10	139	YES	4.6	MULTIDISCIPLINARY SCIENCES	Q2
8	AMERICAN JOURNAL OF CHINESE MEDICINE	7	37	YES	5.7	INTEGRATIVE & COMPLEMENTARY MEDICINE	Q1
						MEDICINE, GENERAL & INTERNAL	Q1
10	EXPERIMENTAL AND THERAPEUTIC MEDICINE	6	150	YES	2.7	MEDICINE, RESEARCH & EXPERIMENTAL y	Q3

citations, followed closely by “American Journal of Respiratory and Critical Care Medicine” with 396 citations. Interestingly, papers related to Traditional Chinese Medicine and pulmonary fibrosis were not only cited by journals in the Integrative Complementary Medicine and Pharmacology & Pharmacy domains but were also substantially referenced by the prestigious medical journal, the “New England Journal of Medicine” (n = 218). This indicates substantial recognition of this field’s research within the medical community, which may be associated with the impact of the COVID-19 pandemic.

Table 2
The top 10 journals of citation counts in the TCM/PF.

Rank	Journal	Citation	Open Access	Impact Factor (2022)	Categories	Quartile
1	JOURNAL OF ETHNOPHARMACOLOGY	486	Optional	5.4	CHEMISTRY, MEDICINAL	Q1
					INTEGRATIVE COMPLEMENTARY MEDICINE	Q1
					PHARMACOLOGY & PHARMACY	Q1
					PLANT SCIENCES	Q1
2	AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	396	Optional	24.7	CRITICAL CARE MEDICINE	Q1
					RESPIRATORY SYSTEM	Q1
3	BIOMEDICINE & PHARMACOTHERAPY	254	YES	7.5	MEDICINE, RESEARCH & EXPERIMENTAL	Q1
					PHARMACOLOGY & PHARMACY	Q1
4	FRONTIERS IN PHARMACOLOGY	249	YES	5.6	PHARMACOLOGY & PHARMACY	Q1
5	PLOS ONE	247	YES	3.7	MULTIDISCIPLINARY SCIENCES	Q2
6	INTERNATIONAL IMMUNOPHARMACOLOGY	237	Optional	7.9	IMMUNOLOGY	Q2
					PHARMACOLOGY & PHARMACY	Q1
7	EVIDENCE-BASED COMPLEMENTARY AND ALTERNATIVE MEDICINE	219	YES	/	INTEGRATIVE & COMPLEMENTARY MEDICINE	Q3
8	NEW ENGLAND JOURNAL OF MEDICINE	218	YES	158.5	MEDICINE, GENERAL & INTERNAL	Q1
8	SCIENTIFIC REPORTS	215	YES	4.6	MULTIDISCIPLINARY SCIENCES	Q2
10	EUROPEAN RESPIRATORY JOURNAL	209	Optional	24.3	RESPIRATORY SYSTEM	Q1

Fig. 4 depicts the dual map overlay of the journal, providing insight into the distribution of topics. The map on the left represents the citing journals and the map on the right represents the cited journals. The labels represent the disciplines covered by the journals, while the colored pathways represent citation relationships. Two primary pathways are discernible. The dual orange citation paths suggest that research findings from the Molecular, Biology and Genetics, as well as the Health, Nursing, and Medicine domains, are frequently cited by journals in the Molecular, Biology and Immunology fields.

3.3. Cooperative relationship network

3.3.1. Country and institutional cooperation network

Through a statistical analysis of the quantity and impact of papers published on TCM/PF by countries, regions, institutions, key nations, and research organizations, their interconnections and collaborative relationships can be established. From the perspective of publication volume, the top ten countries were identified (Table 3). The foremost countries in terms of publication output include China, the United States, South Korea, Japan, the United Kingdom, Iran, Germany, India, Australia, and Italy. The results indicate that China has the highest number of published papers, with a total of 300, accounting for 83.80 % of the overall count. This significantly exceeds the United States, which ranks second with 16 publications, indicating China's dominant position in this field.

By using VOSviewer, we collated all countries with relevant publications, and generated a cluster map (Fig. 5A) through Scimago Graphica. Our analysis revealed that China has also collaborated closely with South Korea, the United States, and the United Kingdom, among others.

The top ten institutions in terms of the number of published papers are all located in China. Seven are TCM universities, with the remaining being medical universities and pharmaceutical universities (Table 4). This indicates that although universities specializing in TCM are the main research institutions, other comprehensive universities and medical schools are also engaged in this field.

3.3.2. Author cooperation network

Fig. 5B displays the annual scientific productivity of the top ten authors. Most authors published research related to TCM and PF, commencing from 2013. Notably, the zenith of the publications arose during the COVID-19 pandemic, from 2019 to 2013, which is shown as the darkest segment in the graph.

Fig. 5C and Table 5 shows a comprehensive overview of the publications and collaborations of the top 10 authors. These authors can be classified into two different clusters, with a large trend of collaboration within the clusters. SONG SIYU, LI YANXIN, LI XIANGYAN, DING LU, WANG JING AND TONG XIAOLIN demonstrated consistent collaboration, while LI JIANSHENG, BAI YUNPING, ZHAO PENG exhibited a close collaborative relationship.

3.4. Analysis of cited and co-cited reference

3.4.1. Highly cited articles

Table 6 lists the most frequently cited articles in the field of TCM/PF. Of the top ten, six are research papers and four are review articles. The most cited paper, with a total of 220 citations, was published by C. Bausewein in the Cochrane Database of Systematic Reviews, making it a seminal work in this field. Among the top ten articles, four were published in the preeminent Journal of

