Review article

A bibliometric analysis of research related Chinese Medicine in the prevention and treatment of corona virus disease 2019

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ABSTRACT

Objective: To perform a bibliometric analysis of published research related to the use of traditional Chinese medicine (TCM) for the treatment of Coronavirus Disease 2019 (COVID-19).

Methods: Research documents related to the use of TCM for prevention and treatment of COVID-19 published up to September 19, 2021, were retrieved from the Web of Science database. Bibliometrix R 4.0 software package was used to analyze data, including countries of publication, research institutions, journals, citations, and keywords. Further analysis was conducted to identify co-occurrence of keywords in the documents, including their titles and abstracts. Cooperative network analyses of authors, institutions, and countries of publication were also conducted. The classification types were statistically analyzed and the research progress of key TCMs was reviewed.

Results: A total of 417 documents were included in our analysis. Of these, 85.13% originated in China. Of the 417 documents, 148 (35.5%) were published in journals with impact factors in quartile 1 and 164 (39.3%) in journals in quartile 2. The documents were mainly published in journals categorized as Medicine. The results of network analysis showed close cooperation between institutions and countries. Excluding disease- and drug-related keywords, the top four keywords were 'Systematic review', 'Network pharmacology', 'Medicine' and 'Molecular docking'. Keyword co-occurrence analysis showed 4 main keywords association groups. Statistical analysis of the TCM studies showed that Lianhua Qingwen capsule, Qingfei Paidu decoction, Shufeng Jiedu capsules and ReDuNing injection were the most studied Chinese medicines. Lianhua Qingwen capsules, Qingfei Paidu decoction, ReDuNing injection, and Shufeng Jiedu capsules were used in clinical, bioinformatics, and basic research. Toujie Quwen granule, Jinhua Qinggan granule, Shuanghuanglian oral liquid, Tanreqing injection, and Xuanfei Baidu decoction were used in clinical and bioinformatics research, although basic research on their mechanisms of action is lacking.

Conclusion: Research intensity and recognition, as well as cooperation, in the field of Chinese medicine for the prevention and treatment of COVID-19 has increased. Research types are generally comprehensive, and investigated several TCM formulations that are specifically recommended by Chinese COVID-19 guidelines. However, comprehensive, in-depth research on their molecular mechanisms of action is still lacking. More basic research is thus needed to identify therapeutic mechanisms to standardize and validate the use of TCM in the prevention and treatment of COVID-19.

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1. Introduction

Coronavirus disease 2019 (COVID-19) manifests primarily as a respiratory tract infection caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Since the outbreak of SARS-CoV-2 at the end of December 2019, a variety of mutant strains, including B.1.7 (Alpha), B.1.351 (Beta), P.1 (Gamma), B.1.167.2 (Delta), B.1.429 (Epsilon), and B.1.526 (Iota) have been identified in different world regions [1, 2]. At present, the treatment of SARS-CoV-2 infection mainly relies on vaccines and antiviral drugs, the latter still being the main treatment in practical applications [3]. At present, antiviral drugs for the treatment of COVID-19 mainly include small molecule drugs (such as protease inhibitors and polymerase inhibitors) and SARS-CoV-2 neutralizing antibodies (e.g. bamlanivimab, etesevimab, casirivimab, and imdevimab) [4]. Due to the enhanced transmission of newer viral lineages, immune escape is more likely to occur, which limits the application of antiviral drugs [2]. Moreover, several studies have shown that bamlanivimab, etesevimab, casirivimab, and imdevimab cannot neutralize omicron mutants [5, 6, 7]. There is evidence that small-molecule antiviral drugs improve mild to moderate COVID-19 symptoms in patients, but there is still a lack of evidence for severe COVID-19 patients and for those infected with newer virus variants [8]. It has been reported that traditional Chinese medicine (TCM), a form of "treatment based on syndrome differentiation", can rapidly relieve the clinical symptoms of patients with COVID-19 and has also a curative effect on patients affected by newer SARS-CoV-2 variants [9, 10]. Therefore, China's National Health and Health Commission and the State Administration of TCM have jointly issued several papers advocating the integrative medicine treatment model and the unique advantages of TCM in the treatment of epidemic diseases [11]. Chinese medicine contains many chemical components, which can act on multiple targets in disease, and there is substantial evidence supporting its beneficial effects in the treatment of COVID-19. In order to classify and summarize the scientific literature reporting on TCM in the prevention and treatment of COVID-19, we used bibliometric methods to analyze relevant research published in the Web of Science database from the outbreak of COVID-19 to September 19, 2021.

2. Information and methodology

2.1. Search and data retrieval methods

The Web of Science (http://webofscience.com) data platform was searched using the following terms: 'Traditional Chinese Medicine', 'Traditional Medicine, Chinese', 'Chinese Medicine, Traditional', 'Zhong Yiyao', 'COVID 19', '2019-nCoV Infections', 'COVID-19 Virus Infections', 'COVID-19 Virus Disease', and 'COVID 19 Virus Disease'. The search was limited to English language documents published in the period from inception to 19 September, 2021. Within the Web of Science, the following databases were searched: Web of Science Core Collection, Science Citation Index Expanded, Social Sciences Citation Index, Current Chemical Reactions, and Index Chemicus.

The search formulas were:

#1- COVID 19 (All Fields) or COVID-19 Virus Disease (All Fields) or COVID 19 Virus Disease (All Fields) or Disease, COVID-19 Virus (All Fields) or Virus Disease, COVID-19 (All Fields) or COVID-19 Virus Infection (All Fields) or COVID 19 Virus Infection (All Fields) or COVID-19 Virus Infections (All Fields) or 2019-nCoV Infections (All Fields)

#2- Traditional Chinese Medicine (All Fields) or Traditional Medicine, Chinese (All Fields) or Chinese Medicine, Traditional (All Fields) or Zhong Yiyao (All Fields)

#3- Cross examination of articles retrieved from #1 and #2

Once all relevant documents had been retrieved, the full record was exported in the Bib txt format.

