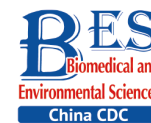


## Letter to the Editor



## Qingfei Paidu Decoction for COVID-19: A Bibliometric Analysis\*

LIU Si Hong<sup>1,&</sup>, MA Yan<sup>2,&</sup>, SHI Nan Nan<sup>2</sup>, TONG Lin<sup>1</sup>, ZHANG Lei<sup>1</sup>, CHEN Ren Bo<sup>2</sup>, FAN Yi Pin<sup>2</sup>,  
JI Xin Yu<sup>2</sup>, GE You Wen<sup>2</sup>, ZHANG Hua Min<sup>3,#</sup>, WANG Yan Ping<sup>2,#</sup>, and WANG Yong Yan<sup>2</sup>

Traditional Chinese medicine (TCM) has been used for thousands of years in fighting epidemics and has achieved remarkable therapeutic effects<sup>[1]</sup>. The coronavirus disease 2019 (COVID-19) pandemic has been effectively controlled in China under a series of policies. In the absence of specific medicine for COVID-19, TCM has played an important role in treating COVID-19, of which, *Qingfei Paidu Decoction* (QFPDD) has attracted more attention based on favorable treatment effects. Notably, the National Administration of Traditional Chinese Medicine (NATCM) released the data of 214 confirmed COVID-19 cases who had been treated with QFPDD from four provinces between January 27<sup>th</sup> and February 5<sup>th</sup>, 2020, with a total effective rate of over 90%. QFPDD has been recommended as a general prescription for the treatment of COVID-19 in the *Diagnosis and Treatment Protocol of novel coronavirus pneumonia COVID-19 (Trial Version 6-8)*. With a deeper understanding of QFPDD, more studies on the theoretical basis, molecular mechanism, and clinical effects of QFPDD for COVID-19 have been published in related journals. Previous studies have found that early treatment with QFPDD can prevent mild and moderate cases of COVID-19 from progressing to severe and critically severe cases and shows favorable outcomes<sup>[2-5]</sup>. Given that the pandemic is still ongoing worldwide, a comprehensive analysis of articles in relation to QFPDD through bibliometric methods can provide references for clinicians using QFPDD to treat COVID-19.

Bibliometrics is the quantitative analysis of any knowledge carriers intended to evaluate the research status of a certain field and predict future development by using mathematical and statistical

methods. This interdisciplinary subject integrates mathematics, statistics, and philology and focuses on quantification. To date, no bibliometric analysis of QFPDD for COVID-19 has been conducted. This study conducted a bibliometric analysis and visual analysis to demonstrate the status of research on QFPDD for COVID-19 and identify hotspots to provide references for the global management of COVID-19.

We searched English databases and search engines, including PubMed, Web of Science, Science Direct, Springer, and Google Scholar, as well as Chinese databases such as CNKI, Wanfang, and VIP databases. We also searched the official websites of the following organizations: the World Health Organization ([www.who.int/](http://www.who.int/)), Centers for Disease Control and Prevention ([www.cdc.gov/](http://www.cdc.gov/)), National Institute for Health and Clinical Excellence ([www.nice.org.uk/](http://www.nice.org.uk/)), NATCM ([www.satcm.gov.cn/](http://www.satcm.gov.cn/)), National Health Commission of the People's Republic of China ([www.nhc.gov.cn/](http://www.nhc.gov.cn/)), the State Council of the People's Republic of China (<http://www.gov.cn/>), and the Chinese Center for Disease Control and Prevention (<http://www.chinacdc.cn/>). The search terms included ("Qingfei Paidu Decoction" OR "QPD" OR "QFPDD" OR "Lung Cleansing & detoxifying Decoction" OR "Lung Cleansing and detoxifying decoction") AND ("Coronavirus" OR "pneumonia" OR "severe acute respiratory syndrome coronavirus 2" OR "SARS-CoV-2" OR "2019-nCoV" OR "SARS-CoV" OR "COVID-19"). The literature search was conducted from the time of virus emergence until March 28, 2021. Bibliometric method was used to analyze the data. Gephi software<sup>[6]</sup> was used to perform bibliographic-coupling analysis (for authors and institutions), co-occurrence analysis, and other visual transformations, intended to analyze the

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1. Institute of Information on Traditional Chinese Medicine, China Academy of Chinese Medical Sciences, Beijing 100700, China; 2. Institute of Basic Research in Clinical Medicine, China Academy of Chinese Medical Sciences, Beijing 100700, China; 3. Institute of Chinese Materia Medica, China Academy of Chinese Medical Sciences, Beijing 100700, China

status and predict trends for theoretical, laboratory, and clinical research on QFPDD for COVID-19.