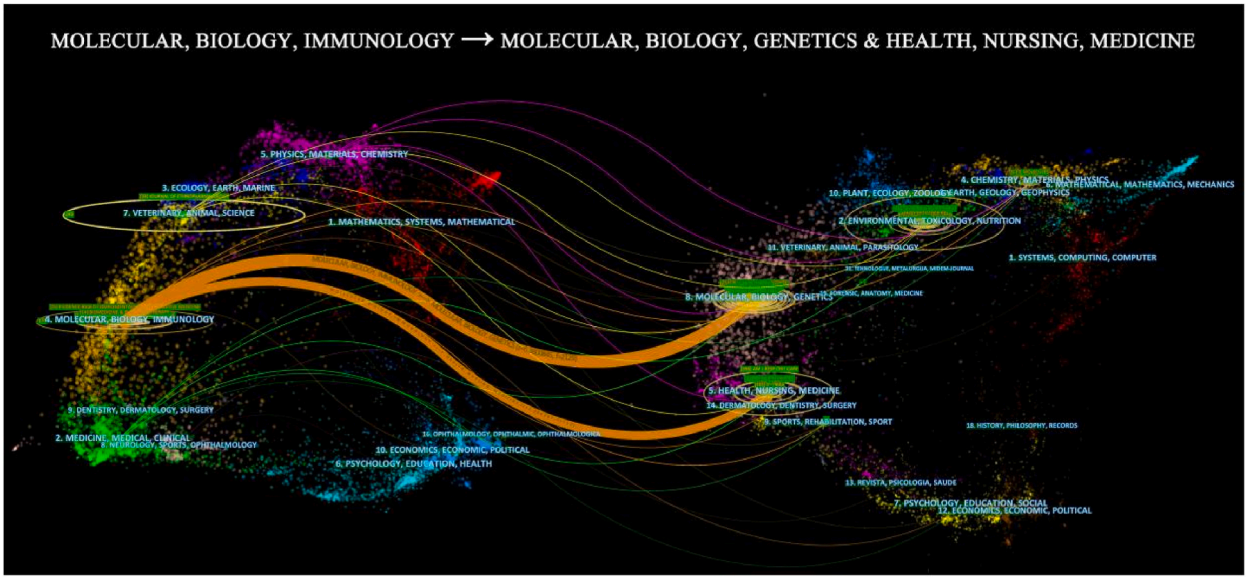

Fig. 4. Dual-map of journal of the distribution of topics.

Table 3
Country distribution of researches.

Rank	Country	Publications	Citations	total link strength
1	P.R.China	299	3479	7656
2	USA	16	503	2322
3	South Korea	15	132	2312
4	Japan	10	126	410
5	UK	8	371	1664
6	Iran	6	93	1370
7	Germany	4	92	445
8	India	4	124	674
9	Australia	3	75	767
10	Italy	3	26	353

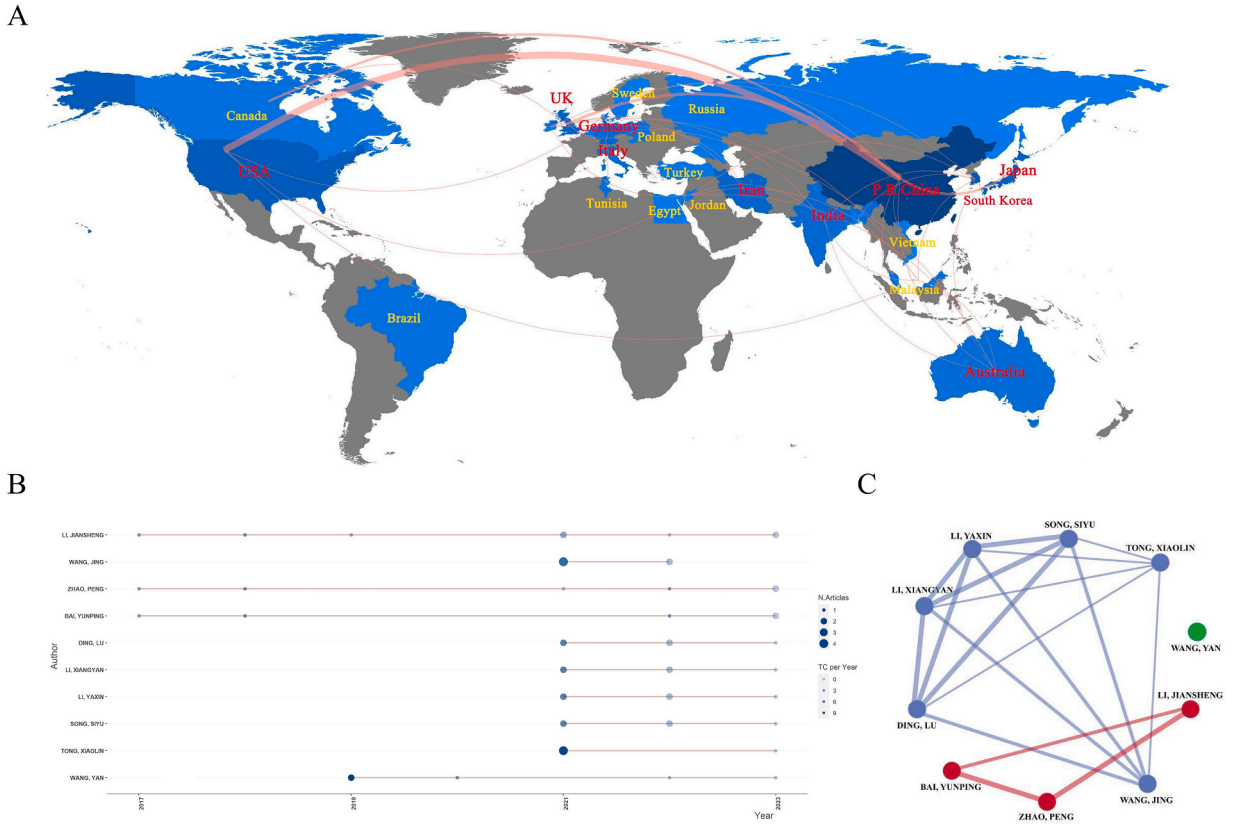

Fig. 5. Cooperative relationship network analysis (A)Country scientific production and international collaboration network in TCM/PF. **(B)**The top ten annual scientific productivity authors, and the size of the circle represents the number of publications, the depth of the circle represents annual citations. **(C)** Publications and collaborations of the top 10 authors. Each dot represents an author, the size of the dot represents the number of publications, and the thicker the lines, the closer the collaboration between the authors.

Ethnopharmacology, suggesting that this journal holds a significant influence in the field. This finding is consistent with the journal's publication and citation volume.