2.2. Data analysis

Bibliometrix (http://www.bibliometrix.org/) R 4.0 software package was used to store and visualize statistics from relevant studies [12]. National functional statistics were used to find the number of papers published by authors based in certain countries or regions. The highest cited country function was used to determine the number of citations of research published by authors per country or region. The most relevant membership function was used to determine the number of papers published per research institution. The word frequency function was used to determine frequency of keywords, with normalization set to association. The clustering algorithm was set to Louvain and unconnected points are removed. Co-occurrence network analysis was used to determine keywords co-occurrence. Cooperative networks were modeled to analyze collaboration between authors and institutions. The results obtained using the Bibliometric package were imported into Excel software to construct the data set and three-line table.

3. Results

3.1. Search results

The search initially yielded 652 documents. After reading the title and abstract of the documents, we excluded 18 documents unrelated to TCM and COVID-19, 13 documents related to TCM but unrelated to COVID-19, and 204 documents related to COVID-19 but unrelated to TCM. Finally, 417 documents were selected. Among those, 212 were published in 2020, and the remaining 205 were published as of September 19, 2021. The 417 documents were cited 7335 times and were published over a period from 2020 to 2021. The documents included 1819 author names, were published in a total of 132 journals, and proceeded from 683 institutions in 46 countries and regions.

3.2. Institutional analysis

The countries from which most of the documents originated were identified. The results showed that most of the published documents described research conducted by authors based in China, India, and the USA (Figure 1A). Authors in China conducted most of the research on TCM for prevention and treatment of COVID-19, being responsible for 355 of the 417 documents (85.13%). The most cited studies were conducted in China, Brazil, and Australia (Figure 1B). The documents published in China were cited 6581 times, accounting for 89.72% of all citations, which affirmed China's contribution to this field of research. The 683 institutions listed in the 417 documents were ranked according to the number of publications for institutions (Figure 1C). Results showed 10 TCM universities among the top 20 institutions, of which the top three were Shanghai University of Traditional Chinese Medicine (n = 88, 21.10%), Chengdu University of Traditional Chinese Medicine (n = 76, 18.23%), and Beijing University of Traditional Chinese Medicine (n = 63, 15.11%). Among non-TCM universities, the institutions with the most publications in this field were Huazhong University of Science and Technology (n = 48, 11.51%), Wuhan University (n = 48, 11.51%) and Capital Medical University (n = 41, 9.83%). The top 20 institutions were all located in China, indicating that these universities are highly active in TCM research.

3.3. Journal analysis

The 132 journals in which the 417 documents were published were categorized into quartiles 1 (Q1) to 4 (Q4) based on their impact factors. One hundred and forty eight of the 417 documents were published in Q1
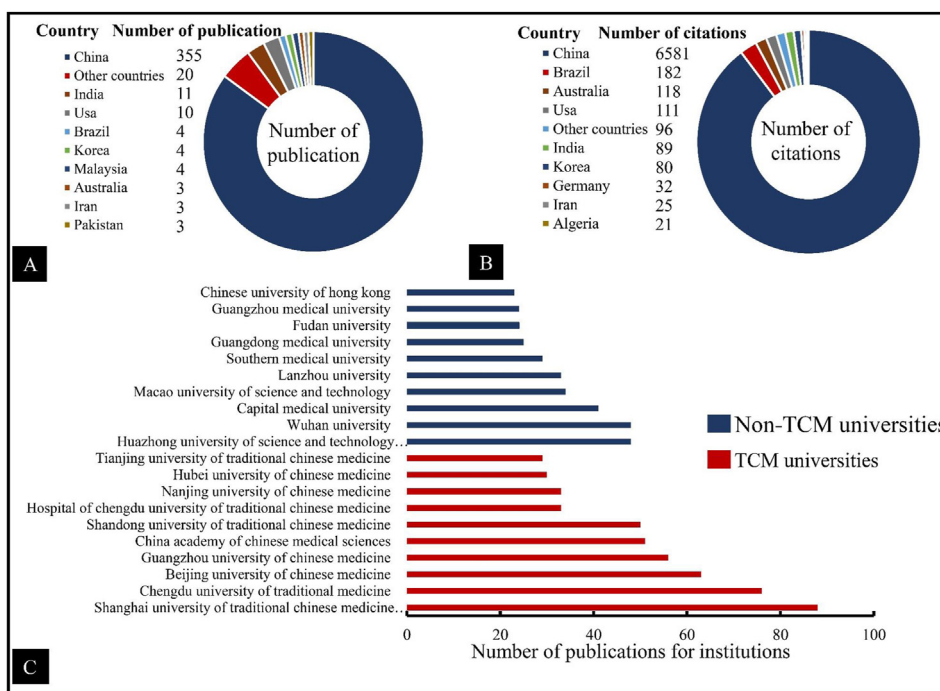
Figure 1. Countries with the highest number of publications (A), number of citations (B) and number of publications for institutions (C).

and 164 in Q2 journals (Figure 2A). Among the 132 journals, the highest number of reports were published in Medicine (Baltimore) (n = 54), Frontiers in Pharmacology (n = 30), and Pharmacological Research (n = 18), all of which have a record of publishing TCM research (Figure 2B). The impact factors of the journals in which the selected documents were published were generally low; only eight had an impact factor >10, and only 11 (2.64%) documents were published in these journals. Thirty-seven journals had an impact factor >5, and 120 (28.87%) of the documents were published in these journals. The journal with the highest impact factor (18) was Signal Transduction and Targeted Therapy. Among the 417 documents, 85 were published in journals categorized as Medicine, General & Internal, 83 as Integrative & Complementary