A total of 453 articles were retrieved. Duplicates, articles not related to the topic, newspaper documents, and popular science articles were excluded. Finally, 155 articles were included (Supplementary Figure S1, available in [www.besjournal.com](http://www.besjournal.com)). Of 155 articles, 129 (83.2%) were Chinese, and 26 (16.8%) were in English. There were 93 (60.0%) theoretical, 23 (14.8%) fundamental (laboratory), and 39 (25.2%) clinical studies. The content of the included articles was mainly related to theory, mechanism, network pharmacology, and clinical effects (Supplementary Figure S2, available in [www.besjournal.com](http://www.besjournal.com)). A total of 155 articles were written by 809 authors from 267 institutions in 28 provinces, municipalities, and autonomous regions in Mainland China and China Macao Special Administrative Region, and seven countries including the United Kingdom, the United States, Canada, Saudi Arabia, South Korea, Sweden, and Australia.

The first article on QFPDD was published in the *Journal of Traditional Chinese Medicine Management* on February 14, 2020. The number of QFPDD articles published peaked in March 2020, mainly in theoretical discussion; in the following months, studies continued to be published and the trend tended to flatten out (Supplementary Figure S3A, available in [www.besjournal.com](http://www.besjournal.com)).

A total of 155 articles were published in 93 journals, of which 10 journals published more than three articles, accounting for 33.5% among 155 papers (Supplementary Figure S3B). In terms of journal language, 23 English journals published 26 articles (16.8%) and 70 Chinese journals published 129 articles (83.2%). The top three Chinese journals with the largest publication volume on QFPDD were *Journal of Traditional Chinese Medicine* (10 articles), *Acta Chinese Medicine* (6 articles), *China's Naturopathy* (6 articles), and *Pharmacology and Clinics of Chinese Materia Medica* (6 articles), while the top three English journals were *Pharmacological Research* (3 articles), *Medicine* (2 articles), and *Biomedicine and Pharmacotherapy* (2 articles).

Citation frequency can, to a certain degree, reflect research hotspots in certain fields and the quality of the articles. Moreover, it can also reflect the authors' research and academic capabilities. The five most frequently cited Chinese articles were published before May 2020, with a wide range of research fields involving theoretical research on QFPDD, as well as network pharmacology and clinical effectiveness (Table 1). The top five most frequently

cited English articles were published before September 2020, which had similar research fields to the five highest-cited Chinese papers (Table 2). This shows that theoretical, laboratory, and clinical research were all research hotspots for QFPDD during the COVID-19 pandemic.

Co-occurrence analysis between authors and institutions indicated that there were 809 authors of the included 155 articles from 267 institutions. To better reflect the cooperation between authors and institutions, the number of published articles, highly productive authors, and institutions was analyzed to conduct co-occurrence analysis between authors and institutions. Figure 1 demonstrates the co-occurrence analysis results between authors who have published more than two articles and their institutions. To further analyze the cooperation between highly productive authors who have published more than three articles, co-occurrence networks of authors and institutions were combined and showed that there were two major author teams conducting QFPDD studies: Wang and colleagues from the Institute of Basic Research in Clinical Medicine of China Academy of Chinese Medical Sciences, and an author group of 66 institutions from 10 provinces that conducted clinical effectiveness research on QFPDD.

Key words reveal the central idea and content of the article, and so the analysis of keywords can reflect hotspots and core research themes in certain fields. This study used Gephi software to analyze the keywords and draw a knowledge graph (Figure 2). The font size in the knowledge graph represents the frequency of the keywords; the larger the font size, the higher the keyword frequency. The node color represents the clustering results of the keywords; keywords of the same color are distributed together and can be considered to form a core theme. Lines connecting keywords indicate their co-occurrence relationship, and the thickness of the line is determined by the co-occurrence frequency; the thicker the line between the nodes and the darker the color, the closer the relationship between the nodes. Therefore, upon observing the node size corresponding to each keyword, the larger nodes are mainly related to formula decomposition, network pharmacology, and clinical effectiveness of QFPDD.