3.4.2. Highly co-cited reference

Table 7 delineates the most frequently co-cited articles in the field of TCM/PF. Among the top ten, the most common co-citations were four research articles and six reviews. The articles most frequently co-cited include three from the top-tier journal in the field of respiratory diseases, the American Journal of Respiratory and Critical Care Medicine, as well as the renowned medical journals, The Lancet and the New England Journal of Medicine. This implies that articles published in these core journals have notable impact within this field.

Burst detection analysis was utilized on highly cited articles and it was discovered that the article by Raghu G (2015) had a burst strength of 7.13, with the main burst period from 2018 to 2020. Hutchinson J (2015) exhibited a burst strength of 6.11, primarily from

Table 4
The top 10 productive institutions involved in the TCM/PF.

Rank	Institution	Publications	Citations	Average Citations/Publication
1	Beijing University of Traditional Chinese Medicine	36	219	6.08
2	Nanjing University of Traditional Chinese Medicine	23	227	9.87
3	Shanghai University of Traditional Chinese Medicine	17	102	6.00
4	Chengdu University of Traditional Chinese Medicine	14	108	7.71
5	China Academy of Chinese Medical Sciences	13	25	1.92
6	Fudan University	13	64	4.92
7	Henan University of Traditional Chinese Medicine	13	199	15.31
8	Tianjin University of Traditional Chinese Medicine	13	60	4.62
9	China Pharmaceutical University	10	66	6.60
10	Dalian Medical University	9	113	12.56

Table 5
The top 10 productivity authors related to the TCM/PF.

Rank	Author	Publications	H-index	Citations	Average Citations/Publication	Institution
1	LI, JIANSHENG	8	22	116	7.73	Henan University of Chinese Medicine
2	ZHAO, PENG	6	18	105	8.08	Henan University of Chinese Medicine
3	WANG, JING	6	10	105	8.08	Chengdu University of Traditional Chinese Medicine
4	TONG, XIAOLIN	5	30	61	5.55	China Academy of Chinese Medical Sciences
5	LI, XIANGYAN	5	21	85	10.63	Changchun University of Traditional Chinese Medicine
6	BAI, YUNPING	5	8	100	11.11	Henan University of Chinese Medicine
7	WANG, YAN	5	6	121	15.13	Hubei University of Chinese Medicine
8	DING, LU	5	4	23	2.56	Changchun University of Traditional Chinese Medicine
8	SONG, SIYU	5	3	129	14.33	Changchun University of Traditional Chinese Medicine
10	LI, YAXIN	5	3	156	19.50	Changchun University of Traditional Chinese Medicine

Table 6
The top 10 cited original researches related to the TCM/PF.

Rank	Citations	Title	First Author	Document type	Year	Journal	IF (2022)
1	220	Non-pharmacological interventions for breathlessness in advanced stages of malignant and non-malignant diseases	C Bausewein	Review	2008	COCHRANE DATABASE OF SYSTEMATIC REVIEWS	8.4
2	89	Controlled Release Pulmonary Administration of Curcumin Using Swellable Biocompatible Microparticles	E Sherbiny	Article	2012	MOLECULAR PHARMACEUTICS	4.9
3	87	Phillyrin attenuates LPS-induced pulmonary inflammation via suppression of MAPK and NF-kappa B activation in acute lung injury mice	Zhong WT	Article	2012	FITOTERAPIA	3.4
4	84	Traditional Chinese medicine for pulmonary fibrosis therapy: Progress and future prospects	Li LC	Review	2017	JOURNAL OF ETHNOPHARMACOLOGY	5.4
5	79	Therapeutic potentials of Houttuynia cordata Thunb. against inflammation and oxidative stress: A review	Shingnaisui	Review	2018	JOURNAL OF ETHNOPHARMACOLOGY	5.4
6	67	Luteolin Ameliorates Experimental Lung Fibrosis Both in Vivo and in Vitro: Implications for Therapy of Lung Fibrosis	Chen CY	Article	2010	JOURNAL OF AGRICULTURAL AND FOOD CHEMISTRY	6.1
7	66	PG490-88, a derivative of triptolide, blocks bleomycin-induced lung fibrosis	Krishna G	Article	2001	AMERICAN JOURNAL OF PATHOLOGY	6
8	65	Salvianolic Acid B Attenuates Experimental Pulmonary Fibrosis through Inhibition of the TGF-beta Signaling Pathway	Liu QM	Article	2016	SCIENTIFIC REPORTS	4.6
9	60	Attenuation of acute lung injury in mice by oxymatrine is associated with inhibition of phosphorylated p38 mitogen-activated protein kinase	Xu GL	Article	2005	JOURNAL OF ETHNOPHARMACOLOGY	5.4
10	59	Sophora alopecuroides L.: An ethnopharmacological, phytochemical, and pharmacological review	Wang RZ	Review	2020	JOURNAL OF ETHNOPHARMACOLOGY	5.4

Table 7
The top 10 co-cited original researches related to the TCM/PF.

Rank	Citations	Title	First Author	Document type	Year	Journal	IF (2022)
1	39	An Official Statement: Idiopathic Pulmonary Fibrosis: Evidence-based Guidelines for Diagnosis and Management	Raghu G	Article	2011	AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	24.7
2	36	Idiopathic pulmonary fibrosis	Richeldi L	Review	2017	LANCET	168.9
3	35	Idiopathic Pulmonary Fibrosis	Lederer DJ	Review	2018	NEW ENGLAND JOURNAL OF MEDICINE	158.5
4	31	Idiopathic pulmonary fibrosis	King TE	Review	2011	LANCET	168.9
5	29	Bleomycin induced interstitial pulmonary disease in the nude, athymic mouse	SZAPIEL SV	Review	1979	AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	24.7
6	28	Traditional Chinese medicine for pulmonary fibrosis therapy: Progress and future prospects	Li LC	Review	2017	JOURNAL OF ETHNOPHARMACOLOGY	5.4
7	27	Global incidence and mortality of idiopathic pulmonary fibrosis: a systematic review	Hutchinson J	Review	2015	EUROPEAN RESPIRATORY JOURNAL	24.3
8	27	An Official ATS/ERS/JRS/ALAT Clinical Practice Guideline: Treatment of Idiopathic Pulmonary Fibrosis: An Update of the 2011 Clinical Practice Guideline	Raghu G	Article	2015	AMERICAN JOURNAL OF RESPIRATORY AND CRITICAL CARE MEDICINE	24.7
9	26	SIMPLE METHOD OF ESTIMATING SEVERITY OF PULMONARY FIBROSIS ON A NUMERICAL SCALE	ASHCROFT T	Article	1988	JOURNAL OF CLINICAL PATHOLOGY	3.4
10	25	A Phase 3 Trial of Pirfenidone in Patients with Idiopathic Pulmonary FibrosisPirfenidone	King TE	Article	2014	NEW ENGLAND JOURNAL OF MEDICINE	158.5

2017 to 2020. Li LC (2017) demonstrated a burst strength of 3.8, with the burst phase predominantly occurring between 2019 and 2020. Cheresh P (2013) registered a burst strength of 3.67, primarily from 2015 to 2017 (Fig. 6).

