

# Traditional Chinese Medicine Pattern Classification and Herbal Medicine for COVID-19: A Comparative Study of Data from Different Sources

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## Abstract

**Background:** Traditional Chinese medicine (TCM) plays a crucial role in the prevention and control of coronavirus disease 2019 (COVID-19). **Objective:** The study aimed to reveal the distribution characteristics of COVID-19 TCM syndrome types and syndrome elements and the law of TCM treatment and medication. **Methods:** The TCM diagnosis and treatment protocol for COVID-19 and clinical research data were obtained through network retrieval, and Revman 5.3 and SPSS 23.0 were employed to analyze the composition of TCM syndromes and the situation of TCMs in meta and frequency. **Results:** The top three TCM syndromes of COVID-19 included damp-heat accumulation in the lung pattern, damp abundance due to spleen deficiency, and epidemic toxin invading the lung pattern, while the syndrome elements were dampness, heat, and toxin. *Gypsum fibrosum*, *Pogostemonis herba*, and *Armeniacae semen* were identified as the commonly used drugs. Different syndrome elements were identified at lung disease location: *Forsythiae fructus*, *Glycyrrhizae radix*, and *Armeniacae semen* can be used for “wind;” *Glycyrrhizae radix*, *Armeniacae semen*, and *Scutellariae radix* can be used for “Heat;” *Armeniacae semen*, *Sheng Gypsum fibrosum*, and *Ephedrae herba* can be used for “Toxin;” *Ephedrae herba*, *Armeniacae semen*, and *Atractylodis rhizome* can be used for “Damp;” *Magnoliae officinalis Cortex*, *Ephedrae herba*, and *Zingiberis Rhizoma recens* can be used for “cold;” and *Armeniacae semen*, *Gypsum fibrosum*, *Ephedrae herba*, and *Lepidii/Descurainiae semen* can be used for “epidemic.” **Conclusion:** The establishment of a treatment scheme based on the classification of disease syndrome elements should be considered for sudden infectious diseases, such as COVID-19. *Pogostemonis herba*, *Armeniacae semen*, *Gypsum fibrosum*, and *Glycyrrhizae radix* should be considered as effective drugs from TCM for the treatment of COVID-19.

**Keywords:** COVID-19, diagnosis and treatment protocol for COVID-19, syndrome, syndrome element, traditional Chinese medicine, traditional Chinese medicine syndrome investigation

## INTRODUCTION

Traditional Chinese medicine (TCM) is a general designation for the medicines derived from all ethnic groups in China, including Han medicine and other ethnomedicine in China. TCM is a medical and pharmaceutical system that reflects the country's understanding of life, health, and diseases. Accordingly, TCM is rich in history and has unique theories and technical methods. Critical cases of coronavirus disease 2019 (COVID-19) often lead to fatality.<sup>[1]</sup> Early detection of COVID-19 is thus necessary, and active comprehensive intervention should be administered to patients with mild, common, and severe COVID-19 to prevent advancement to critical stage. TCM has had important contributions to the prevention and treatment of COVID-19.

After numerous clinical studies, several effective prescriptions represented by “Three Drugs and Three Prescriptions” have been screened out.<sup>[2]</sup> From January 15, 2020, to March 4, 2020, the National Health Commission of the People's Republic of China (NHC) issued a total of seven editions of “diagnosis and

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treatment protocol for COVID-19" (DTP). The name of the disease was changed from "pneumonia caused by the novel coronavirus" to "COVID-19." Clinical manifestations and case definitions of COVID-19 were continuously refined, and the diagnosis process has been optimized and simplified. According to the DTP issued by the NHC, all regions have formulated a TCM diagnosis and treatment protocol for COVID-19, with focus on treatment in specific regions based on the local COVID-19 disease condition, climate characteristics, and varied physical conditions of patients.

Disease research primarily aims to determine the diagnosis and then the treatment methods and efficacy evaluation criteria, and finally provide accurate feedback. Therefore, we carried out a comparative study of COVID-19 symptom description of traditional Chinese and modern medicine.<sup>[3]</sup> The characteristics of TCM syndromes and syndrome elements were analyzed based on a COVID-19 clinical survey. The medication characteristics based on a single-case study were discussed, and a comprehensive comparative analysis of DTP across the country was performed to summarize the TCM syndrome characteristics of the disease, reveal the TCM medication characteristics of COVID-19 based on syndrome element classification, and provide a reference for the treatment of "a group treated with one prescription" for the disease. On May 25, 2020, local time, the World Health Organization revealed that epidemiological studies demonstrated the susceptibility of many people to the disease. Accordingly, if the virus existed, it could infect humans, regardless of the temperature and month. Further, if people were in close contact with each other, the epidemic would proceed. Currently, the pandemic is still rampant. Further, there are no specific drugs available to treat COVID-19. Hence, countries must not only aim to prevent another peak of the current epidemic but also prevent the next wave. The effect of TCM in preventing and treating COVID-19 must thus be explored to provide a reference for the control of the world pandemic.

## DATA AND METHODS

### Inclusion of literature

TCM-DTP protocols from various regions of the country were collected from the websites of regional health committees or TCM societies, including PubMed, ClinicalKey, Cochrane, "COVID-19 Scientific Research Achievements Academic Exchange Platform (<http://medjournals.cn/2019NCP/index.do>)," the China National Knowledge Infrastructure, "COVID-19 Special Research Achievements Network First Platform (OA) ([cajn.cnki.net/gzbd/brief/Default.aspx](http://cajn.cnki.net/gzbd/brief/Default.aspx))," in English or Chinese, and "(COVID-19) and (Chinese medicine)" were used as part of the search strategy. Data up to May 1, 2020, were included in the analysis. Two researchers independently screened the literature and recorded the information related to diagnosis and treatment.