Medicine, and 79 as Pharmacology & Pharmacy (Figure 2C). The h-index is the number of articles published in a journal that have been cited at least h times. The 20 journals with the highest h-indices were identified, and were found to feature 237 (56.83%) of the documents. H index ranking showed that Pharmacological Research had the highest index, indicating high recognition of this journal in the field of TCM (Figure 2D). Between 2020 and 2021, the journal published 18 articles on TCM treatment of COVID-19. These articles were cited a total of 802 times, and the highest number of citations was for Li et al. [13]. This study found that Lianhua Qingwen significantly inhibited SARS-Cov-2 replication, affected virus morphology, and exerted antiviral and anti-inflammatory activities *in vitro*.
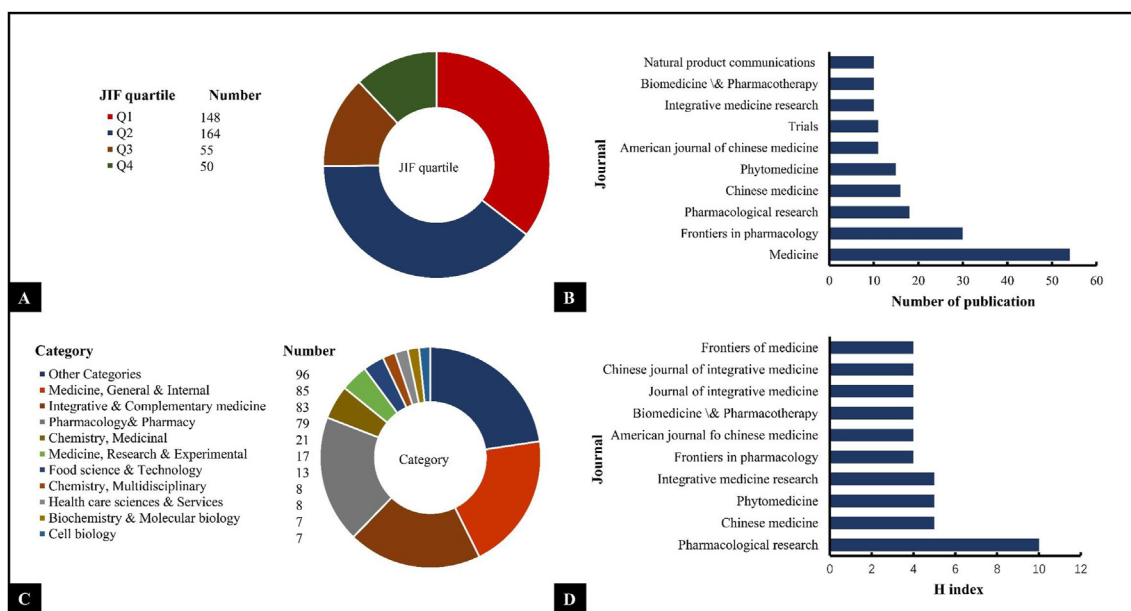

Figure 2. The impact factor of journals (journal impact factor; JIF) publishing the 417 documents categorized as quartiles 1 to 4 (A), the number of publications per journal (B), per journal category (C) and the author H index of documents published per journal (D).

3.4. Cooperation network

A cooperative analysis of the 417 documents selected was conducted. Results identified seven main institutional cooperation groups (Figure 3A): (1) Huazhong University of Science and Technology cooperated closely with Wuhan University, Capital Medical University, Fudan University, and Peking University; (2) Shanghai University of TCM cooperated closely with Shanghai Jiaotong University and Hubei University of Chinese Medicine; (3) Chengdu University of TCM cooperated closely with Hospital of Chengdu University of TCM and Sichuan University; (4) Southern Medical University cooperated closely with Wuhan Institute of Virus Research; (5) Zhejiang University cooperated closely with Zhejiang University of Chinese Medicine; (6) Beijing University of Chinese Medicine cooperated closely with China Academy of Chinese Medical Sciences, Guangzhou Medical University, Shandong University of TCM, and Macao University of Science and Technology; and (7) Tianjin University of TCM cooperated closely with Lanzhou University, Guangdong Provincial Hospital of TCM, Guangzhou University of Chinese Medicine, and Sun Yat-sen University. National cooperation analysis showed close cooperation between China and the USA, Australia, Canada, and other countries, between France and Ireland and Italy, and between India and South Africa, the UK, and Malaysia (Figure 3B) (see Figure 4).

3.5. Keyword analysis

Keywords provide an indication of the research focus of an article. From the 417 documents selected for analysis, we extracted 939 keywords. The three keywords with the highest frequency of occurrence were Covid-19 (n = 242), Traditional Chinese medicine (n = 97), and SARS-Cov-2 (n = 75). Excluding those keywords related to diseases and drugs, the four keywords with the highest frequency were Systematic review (n = 43), Network pharmacology (n = 42), Medicine (n = 35) and Molecular docking (n = 35) (Figure 4). These results indicate that the research analyzed focused mainly on information system evaluation and clinical and pharmacological research.