3.5. Analysis of keywords

Keyword co-occurrence can effectively reflect research hotspots in the field, while emergent keywords can forecast frontier topics. Research hotspots and frontier topics were explored through keyword distribution analysis.

3.5.1. Cluster and trends analysis of high-frequency keywords

The top ten keywords include: pulmonary fibrosis, traditional Chinese medicine, murine model, TGF-β, regulation, protein expression, inflammation, acute lung injury, cell model, and idiopathic pulmonary fibrosis (Fig. 7A, Table 8).

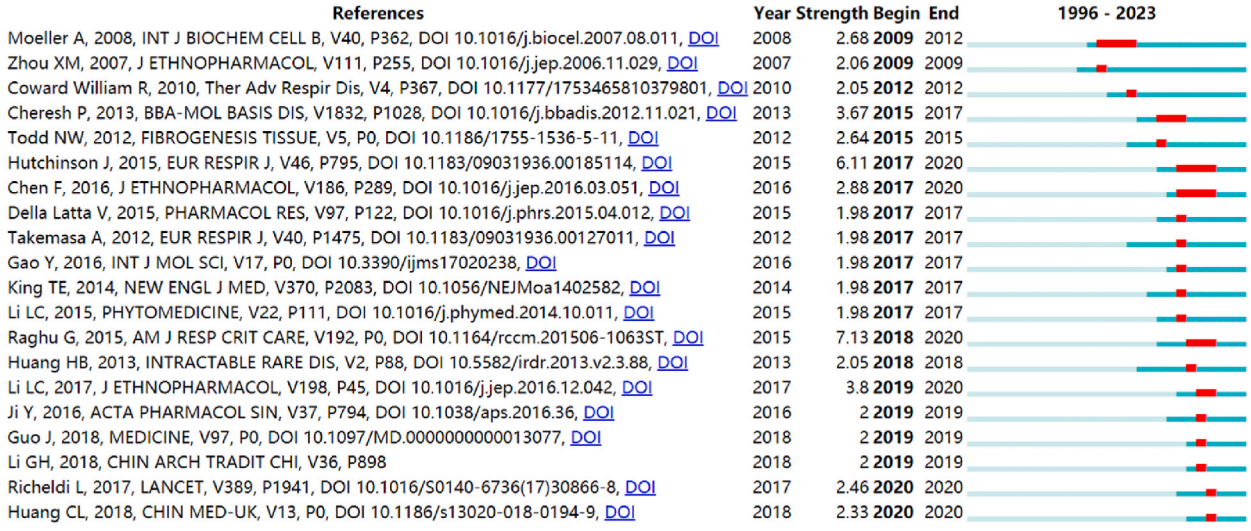

Fig. 6. Top 20 references with the strongest citation bursts.
The years between 'begin' and 'end' represent the period in which references have more influence. The years with light blue indicate that the references have not yet appeared, the years with dark blue indicate that the references have less influence, and the years with red indicate that the references have strong influence.