The study demonstrated that the major authors and institutions conducting QFPDD research were from China. The research from Chinese authors was in an absolute leading position for all included articles. Of the five journals with the largest publication number of QFPDD articles, the top four

Table 1. Top 5 Chinese papers cited from February 2020 to March 2021

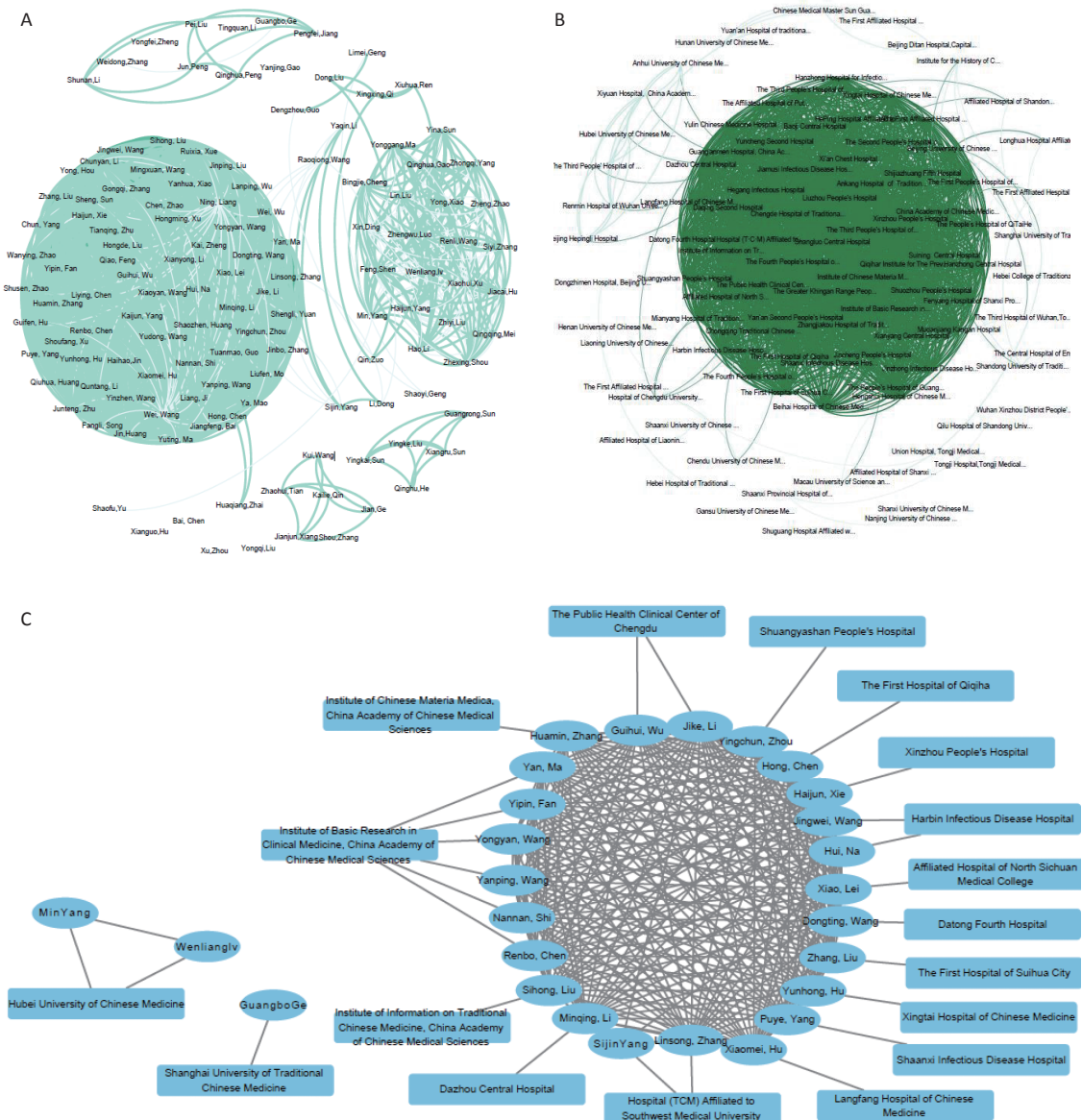
Title	First author	Corresponding author	Date of publication	Journal	Cited frequency
Analysis on traditional Chinese medicine theory of Qingfei Paidu Decoction in fast and effective treatment of coronavirus disease 2019 (COVID-19)	Boshou Xue	Yanxing Xue	20-Feb	<i>Journal of Traditional Chinese Medicine</i>	106
Investigating mechanism of Qing-Fei-Pai-Du-Tang for treatment of COVID-19 by network pharmacology	Jing Zhao	Weidong Zhang	20-Feb	<i>Chinese Traditional and Herbal Drugs</i>	74
Clinical observation of Qingfeipaidu Decoction in the treatment of COVID-19	Raoqiong Wang	Sijin Yang	20-Mar	<i>Pharmacology and Clinics of Chinese Materia Medica</i>	48
Preliminary exploration of the mechanism of Qingfei Paidu decoction against novel coronavirus pneumonia based on network pharmacology and molecular docking technology	Hao Wu	Chen-ning Zhang	20-Feb	<i>Acta Pharmaceutica Sinica</i>	45
The significance and role of Qingfei Paidu Decoction recommended by the National Health Commission and the National Administration of Traditional Chinese Medicine	Qinghu He	Guangrong SUN	20-May	<i>Journal of Traditional Chinese Medicine</i>	27