3.6. Co-occurrence network

The results of keyword co-occurrence analysis showed four groups of co-occurring words, as follows: (1) 'Covid-19' with 'Traditional Chinese Medicine' and 'SARS-Cov-2'; (2) 'Severe acute respiratory syndrome' with 'Coronavirus disease 2019', 'Meta-analysis' and 'Systematic review'; (3) 'Network pharmacology' with 'Molecular docking', 'Pulmonary fibrosis', and 'Pneumonia'; and (4) 'Traditional medicine' with 'Chinese medicine' and 'Medicine' (Figure 5A). The results of title co-occurrence analysis showed four groups of associated words within the documents' titles, as follows: (1) 'Covid-19' with 'Traditional', 'Chinese' and 'Medicine'; (2) 'Network' with 'Pharmacology' and 'Mechanism'; (3) 'Trial' with 'Patients', 'Study', and 'Effects'; and (4) 'Meta-analysis' with 'Protocol', 'Review', and 'System' (Figure 5B). Results of co-occurrence analysis of abstracts showed three association groups: (1) 'Covid' and 'Traditional', 'Chinese', 'Medicine', 'Treatment', and 'Disease'; (2) 'Clinical' and 'Study', 'Methods', and 'Patients'; and (3) 'Analysis' and 'Effects' and 'Potential' (Figure 5C).

3.7. Analysis of literature focusing on TCM treatment for COVID-19

We further screened the 417 selected articles to specifically analyze those reporting on the therapeutic effects of TCM treatment for COVID-19. As a result, we excluded 189 review articles, 6 cross-sectional studies on people 's views on TCM and the diagnostic characteristics of COVID-19, and 22 articles reporting on data mining in TCM through association rules, deep learning, and construction of prediction models. Among the 200 remaining documents there were 39 clinical studies, 5 protocols of clinical studies, 29 experimental studies, 53 network pharmacology analyses, 9 molecular docking analyses, 23 systematic reviews, and 42 protocols of systematic reviews. A total of 93 different treatments were reported in the 200 documents. Among the 93 treatments, Lianhua Qingwen capsule (n = 16), Qingfei Paidu decoction (n = 9), Shufeng Jiedu capsule (n = 8), Reduning injection (n = 4), Toujie Quwen granule (n = 3), Shenhuang granule (n = 3), and Jinhua Qinggan granule (n = 3) were the most frequently used. Xiyanping injection (n = 2), Xuanfei Baidu decoction (n = 2), and Shuanghuanglian oral liquid (n = 2), were used less frequently (Table 1). Of the 10 Chinese medicines with the highest frequency of occurrence, 7 are recommended in the guidelines for the prevention and treatment of COVID-19 in China [14]. These 7 Chinese medicines are Lianhua Qingwen capsule, Qingfei Paidu decoction, Shufeng Jiedu capsules, Reduning injection, Jinhua Qinggan granules, Xiyanping injection, and Xuanfei Baidu decoction.

3.8. Research status of core Chinese medicine

Using the China National Knowledge Infrastructure (https://www.cnki.net/) and Web of Science databases (http://webofscience.com), we summarized research progress on the 10 Chinese herbal compounds
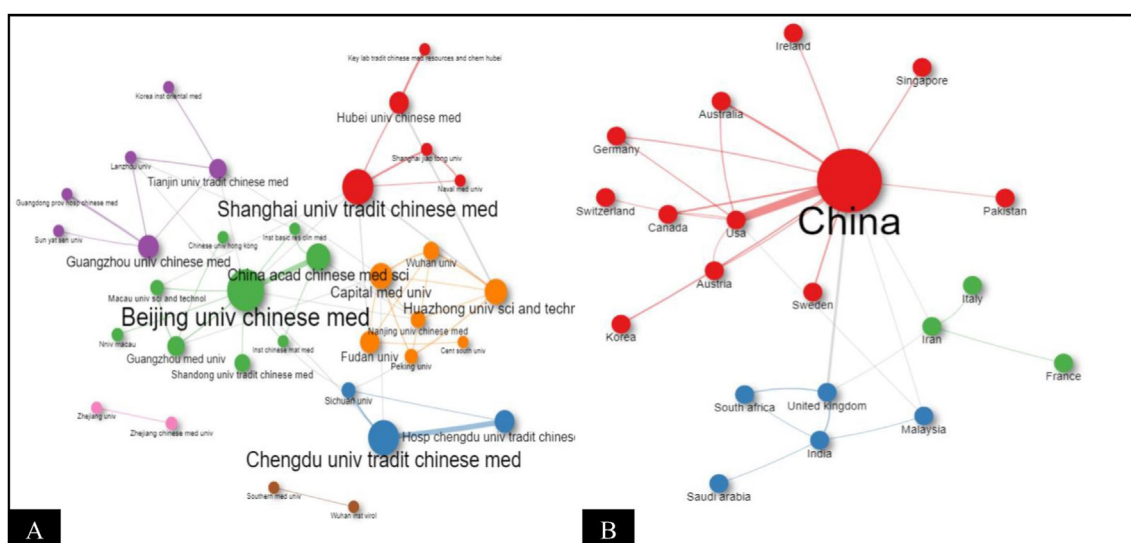

Figure 3. Networks of cooperation between institutions (A) and countries (B).

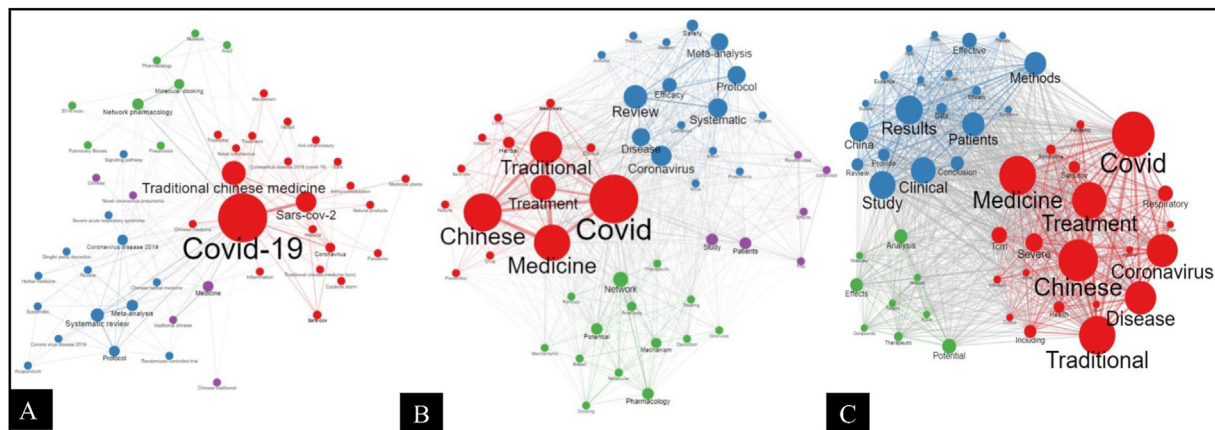**Figure 4.** Word cloud showing the frequency of key words.