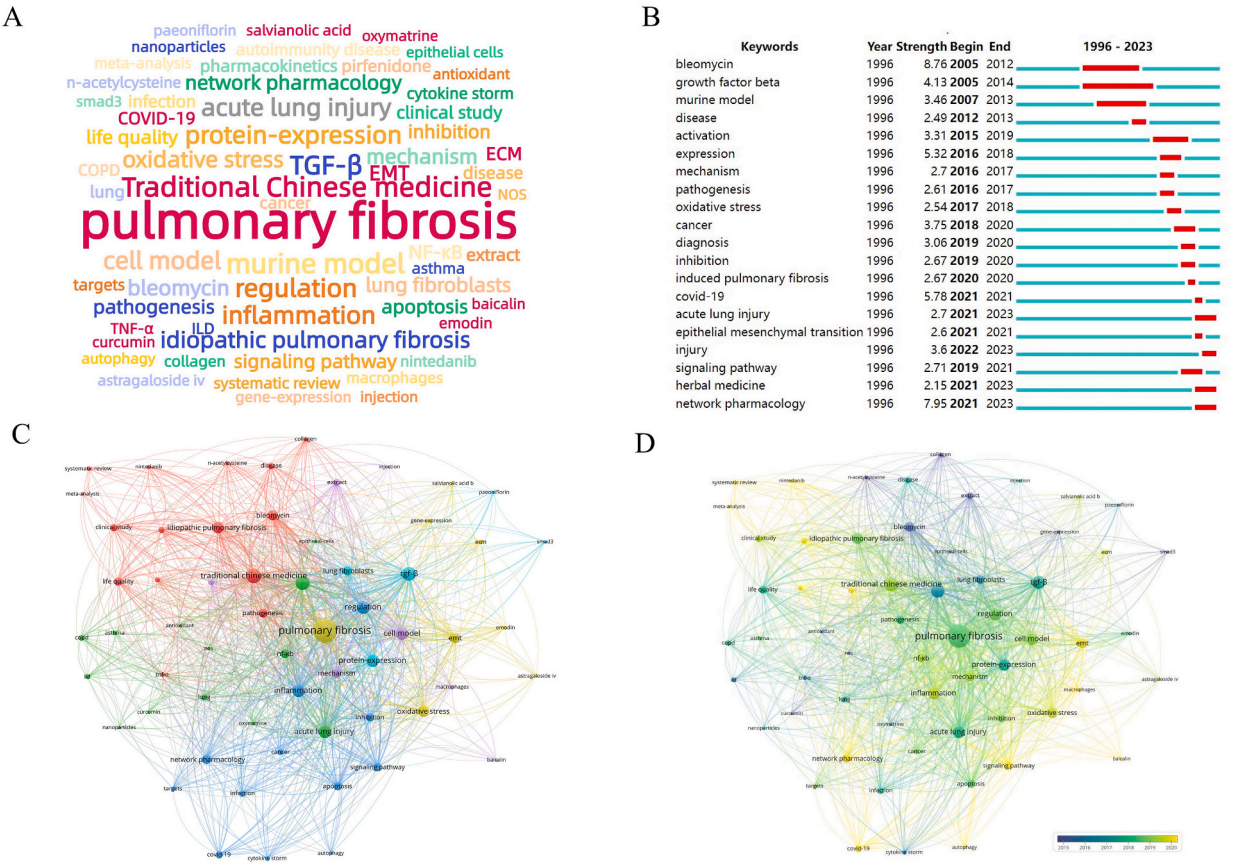

Fig. 7. Keywords analysis of TCM/PF. **(A)**1Distribution of top 60 keywords in TCM/PF. The larger the font, the more frequent the representation. **(B)** Top 20 strongest keyword bursts. The year between 'begin' and 'end' represents the period of keywords having more influence. The year with blue indicates that the keywords have not yet appeared or have less influence, and the year with red indicates the keywords having strong influence. **(C)** Cluster and trends analysis of high-frequency keywords. Different colors indicate different clusters, and the size of the dot indicates the frequency of the keyword occurrence. **(D)** Cluster and trends analysis of high-frequency keywords by years. The blue dot representing the earliest keyword, the yellow dot represents the latest keyword.

Table 8
Top 20 keywords in TCM/PF.

Rank	keyword	occurrences
1	pulmonary fibrosis	209
2	Traditional Chinese medicine	80
3	murine model	78
4	TGF-β	75
5	regulation	67
6	protein-expression	63
7	inflammation	62
8	acute lung injury	61
9	cell model	61
10	idiopathic pulmonary fibrosis	52
11	oxidative stress	51
12	EMT	45
13	bleomycin	43
14	mechanism	40
15	lung fibroblasts	36
16	network pharmacology	36
17	NF-κB	34
18	pathogenesis	32
19	apoptosis	30
20	signaling pathway	30

Keyword bursts were used to identify words that had frequent prominence within a time period. As shown in Fig. 7B, the blue line represents a timeline with the red segment on the blue timeline indicating burst detection, specifying the start year, end year, and burst duration. Notably, the strongest burst was observed for Bleomycin (8.76), followed by Network Pharmacology (6.31), COVID-19 (5.78), Expression (5.32), Growth Factor Beta (4.13), and Cancer (3.75). Keywords still in their burst period include Network Pharmacology, Acute Lung Injury, and Injury. Prior to 2015, the primary research focus was on Bleomycin, Growth Factor Beta, Murine Model, and Disease. Between 2015 and 2020, the major research focus shifted to Activation, Expression, Mechanism, Pathogenesis, Oxidative Stress, Cancer, Diagnosis, Inhibition, and Induced Pulmonary Fibrosis. Post-2020, the current hotspots are Network Pharmacology, COVID-19, Acute Lung Injury, Epithelial Mesenchymal Transition, and Injury.

3.5.2. Cluster and trends analysis of high-frequency keywords

Based on the frequency of co-occurrence of five or more keywords (top 60 keywords), a cluster analysis was performed. Each cluster of keywords was treated as a category and subsequently merged with the category with the highest degree of similarity. All keywords were ultimately divided into a category by the same color code. Fig. 7C illustrates the clustering analysis outcomes in the field of TCM/PF, revealing six separate categories.

Cluster 1(Red Topic): This cluster primarily focuses on the intersection of pathogenesis, clinical treatment options, disease progression, and patient prognosis of diseases related to PF (Keywords: Autoimmunity Disease, Bleomycin, Clinical Study, Collagen, Disease, Idiopathic Pulmonary Fibrosis, Life Quality, Meta-analysis, *N*-acetylcysteine, Nintedanib, Pathogenesis, Pirfenidone, Systematic Review, TNF-α, Traditional Chinese medicine).

Cluster 2 (Green Topic): This category is mainly about the investigation of the treatment and related mechanisms of comorbidities associated with PF(Keywords: Acute Lung Injury, Antioxidant, Asthma, COPD, Curcumin, Epithelial-cells, ILD, Lung, Murine Model, Nanoparticles, NF-kB, NOS, Oxymatrine).

Cluster 3 (Dark Blue Topic): This cluster predominantly concerns the pathogenesis of PF related to COVID-19 and the study of potential intervention methods (Keywords: Apoptosis, Autophagy, COVID-19, Cytokine Storm, Infection, Inflammation, Inhibition, Network Pharmacology, Regulation, Signaling Pathway, Targets).

Cluster 4 (Yellow Topic): This cluster primarily pertains to the gene expression and oxidative stress studies in PF (Keywords: Astragaloside IV, ECM, Emodin, EMT, Gene-Expression, Oxidative Stress, Pulmonary Fibrosis, Salvianolic Acid).

Cluster 5(Purple Topic): This category is predominantly about the cellular models and pharmacokinetic studies of various therapeutic interventions of PF (Keywords: Baicalin, Cell Model, Extract, Injection, Macrophages, Mechanism, Pharmacokinetics).

Cluster 6(Light Blue Topic): This category primarily explores the promoting effect of pulmonary fibroblasts on PF, as well as the related intervention targets and potential therapeutic compounds (Keywords: Lung Fibroblasts, Paeoniflorin, Protein-Expression, SMAD3, TGF-β).

Similar to the concurrent Fig. 7C, the overlay visualization map is an effective method to predict future trends and hotspots. As shown in Fig. 7D, VOSview assigns different color-codes to each keyword in the image based on the average time of appearance across all publications, with blue circles representing the earliest keywords and yellow circles denoting the most recent ones. From 2013 to 2023, the development dynamics of the six clusters were relatively uneven, with yellow nodes predominantly observed in Clusters 1 and Clusters 3. This indicates a concentrated research focus on the association between PF and COVID-19, as well as the clinical treatment of PF.