Table 2. Top 5 English papers cited from February 2020 to March 2021

Title	First author	Corresponding author	Date of publication	Journal	Cited frequency
Treatment efficacy analysis of traditional Chinese medicine for novel coronavirus pneumonia (COVID-19): an empirical study from Wuhan, Hubei Province, China	Erdan Luo	Yonghua Zhao	20-Mar	<i>Chinese Medicine</i>	43
Chemical composition and pharmacological mechanism of Qingfei Paidu Decoction and Ma Xing Shi Gan Decoction against coronavirus disease 2019 (COVID-19): in silico and experimental study	Ruocong Yang	Tiegang Liu	20-Jul	<i>Pharmacological Research</i>	32
Review on the potential action mechanisms of Chinese medicines in treating coronavirus disease 2019 (COVID-19)	Yu-Feng Huang	Hua Zhou	20-Aug	<i>Pharmacological Research</i>	26
Protection against COVID-19 injury by qingfei paidu decoction via anti-viral, anti-inflammatory activity and metabolic programming	Jian Chen	Zhi-Qiang Liang	20-Sep	<i>Biomedicine &amp; Pharmacotherapy</i>	18
The important role of polysaccharides from a traditional Chinese medicine-lung cleansing and detoxifying decoction against the COVID-19 pandemic	Peng Cao	Peng Cao	20-Jul	<i>Carbohydrate Polymers</i>	14

were Chinese journals, and the only English journal with three papers ranked fifth. Four out of the top five most highly cited articles on QFPDD were in Chinese, while one was in English. The results may be related to the fact that QFPDD is a TCM decoction, and Chinese journals may pay more attention to TCM than non-Chinese journals. The publication bias due to language as well as the unapproved marketing of QFPDD by the National

Medical Products Administration during this study period may also help to explain the results mentioned above. Despite this, QFPDD has received wide attention from other countries. The results of this study showed that 14 research groups from seven countries, including Canada and South Korea, carried out or participated in QFPDD research. Notably, a study conducted by the Korean Medical Association on the use of Korean and Chinese