Figure 5. Co-occurrence of key words in the 417 documents as a whole (A), the documents titles (B) and their Abstracts (C).

most frequently listed in the selected documents. The results showed that Lianhua Qingwen capsules, Qingfei Paidu decoction, Reduning injection, and Shufeng Jiedu capsules were used in clinical, bioinformatics, and basic research. Toujie Quwen granule, Jinhua Qinggan granule, Shuanghuanglian oral liquid, Tanreqing injection, and Xuanfei Baidu decoction were used in clinical and bioinformatics research, while basic research on

Table 1. Study designs and Chinese medicine treatment used in the included research.

Category	Number of publications	Chinese medicine treatment (Number of publications)
Network pharmacology	53 (12.71%)	Shufeng Jiedu capsules (4), Qingfei Paidu decoction (3), Lianhuaqingwen capsule (3), Xuebijing injection (3), Maxing Shigan decoction (2), Huashi Baidu formula (2), Zukamu granules (2), Fufang Banlangen (2), Traditional chinese medicine (2), Mahuang combine with Gancao (1), Angong Niuhuang wan (1), Saikosaponins (1), Mahuang combine with Kuxingren (1), Quercetin (1), Cold-Damp Plague Formula (1), Feiluoning Mixture (1), Qingfei dayuan granules (1), Toujie Quwen granules (1), Reduning injection (1), Pudilan (1), Licorice (1), Shenfu decoction (1), Rhizoma Polygonati (1), Jinhua Qinggan granules (1), Dayuanyin (1), Shen Zhu san (1), Hypericum japonicum Thunb. ex Murray (1), Qixuekang (1), Jingyin granule (1), HuaShi XuanFei formula (1), Maxingyigan decoction (1), Chlorogenic acid (1), Xingren (1), Huangqi combined with Baizhu (1), Poria (1), Hanshi Zufei fang (1), Yinma Jiedu granules (1), Fangji Qingfei decoction (1), Gancao (1).
Protocol of system review	42 (10.07%)	Traditional chinese medicine (13), Acupuncture (5), Lianhuaqingwen capsule (3), Qingfei Paidu decoction (2), External treatment of traditional chinese medicine (2), Xuebijing injection (1), Huashi Baidu formula (1), Shufeng Jiedu capsules (1), Reyanning Mixture (1), Fire needle (1), Chinese patent medicine injection (1), Baduanjin (1), Qigong (1), Xiaoqinglong decoction (1), Maxingshigan decoction (1), Toujie Quwen granule (1), Glycyrrhizic acid (1), Reduning injection (1), Xuanfei Baidu granules (1), Xiyanping (1), Moxibustion (1).
Clinical study	39 (9.35%)	Traditional chinese medicine formula (12), Shenhuang granule (2), Reduning injection (2), Atural Herbal medicine (1), Chinese herbal medicine granules (1), Traditional chinese medicine enema therapy (1), Shufeng Jiedu capsules (1), Auricular point pressure (1), Qingfei Paidu decoction (1), Tanreqing capsule (1), Fei Yan No. 1 (1), Traditional chinese and western medicine management (1), Artemisinin-piperaquine (1), Yindan Jiedu granules (1), Jinhua Qinggan granules (1), Shuanghuanglian oral liquid (1), Liuzijue (1), Xuanfei Baidu decoction (1), Taiwan Chingguan Yihau (1), He-Jie-Shen-Shi decoction (1), Lianhuaqingwen capsules (1), Bufei huoxue capsules (1), Huoxiang Zhengqi dropping pills (1), Maxingshigan-Weijing (1), Anluohuaxian (1), Xiyanping injection (1).
Experimental study	29 (6.95%)	Qingfei Paidu decoction (3), Lianhuaqingwen capsule (3), Maxing Shigan decoction (2), Rhamnocitrin (2), Shufeng Jiedu capsules (1), Respiratory detox shot (1), Traditional chinese medicines (1), Andrographolide (1), Three salvianolic acids (1), Tianma combined with Gouteng (1), Ephedra sinica (1), Liu Shen capsule (1), Reynoutria Rhizomes (1), Babaodan (1), Perilla (1), Indigo Naturalis (1), Vitamin K3 and its analogues (1), Danshensu (1), Huashi Baidu formula (1), Salvianolic acid C (1), D-Limonene (1), Glycyrrhizic acid (1), Isorhamnetin (1), Fufang yinhua jiedu granules (1).
System review	23 (5.52%)	Traditional chinese medicine (16), Lianhuaqingwen capsule (6), Acupuncture (1).
Molecular docking	9 (2.16%)	Liquorice (2), Theaflavin (1), Andrographis paniculata phytochemicals (1), Saikosaponins (1), Shuanghuanglian preparations (1), Respiratory Detox Shot (1), Convalescent chinese prescription (1), Jinhua Qinggan granules (1), Shufeng Jiedu capsules (1), Puerarin and quercetin and kaempferol (1).
Protocol of clinical study	5 (1.2%)	Acupressure therapy and Liu Zi Jue (1), auricular point pressure (1), Shenhuang granule (1), Liu Zi Jue (1), Baidu Jieduan granules (1).

their mechanisms of action is lacking. A summary description of the research settings in which the above TCM preparations were used is provided in Table 2.