4. Discussion

TCM has garnered international recognition and application as a complementary and alternative medicine due to its over two-thousand-year history of clinical efficacy and relatively fewer adverse effects [8]. In this study, we combine bibliometric analysis with network visualization to depict the current research landscape of TCM intervention in PF. By comprehensively analyzing the contributions of countries, institutions, journals, and authors in this field, we aim to predict future research directions and hot topics.

4.1. General trends in the research of TCM/PF

Since its emergence in 1996, the annual publications in this field has shown an overall upward trend. From 1996 to 2004, only 1 or 2 relevant studies were published each year. Although there was a gradual increase of researches from 2005 to 2012, the growth rate remained relatively modest. The possible reason for this phenomenon could be that the research field was in its nascent stages of formation, and there might not have been a well-established research team and methods yet. Since 2013, the annual publications has continued to increase, with the growth rate accelerating significantly after 2019. There are several factors contributing to this trend. Firstly, the gradual maturation of research techniques and methods may lead to an increasing number of researchers interested in TCM/PF, further promoting the development of this field. Between 1996 and 2004, research methods related to TCM/PF were relatively simple, primarily focusing on histopathological analysis, ELISA, Western blot, and RT-qPCR to detect single pulmonary fibrosis-related markers [9,10]. From 2005 to 2012, as studies increased, research began to explore the mechanisms underlying pulmonary fibrosis, such as interventions targeting the TGF-β/Smad signaling pathway [11], p38MAPK signaling pathway [12], and others. Besides, there was a growing focus on targeting relative cells involved in the pulmonary fibrosis process, such as pulmonary fibroblasts [13], eosinophils [14], and airway epithelial cells [15]. Since 2013, a broader range of research methods, including proteomics and systemic sclerosis, have been employed in the study of TCM/PF [16,17]. Moreover, the research scope has expanded beyond basic research to include clinical studies in the field of TCM/PF [18,19]. Additionally, the global COVID-19 pandemic, which began at the

end of 2019, propelled research related to PF, as it is a major sequela of the COVID-19 [20]. As a result, research on PF evolved into a global research hotspot from 2019 to the present.

4.2. Countries and institutions that influence the direction of research of TCM/PF

Based on the number of publications, citations metrics and the top rank for co-authorship analysis, P.R.China emerges as the forefront contributor in the research on TCM/PF. Additionally, China has a prominent position in co-authorship analysis, indicating a significant level of collaboration between Chinese researchers and researchers from other countries such as USA, Japan and South Korea. This suggests China's global leadership in research of TCM/PF. Based on the analysis of publishing institutions, it is evident that the main contributors in this field are located in China, with various Traditional Chinese Medicine universities spearheading the research. The top three institutions include Beijing University of Chinese Medicine, Nanjing University of Chinese Medicine, and Shanghai University of Traditional Chinese Medicine. Among these, Beijing University of Chinese Medicine stands out with a significantly higher volume of publications compared to its counterparts, showcasing its comprehensive strength in this research field. Although Nanjing University of Chinese Medicine and Shanghai University of Traditional Chinese Medicine have slightly fewer publications than Beijing University of Chinese Medicine, they still maintain a leading position among other TCM universities. It is interesting to note that while these three universities had a significant influence on research in this field, the top 10 authors with the highest publication counts do not come from these institutions. And this inconsistency is partly due to the presence of many independent researchers among the top three institutions with the highest publications. These researchers may have recently participated the field of TCM/PF, resulting in lower publications and a lack of collaboration both within and between institutions. Additionally, the inconsistency may be related to the absolute number of researchers within these institutions. In cases where the ten authors with the highest number of publications belong to institutions with fewer researchers in the same field, this can further contribute to the observed inconsistency. Such inconsistencies are common in emerging and highly specialized research field. This, to some extent, suggests that TCM/PF is still relatively niche and emerging.

4.3. Past, present, and future hot topics of TCM/PF

The analysis of the composition, distribution and clustering of keywords effectively expedites the comprehension of research progress and distribution of hot topics in the respective field. A certain consistency was observed between the keyword bursts and publication volume in this field, with pivotal points in 2013 and 2019.

Before 2013, the burst keywords were mainly focused on bleomycin, TGF-β, and animal models. Bleomycin, a widely used class of anticancer drugs in clinical practice, is known for its toxic side effect of causing PF. The current consensus in the academic community is that bleomycin provokes DNA breakage, leading to the generation of free radicals, which in turn induces oxidative stress responses, resulting in apoptosis or necrosis of alveolar cells and ultimately causing PF [21]. To this day, bleomycin remains one of the most commonly used and classic methods for modeling PF in experimental animals [22,23]. TGF-β is a multifunctional cytokine that is ubiquitously expressed, controlling tissue homeostasis by regulating cellular processes such as apoptosis, proliferation, and differentiation. The TGF-β family in mammals comprises three major isoforms, among which TGF-β1 has the highest proportion and the strongest activity. It is widely recognized as one of the most potent fibrogenic factors, and in vitro, TGF-β1 is commonly used to induce the proliferation and differentiation of fibroblasts [24,25]. In essence, the characteristics of the aforementioned burst keywords reflect that research on TCM intervention in PF is still in its nascent stages.

During the period from 2014 to 2019, there was a significant shift in burst keywords, with an evident increase in terms related to mechanisms, regulation, and oxidative stress, which are associated with the pathogenesis and signaling pathways of pulmonary fibrosis. This indicates that research on traditional Chinese medicine intervention in PF has evolved, gradually shifting towards more in-depth investigations of its underlying mechanisms.

From 2019 to the present, encompassing the global pandemic of COVID-19 and the current post-pandemic era, the burst keywords have been closely associated with COVID-19. Acute lung injury and epithelial mesenchymal transition have emerged as burst points. As one of the main sequelae of COVID-19, the incidence of PF correlates with the severity (criticality rate) of COVID-19, correlates with patient age and immune factors [20]. To some extent, this highlights the characteristic of early intervention with TCM in PF management. Concurrently, keywords such as network pharmacology and inhibition have also emerged as burst points during the same period. Network pharmacology combines network topology and pharmacological insights to explore the interactions between drugs and biological systems, as well as the molecular mechanisms of drug therapy [26]. It aims to reveal the relationships between drugs and their targets, as well as the mechanisms of drugs in specific diseases. As a principal therapeutic approach in TCM, TCM formulas are characterized by their multi-target and multi-pathway therapeutic features. Therefore, the burst of the aforementioned keywords indicates that TCM treatment of PF during this period has mainly focused on post COVID-19 PF and screening for bioactive monomeric compounds in TCM formulas with therapeutic potential. With the ongoing challenges posed by the COVID-19 pandemic in certain countries or regions, it is foreseeable that this may continue to be a major research direction in the field.