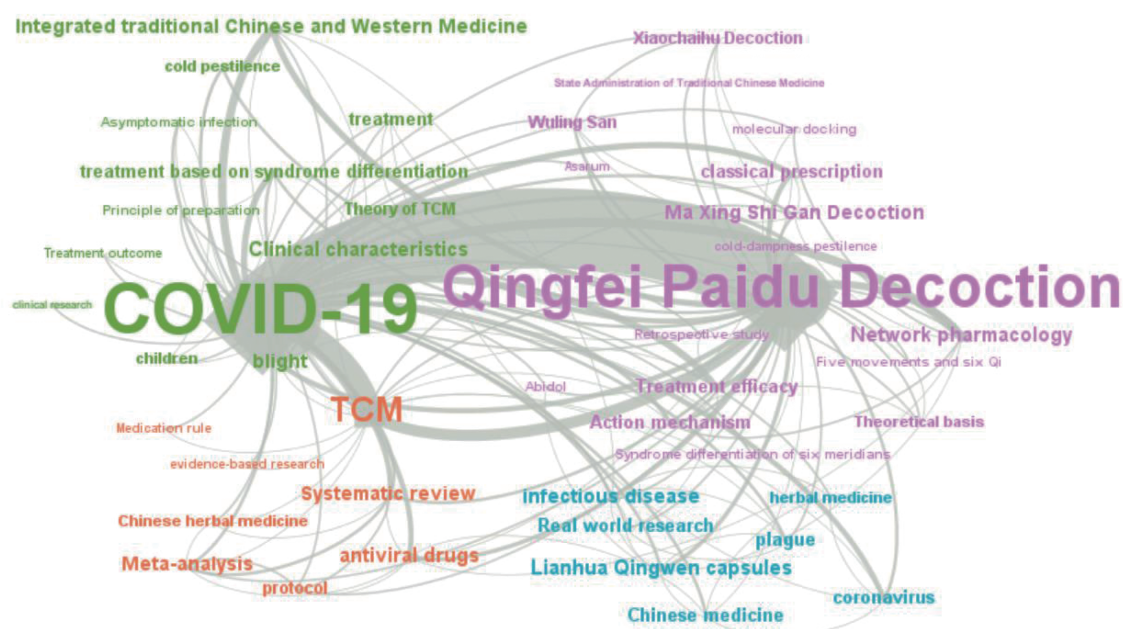
**Figure 1.** Bibliometric analysis of the co-authorship and study organizations. (A) The co-authorship map of authors indicating authors that cooperate in the field of COVID-19 transmission. (B) The co-authorship map of organizations indicating the organizations that cooperate in the field of COVID-19 transmission. (C) The main co-authorship map of organizations. China Academy of Chinese Medical Science has published 31 related papers and cooperates with other 86 institutions.



resolving toxins, and dispelling pathogens. COVID-19 is characterized by cold, dry, and damp conditions, and QFPDD can effectively treat these corresponding symptoms<sup>[7]</sup>. Basic research on QFPDD mainly focused on chemical component characteristics, pharmacokinetics, and pharmacodynamics intended to explain the complex mechanism in the treatment of COVID-19 and explore the anti-inflammatory, antiviral, and immune functions, indicating the multi-component, multi-target, and multi-pathway characteristics of TCM<sup>[8-10]</sup>. Clinical studies have discussed the effectiveness and safety of QFPDD and found that early application can significantly improve clinical symptoms, promote absorption of lung lesions, decrease the incidence of severe cases, and reduce mortality<sup>[2-5,11]</sup>.

According to our bibliometric analysis, exploration of clinical effectiveness will be a hotspot of QFPDD research; however, the present clinical research on QFPDD lacks sufficient breadth and depth. As the sample size of current clinical studies was relatively small, larger multicenter clinical studies with longer follow-up periods are needed to explore the long-term effectiveness of QFPDD. In addition to more comprehensive pharmacodynamic studies *in vivo* and *in vitro*, clinical studies with long-

The theoretical articles on QFPDD mainly focused on the composition, combination of medicinals, and effectiveness of 21 herbs. QFPDD can soothe and release exterior and interior symptoms, as well as unblock and regulate *sanjiao*, with the function of dispelling cold-damp and heat-turbid symptoms, moistening the lung and fortifying the spleen.



**Figure 2.** Bibliometric analysis of themes (keywords). Most recent studies focused on classical prescription (Maxing Shigan decoction, Wuling Powder, Xiaochaihu decoction, and Shegan mahuang decoction to study the formulation theory and drug composition), network pharmacology, and treatment efficacy. The font size of keywords represents their frequency in the literature. Distances between items indicate correlation.

term follow-up should also be conducted to evaluate the effectiveness of QFPDD and provide higher-level evidence for the treatment of COVID-19.

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<sup>&</sup>These authors contributed equally to this work.

<sup>#</sup>Correspondence should be addressed to Prof. ZHANG Hua Min, PhD, 86-10-64032658, E-mail: zhanghm@mail.cintcm.ac.cn; Prof. WANG Yan Ping, PhD, 86-10-64087789, E-mail: wangyanping4816@163.com

Biographical notes of the first authors: LIU Si Hong, female, born in 1989, assistant research, majoring in date mining of TCM's ancient books; MA Yan, female, born in 1980, MD, majoring in epidemiology, prevention and control of infectious disease.

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