4. Discussion

TCM has unique advantages and important roles in the prevention and treatment of COVID-19, as it was shown to effectively alleviate symptoms, improve immunity, and curb the progression of the epidemic [56, 57]. In this work, a bibliometrics approach was implemented to identify the most relevant research conducted on TCM for the prevention and treatment of COVID-19.

The first research report on TCM in the treatment of SARS-Cov-2 infection was published in January 2020. Of the 417 documents retrieved in the present study, 212 were published in 2020, and the remaining 205 were published in 2021. Since at the time of writing (September 2021) three months remain until the end of 2021, the number of studies on TCM treatment for COVID-19 published in 2021 will surely exceed those published in 2020. This in turn suggests that the intensity of research in this field is increasing. After the reporting of the beneficial effects of TCM on COVID-19 symptoms, TCM principles and therapies have attracted increasing interest from researchers in countries other than China. For example, researchers based in Singapore, India, USA, and Brazil have conducted research on the anti-SARS-Cov-2 effects of TCM. In addition, guidelines on the use of TCM for the prevention and treatment of COVID-19 were released in Malaysia [58].

The Journal Citation Reports (JCR) database classifies journals according to disciplines, and within each discipline it divides them into four quartiles based on the corresponding impact factors. Therefore, journals in Q1 and Q2 have relatively high numbers of citations. Our results show that most documents (74.82%) on TCM for prevention and treatment of COVID-19 were published in Q1 and Q2 journals. This proportion was significantly higher than that reported by Li et al [59]. Thus, our findings suggest that TCM research results are standardized and have reference

significance in guiding the prevention and treatment of COVID-19. Still, only 11 of the included documents were published in journals with impact factor >10, suggesting that further work is needed to improve research on TCM for the prevention and treatment of COVID-19.

Institutions that published research on TCM as treatment for SARS-Cov-2 infection were mainly Chinese Medicine and comprehensive universities in China. However, our analysis showed that the research carried out in these institutions was not performed in a completely independent manner. Instead, extensive cooperation between multiple researchers and research institutions was detected, involving collaboration among related professional fields and regions. For example, Beijing University of TCM and China Academy of TCM share a common research domain and are located in the same region. Shanghai Jiaotong University and Shanghai University of Chinese Medicine are both in Shanghai. Guangzhou University of TCM and Zhongshan University are both in Guangzhou. Shanghai University of Chinese Medicine and Hubei University of Chinese Medicine belong to the same field of universities. In addition, international collaborative efforts have increased, with China and the United States having the closest cooperation. This may be related to the large number of Chinese researchers and Chinese students working and studying in the United States [60].

Analysis of keyword frequency in the included documents indicated that research on the anti-SARS-Cov-2 effects of TCM involved mainly clinical research, systematic evaluation, network pharmacology, and molecular docking. Keyword co-occurrence analysis results showed that specific words are associated with each of these research types. For example, the terms COVID-19, Traditional Chinese Medicine, and SARS-Cov-2 may be associated with clinical studies. The terms severe acute respiratory syndrome, signaling pathway, Traditional Chinese Medicine, and coronavirus disease 2019 may be related to basic research. Network pharmacology is often associated with molecular docking, and pulmonary fibrosis may be associated with network pharmacology. Randomized controlled trials and meta-analyses were related to systematic evaluation. We sorted out the 417 documents according to the different

Table 2. Research status of core Chinese medicine.