4.4. The pioneer and mainstay in the field of TCM/PF

The earliest research dates back to 1996, when Kang HS and colleagues discovered that the TCM herb *Stephania tetrandra S Moore*, when applied in a silicosis model, reduced the number of pulmonary fibroblasts and collagen synthesis in lung. This effect was achieved by inhibiting IL-6, thereby exerting anti-inflammatory and anti-fibrotic effects [9]. Currently, the prominent researchers, or high

prolific authors, are mainly divided into two major research teams. One of the research teams is led by LI JIANSHENG, BAI YUNPING, ZHAO PENG, and others, affiliated with Henan University of Chinese Medicine. Their research is primarily focused on exploring the anti-pulmonary fibrosis mechanisms of the TCM formula "Jinshui Huanxian formula". In 2018, this research group made preliminary findings suggesting that the Jinshui Huanxian formula exerts its anti-fibrotic effects by activating the Nrf2 signaling pathway and reducing oxidative stress response [27]. In 2021, they delved further into monomeric compounds of the Jinshui Huanxian formula using network pharmacology and other experimental techniques [28]. In 2022, their research extended to serum pharmacochemistry analysis of the formula, which revealed that these monomeric compounds may inhibit the activation of pulmonary fibroblasts by suppressing the EGFR/PI3K/AKT signaling pathway [29]. Within the same year, a preliminary clinical study on the use of Jinshui Huanxian formula for treating IPF was conducted. It found that this formula can improve lung function and quality of life in IPF patients, providing evidence for further clinical application of this TCM formula [30]. Further investigations in 2023 utilizing transcriptomic technology revealed that the main monomeric compounds in the Jinshui Huanxian formula are closely associated with the inhibition of pulmonary fibroblasts activation through the suppression of the mTOR signaling pathway [31]. In addition, this research team has also conducted exploratory studies of TCM techniques, such as Daoyin [32], and other TCM formulas like "Yangqing Kangxian formula" [33] and "Yangqing Chenfei formula" [34] for the treatment of pulmonary fibrosis.

Another research team, led by individuals including TONG XIAOLIN, WANG JING, LI XIANGYAN, DING LU, SONG SIYU, and LI XIAXIN, affiliated with Changchun University of Traditional Chinese Medicine, China Academy of Chinese Medical Sciences, and Chengdu University of Traditional Chinese Medicine, focuses their research primarily on the "Qimai Feiluoping decoction" and "Wenfei Buqi Tongluo formula", both of which are TCM formulas. In 2021, this team utilized network pharmacology techniques to explore monomeric compounds of this formula through cellular experiments, and they demonstrated that the formula possesses certain anti-fibrotic effects [35]. Subsequently, in 2023, through the application of UHPLC/IM-QTOF-MS analysis and 4D-label-free proteomics analysis, coupled with animal experiments, the research team further uncovered that this decoction inhibits mitochondrial complex I-mediated oxidative stress to mitigate pulmonary fibrosis [36]. In 2021, the research team conducted preliminary in vitro experiments to explore the therapeutic potential of the "Wenfei Buqi Tongluo Formula" in treating pulmonary fibrosis. Their findings suggested that this formula might exert its effects through the inhibition of the TGF-β/Smad3 signaling pathway, thereby reducing EMT and inhibiting extracellular matrix accumulation [37]. In addition, during the period from 2021 to 2022, several significant research papers were published in this field. One publication focused on a systematic review and meta-analysis of the efficacy and safety of *Tripterygium Wilfordii Hook F* in treating interstitial lung diseases associated with connective tissue disorders [38]. Another review highlighted the therapeutic effects and molecular mechanisms of commonly used traditional Chinese herbal bioactive compounds, including their role in treating respiratory system diseases such as PF [39]. Furthermore, another review discussed the potential of monomeric compounds from Chinese herbal medicines to prevent and treat PF by inhibiting TGF-β1-mediated cellular processes [40]. These studies collectively contribute to a deeper understanding of the therapeutic potential of TCM in treating PF. The research achievements and methodologies developed by the aforementioned prominent research groups have, to a certain extent, provided valuable insights for other emerging research teams. This involves identifying TCM formulas with anti-fibrotic properties, conducting comprehensive studies on important TCM monomeric compounds to understand their mechanisms, and eventually progressing towards clinical trials after obtaining substantial research findings.

4.5. Significant monomeric compounds of TCM/PF

While TCM formulas possess distinct characteristics and are more frequently employed in clinical practice, their flexible prescription patterns and complex compositions render exploring their mechanisms a challenge. Moreover, conducting sustained research on a specific TCM formula is intricate due to the dynamic nature of herbal combinations. In contrast, individual chemical compounds derived from Traditional Chinese herbs exhibit fixed chemical structures, allowing different research groups to study specific monomeric compounds of high medicinal value. Consequently, this research landscape is reflected in the keyword analysis, wherein five prominent TCM monomeric compounds, namely emodin, curcumin, salvianolic acid, baicalin, and oxymatrine, have surfaced with increased frequency and centrality.

Emodin, primarily sourced from the traditional Chinese herb *Rhei Radix Et Rhizoma*, saw its earliest research in treating PF in 2009. A study discovered that oral administration of emodin effectively reduced the levels of TGF-β1 and HYP in vivo experiments. Additionally, in vitro experiments demonstrated that emodin inhibited the collagen protein secretion function of lung fibroblasts [41]. However, the study did not elucidate the underlying mechanisms of these effects. By 2015, further in-depth research into emodin revealed that its ability to reduce collagen was closely related to inhibiting the activation of the PI3K/Akt signaling pathway, thereby alleviating inflammatory reactions [42]. Subsequently, in 2017, emodin's mechanism of reducing TGF-β1 expression was uncovered to be intricately linked to the activation of the Notch signaling pathway, which in turn suppressed EMT [43]. The latest research done in 2023 found that emodin's inhibition of EMT is also associated with its upregulation of miR-182-5p and downregulation of c-MYC [44]. Furthermore, research and reviews from 2021 highlighted emodin as a crucial monomeric compound of TCM, with potential therapeutic effects for both COVID-19 and PF [45–47]. Therefore, emodin holds significant potential to become a novel generation drug for treating PF in the future.

Curcumin is mainly derived from *Curcumae Longae Rhizoma*, *Curcumae Radix*, and *Curcumae Rhizoma*. Unlike emodin when administered orally, curcumin's trajectory takes a different course. While its oral administration was found to possess certain inhibitory effects on PF in 2009 [48], subsequent studies in 2012 indicated that pulmonary delivery might offer more advantages [49]. A study in 2018 introduced curcumin large porous microparticles for pulmonary delivery, which exhibited reduced phagocytosis by alveolar macrophages, significantly decreased HYP, and suppressed type I collagen synthesis, ultimately resulting in PF inhibition

[50]. Advancements in delivery methods in 2021 further enhanced curcumin's ability to decrease TNF-α expression in the lungs [51]. During the same year, a review discussing the combination of TCM with pulmonary delivery for PF treatment identified curcumin as one of the key research areas [52]. Therefore, prospective research on curcumin may continue to focus on optimizing and improving delivery methods.

Salvianolic acid, primarily derived from *Radix Salvia Miltiorhizae* in TCM, comprises of type A and B [53,54]. In 2014, two studies revealed that both salvianolic acid A and salvianolic acid B inhibited lung fibroblast proliferation, induced apoptosis, and suppressed PF [54,55]. Subsequently, in 2016, it was found that their mechanisms were associated with the inhibition of the TGF-β signaling pathway [56]. Similar to curcumin, the oral bioavailability of salvianolic acid is relatively low. Consequently, since 2021, research on the efficacy of salvianolic acid in treating PF has pivoted towards pulmonary delivery administration [57]. Furthermore, studies on TCM formulas like Yangfei Huoxue decoction [58] and Shuangshen Pingfei formula [59], which utilize salvianolic acid as a core monomeric compound, have been initiated for PF. Moving forward, research on salvianolic acid might continue to focus on refining delivery methods and exploring its mechanisms of action.

Baicalin, mainly derived from the roots of *Scutellariae Radix*, is well-recognized for its anticancer and antioxidant effects [60,61]. Similar to salvianolic acid, its research began relatively later. In 2015, it was initially discovered that baicalin could inhibit IL-6 and IL-23, reducing the number of Th17 cells and alleviating lung inflammation and PF [62]. Subsequently, in 2020, baicalin was found to mitigate PF through the inhibition of apoptosis in lung fibroblasts, mediated by the PI3K/AKT signaling pathway [63]. Furthermore, a metabolomics study conducted in 2021 on the use of baicalin for PF identified that its mechanisms of improving PF are associated with the regulation of metabolic processes such as taurine and hypotaurine, glutathione, and glycerophospholipids [64]. Thus, future research could delve more extensively into the study of its metabolites.

Oxymatrine, a bioactive alkaloid extracted from the Chinese herb *Sophorae Flavescentis Radix*, was identified as early as 2008 to possess inhibitory effects on lung fibroblast proliferation and reduce HYP expression [13]. A study in 2012 confirmed its mechanism for treating PF, which involves inhibiting iNOS expression and the TGF-β/Smad pathway [11]. In 2016, modified Kushen Gancao formula, a Chinese herbal formula which is known to feature oxymatrine as its main monomeric compound, further substantiated its efficacious inhibitory effects on PF [65]. By 2023, further research revealed that oxymatrine can activate the PI3K/AKT signaling pathway, thereby attenuating TGF-β-mediated mitochondrial apoptosis in alveolar epithelial cells, and inhibiting the occurrence of EMT [66]. Similarly, in the same year, a review on the use of individual TCM monomeric compounds for PF also highlighted oxymatrine as one of the promising avenue for future research [67]. Hence, oxymatrine holds a favorable research prospect for treating PF.

4.6. Limitations of this study

This study acknowledges certain limitations that warrant consideration. Firstly, the field of TCM/PF is considered niche and emerging, resulting in a limited pool of relevant literature. Consequently, the overall volume of literature included in the analysis is relatively small, potentially limiting the comprehensiveness of the investigation. Furthermore, we confined our search to English-language papers included in the Web of Science Core Collection database. Some papers published in Chinese, particularly from a prolific TCM publishing country like China, may not have been included in the analysis, which could potentially introduce bias into the results. Thirdly, the results of keyword analysis may be influenced by incomplete keyword extraction. Additionally, newly published articles with keywords showing low correlation might be overlooked, potentially resulting in oversight of the latest research trends.

5. Conclusion

In conclusion, this study employed scientometric and visual analysis methods to provide a preliminary insight into the global research status and trends of TCM in treating PF. The results revealed a consistent increase in the volume of research focused on TCM treatment for PF over the years. The surge in post-COVID-19 related PF has further intensified this trend, prompting a rapid growth in TCM related studies. Currently, researches primarily focus on both the animal and cellular experiments of TCM formulas and individual monomeric compounds. Due to the flexible and diverse compatibility of TCM formulas, and the incomplete exploration of the active monomeric compounds, studies related to the treatment of PF with TCM formulations appear relatively scattered. However, as research advances and more investigations into individual monomeric compounds emerge, a more concentrated research direction is anticipated, gradually unveiling a plethora of clinical research outcomes. In summary, TCM stands as a promising resource for addressing PF. With increasing insights into the mechanisms of TCM, it is foreseeable that TCM could become a complementary therapeutic approach alongside mainstream medicine, offering a new dimension in the treatment of PF.

Data availability statement

All data generated or analyzed during this study are included in this article. Further information could be made available on request with the corresponding author.

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CRediT authorship contribution statement

Bokai Wei: Writing – review & editing, Writing – original draft, Conceptualization. **Haozheng Li:** Software, Methodology, Formal analysis. **Chengyu Wang:** Writing – review & editing, Visualization, Software, Methodology, Formal analysis. **Jing Hu:** Writing – review & editing, Resources, Project administration, Funding acquisition, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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