Treatment	Chinese medicine included	Clinical research	Bioinformatics research	Basic research
Lianhua Qingwen capsules (LHQW)	Lianqiao、Jinyinhua、Mahuang、Kuxingren、Shigao、Banlangen、Mianmaguanzhong、Yuxingcao、Huoxiang、Dahuang、Hongjingtian、Bohenao、Gancao	LHQW significantly improved the cure rate. Significantly reduced median time to symptom recovery. Significantly shortened the duration of fever, fatigue, cough. Improve chest CT performance improvement rate [15].	Hepatitis B, Kaposi sarcoma-associated herpesvirus infection, Hepatitis C, Human cytomegalovirus infection, Human immunodeficiency virus 1 infection, Influenza A, Epstein-Barr virus infection, Human papillomavirus infection, Human T-cell leukaemia virus 1 infection, Viral carcinogenesis, Viral protein interaction with cytokine and cytokine receptor, Viral myocarditis [16].	Rhein, forsythoside A, forsythoside I, neochlorogenic acid and its isomers exhibited high inhibitory effect on ACE2 [17]. LHQW significantly deactivated NF-κB and reversed the SOCS3 expression in inflammatory macrophages [18]. LHQW significantly inhibits the Sars-cov-2 replication, affects virus morphology and exerts anti-inflammatory activity in vitro [13].
Qingfei Paidu decoction (QFPDD)	Mahuang, Gancao, Xingren, Shigao, Guizhi, Zexie, Zhuling, Baizhu, Fuling, Chaihu, Huangqin, Banxia, Shengjiang, Ziyuan, Donghua, Shegan, Xixin, Shanyao, Zhishi, Chenpi, Huoxiang	QFPDD significantly antipyretic and anti-inflammatory. Significantly reduced the degree of multiple organ damage [19, 20]. Significantly reduced risk of in-hospital death without liver and kidney damage [21]. The clinical symptoms and inflammatory indicators were significantly improved. Significantly promoted the absorption of lung lesions [22, 23]. Significantly improved the tongue [24]. Significantly shortened the time of nucleic acid negative and hospitalization time [25].	TNF signaling pathway, NOD-like receptor signaling pathway, Toll-like receptor signaling pathway, MAPK signaling pathway and cytokine receptor interaction [26]. Hypoxia inducible factor-1 pathway, Toll-like receptor pathway [27].	QFPDD may act through regulating USP14 to promote ATF2 degradation. QFPDD alleviates inflammatory reaction in the spleen [28]. QFPDD significantly inhibits coronavirus replication [29]. Significantly up-regulated the relative abundance of Romboutsia, Turicibacter, Clostridiumsensustricto1. Significantly reduced the relative abundance of norank_f_Lachnospiraceae [30].
ReDuNing injection	Qinghao, Jinyinhua, Zhizi	Reduning injection significantly increased the remission rate of symptoms. Significantly shortened the remission time of clinical symptoms, nucleic acid detection negative time, hospitalization time and fever time [31]. Significant inhibition of Sars-cov-2 proliferation and viral plaque formation. Significantly reduced the production of inflammatory cytokines in infected cells [32].	Oxidative stress response pathway, MAPK signaling pathway, chemokine pathway and other inflammatory storm-related pathways [33]. Jak-STAT signaling pathway, PI3K-Akt signaling pathway, TGF-β signaling pathway [34].	Reduning injection significantly reduced serum CRP, IL-5 levels in mice with respiratory tract infection [35]. Significantly reduced the lung index of mice. Significantly reduced lung tissue pathological damage. Significantly reduced viral load and IL-6, TNF-α levels [36].
Shufeng Jiedu capsules	Huzhang, Lianqiao, Banlangen, Chaihu, Baijiangcao, Mabiancao, Lugen, Gancao	Shufeng Jiedu capsule showed aboriginal antipyretic effect. Significantly improved pneumonia symptoms [37]. The levels of serum IL-6, IL-21, TNF-α and HMGB1 in patients were significantly decreased [38]. Significantly improved WBC, Neu%, LYM, Lym%, PA, ESR, LDH, CPR levels [39].	Human cytomegalovirus infection, Kaposi sarcoma-associated herpesvirus infection, interleukin-17 signaling pathway, tumor necrosis factor signaling pathway, helper T cell 17 cell differentiation and hypoxia inducible factor 1 signaling pathway [40].	Shufeng Jiedu capsule significantly reduced the pathological damage of lung tissue. Significantly increased lung function indicators PIF, MV, PEF, CD3+, CD4+ and CD4+/CD8+ levels. Significantly increased SOD, GSH-Px activity. Significantly reduced CD8 +, TNF-α, hs-CRP, MDA levels [41].
Toujie Quwen granules ("Fei Yan No. 1")	Chaihu, Huangqin, Banxia, Dangshen, Gualou, Binglang, Caoguo, Houpo, Zhimu, Shaoyao, Gancao, Chenpi, Huzhang	Fei Yan No. 1 significantly increased the proportion of SARS-CoV-2 nucleic acid negative patients [42]. Significantly improve the clinical efficacy. Significantly reduce TCM syndrome score and patients with CRP, PCT, D-dimer levels [43].	Neuroactive ligand-receptor interaction, apoptosis, renin-angiotensin system, calcium signaling pathway, arachidonic acid metabolism, vascular smooth muscle contraction, toxoplasmosis, Inflammatory mediator regulation of transient receptor potential channels, acute myeloid leukemia, central carbon metabolism in cancer, platelet activation, and nuclear factor kappa-B signaling pathway [44].	Not yet
Jinhua Qinggan granules	Jinyinhua, Zhebeimu, Huangqin, Niubangzi, Qinghao	Jinhua Qinggan granules significantly shortened the nucleic acid negative time [45]. Significant promotion of pneumonia inflammatory exudates absorption and no obvious adverse reactions occurred. The duration of cough, fatigue and other symptoms was shortened [46].	TNF signaling pathway, influenza A signaling pathway, HIF-1 signaling pathway, NOD-like receptor signaling pathway, Toll-like receptor signaling pathway, VEGF signaling pathway, MAPK signaling pathway, and T cell receptor signaling pathway [47].	Not yet

Table 2 (*continued*)

Treatment	Chinese medicine included	Clinical research	Bioinformatics research	Basic research
Shuanghuanglian oral liquids	Jinyinhua, Huangqin, Lianqiao	Shuanghuanglian oral liquid significantly increased the negative conversion rate of Sars-cov-2 in nucleic acid swab test. High-dose Shuanghuanglian oral liquid significantly promoted the absorption of inflammatory lesions of pneumonia [48].	Hepatitis B signaling pathway, tumor necrosis factor signaling pathway, pulmonary tuberculosis signaling pathway, pertussis signaling pathway, Salmonella infection signaling pathway, influenza A signaling pathway, and herpes simplex virus infection signaling pathway [49].	Not yet
Tanreqing capsule	Huangqin, Xiongdanfen, Shanyangjiao, Jinyinhua, Lianqiao	Tanreqing capsule significantly shortened the time of fecal nucleic acid turning negative and the time of pharyngeal- fecal nucleic acid turning negative [50].	Interleukin-17 signaling pathway, T cell receptor signaling pathway, arachidonic acid metabolism, cAMP signaling pathway, PI3K-Akt signaling pathway, influenza A [51].	Not yet
Xiyanping injection	Chuanxinlian	Xiyanping injection significantly reduced cough relief time, antipyretic time and virus clearance time. In the course of treatment, patients treated with Xiyanping injection had less disease progression to severe stage [52].	Kaposi sarcoma-associated herpesvirus infection, Human cytomegalovirus infection, AGE-RAGE signaling pathway in diabetic complications, Hepatitis B, Pancreatic cancer, Coronavirus disease-COVID-19, C-type lectin receptor signaling pathway, Influenza A, VEGF signaling pathway, TNF signaling pathway, Epstein Barr virus infection, Osteoclast differentiation, FoxO signaling pathway, Human T-cell leukemia virus 1 infection, Cellular senescence, PD-L 1 expression and PD-1 checkpoint pathway in cancer, Hepatitis C, IL-17 signaling pathway, Endocrine resistance, Chagas disease [53].	Not yet
Xuanfei Baidu decoction	Mahuang, Xingren, Shigao, Cangzhu, Yiyiren, Huoxiang, Huzhang, Tinglizi, Mabiancao, Lugen, Qinghao, Juhong, Gancao	Xuanfeibaidu decoction significantly improved the clinical symptoms of patients. Significantly increased the number of white blood cells and lymphocytes. Significantly reduced C-reactive protein and ESR [54].	Kaposi's sarcoma-associated herpesvirus infection, Chagas disease (American trypanosomiasis), tuberculosis, hepatitis B, TNF signaling pathway, IL-17 signaling pathway, pertussis, influenza A, toxoplasmosis, malaria, salmonella infection, leishmaniasis [55].	Not yet

types of literature. The results showed that there were 41 clinical studies, 29 experimental studies, 53 network pharmacology studies, nine molecular docking studies, and 23 systematic reviews. This evidence indicates that recent research on TCM and SARS-Cov-2 is multifaceted.

The book Epidemiology of Traditional Chinese Medicine points out that epidemic diseases feature strong infectivity, acute onset, can cause large-scale, significant harm, and their clinical manifestations are similar across gender and age groups [61]. Therefore, COVID-19 belongs to the category of 'epidemic disease' in TCM. In view of the high humidity in Wuhan, and the overweight tongue of patients with COVID-19, with tooth marks, thick, greasy, and even "rotten" fur (coating), most TCM experts believe that COVID-19 belongs to the category of "damp-ness-toxin epidemic" [62, 63, 64]. The 8th edition of China's Guidelines for the Prevention and Treatment of COVID-19 discusses the characteristics of viral infection and introduces three major stages of this disease: medical observation period, clinical treatment period, and recovery period [14]. The Guidelines propose Chinese medicine strategies based on the characteristics of diseases in different periods. The present results show that 7 of the 10 Chinese medicines most frequently used in the analyzed documents were recommended by the Chinese guidelines for the prevention and treatment of COVID-19 [14]. Our analysis showed that Lianhua Qingwen capsules, Qingfei Paidu decoction, Reduning injection, and Shufeng Jiedu capsules were used in clinical studies,

bioinformatics studies, and basic research. This suggests that these four formulations are the core TCM therapies against SARS-Cov-2 infection.

While extensive clinical evidence of the therapeutic effect of TCM against SARS-Cov-2 infection is available, there are few studies on the underlying molecular mechanisms. Most of these, such as those using network pharmacology and molecular docking analyses, are based on bioinformatics predictions of molecular mechanisms. In contrast, few cell or animal experiments have been conducted in this field and the research is not sufficiently detailed.

There is preliminarily evidence for the potential therapeutic mechanism of Qingfei Paidu decoction against SARS-Cov-2 infection. Liu et al. used UHPLC-Q-Orbitrap HRMS technology to show that Qingfei Paidu decoction contains 39 chemical constituents [65]. Using 16S rDNA sequencing analysis, Wu et al. found that administration of Qingfei Paidu decoction modified the composition of the intestinal flora in rats, significantly upregulating the relative abundance of *Romboutsia*, *Turici-bacter*, and *Clostridium sensu stricto* 1 species, and downregulating the abundance of norank_f_*Lachnospiraceae* [30]. In turn, Wang et al. found that Qingfei Paidu decoction blocked the entry process of the SARS-Cov-2 virus by inhibiting its adsorption, and played an antiviral role by upregulating the expression of interferons (IFNs) and interferon-stimulated genes (ISGs) [29]. Therefore, there is a clear need for more basic research to elucidate the molecular mechanisms underlying the

therapeutic effects of TCM formulations on the pathogenesis and symptomatology of SARS-Cov-2.

5. Conclusion

This study reviewed published documents on TCM in the prevention and treatment of COVID-19 and addressed reporting aspects such as publication year, journal, country, institution, title, abstract, and keywords. In addition, the relevant literature was analyzed to identify the core TCM drugs tested for the prevention and treatment of COVID-19, and these findings were in accord with the drugs recommended by TCM guidelines related to COVID-19 treatment. We also found that research intensity and recognition, as well as cooperation, in the field of Chinese medicine applied to the prevention and treatment of COVID-19 has increased over the duration of the pandemic. Research types evaluated are in general comprehensive, and widely used TCM drugs are mainly recommended by Chinese COVID-19 guidelines. However, to date, comprehensive, in-depth research addressing the molecular mechanisms of TCM preparations remains very scarce. More basic research is thus needed to identify therapeutic mechanisms and promote a better use of TCM in the prevention and treatment of COVID-19. Our study has the following limitations: 1) We only included literature available in the Web of Science database and did not examine other databases such as CNKI, WANFANG, WEIPU, PubMed, etc. Accordingly, we may have missed relevant published articles on the study subject; 2) We estimated the number of published studies reporting the use of TCM formulations, but did not conduct an in-depth analysis of the actual usage conditions; 3) The TCM diagnosis of COVID-19, the principle and timing of drug use, comparison of efficacy between different drugs, and comparison of evidence quality were not analyzed in depth. Therefore, the clinical guidance provided by this study is limited.

Declarations

Author contribution statement

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The authors declare no conflict of interest.

Additional information

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