### Data collection and processing

Based on the extraction table, TCM syndrome classification, therapeutic principles and methods, prescriptions, and other

contents were included and standardized. The syndrome elements were extracted according to the *Differentiation of Syndrome Elements*.<sup>[4]</sup> Disease nature syndrome elements and disease location syndrome elements were also extracted. The "three prescriptions" of the "three prescriptions and three drugs" were Qingfei Paidu decoction (QPD), Xuanfei Baidu Formula (XBF), and Huashi Baidu Formula (HBF). The clinical summary analysis selected clinical research based on a single-case analysis (herein referred to as a single-case study) [Figure 1]. For meta-analysis, all included trials met the following selection criteria: a prospective, cross-sectional, and retrospective study on the composition of TCM syndrome types. The exclusion criteria were as follows: case report, academic discussion, ideas, methods, reviews, duplicate publications, and lack of data on the composition ratio of the syndrome in TCM. For the meta-analysis, the checklist of the Agency for Healthcare Research and Quality<sup>[5]</sup> was used to assess the quality and bias risk of the included studies.

### Statistical methods

The TCM syndromes and syndrome elements data were analyzed through a meta-analysis of uncontrolled binary data based on RevMan5.3.<sup>[5,6]</sup> The DTP published by local health committees and TCM administration were searched, and the frequency or composition was analyzed and compared with the "three prescriptions" and single-case studies of the "three prescriptions and three drugs" using SPSS 23.0 (IBM Corp., Armonk, NY, USA) to prove the clinical value of the research results.

## RESULTS

According to the accessibility of network information resources, 33 DTP issued by 29 provincial health committees or Chinese Medicine Associations in China, including those of Beijing, Tianjin, Hebei, Shanxi, Mongolia, Heilongjiang, Jilin, Liaoning, Shanghai, Jiangsu, Zhejiang, Anhui, Fujian, Jiangxi, Shandong, Henan, Hunan, Guangdong, Guangxi, Qiong, Sichuan, Guizhou, Yunnan, Tibet, Shaanxi, Gansu, Qing, and Ningxia, were included in this study. Further, 23 TCM syndrome investigation studies and 25 TCM single cases reports were included.

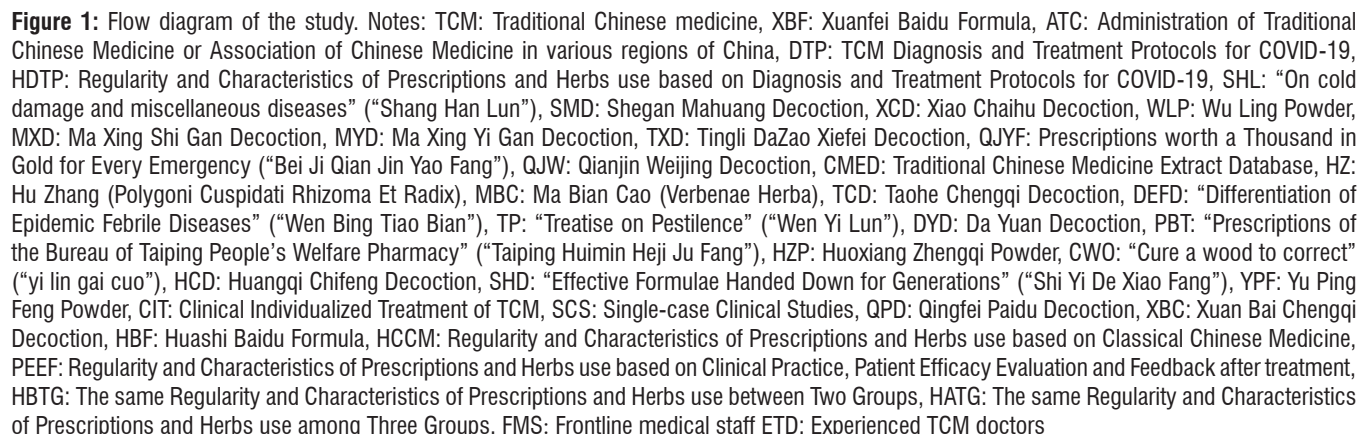
### Traditional Chinese medicine syndromes and meta-analysis based on a clinical survey of COVID-19 in different areas

#### Methodological quality assessment

The selected articles were assessed to determine methodological quality. The quality score of each study is presented in Table 1. One study had high quality and 22 studies had moderate quality. There were no articles with a low-quality rating [Table 1].

### Traditional Chinese medicine syndromes and meta-analysis

Based on an epidemiological survey, more TCM syndromes of COVID-19 exist in different regions of China than those listed in DTP. Such finding reflects the difference between diagnosis and treatment protocol and clinical practice to a certain extent. A total of 24 studies were included, and the



According to the recommended frequency, the top six rankings were Mai Dong (93.75%), Gan Cao (*Glycyrrhizae radix*) (81.25%), Nan Sha

**Table 1: Quality control of the selected studies according to the criteria of the Agency for Healthcare Research and Quality**

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total score*
Zhou et al., 2020 <sup>[7]</sup>	Y	Y	Y	Y	Y	U	U	U	U	U	U	5
Meng et al., 2020 <sup>[8]</sup>	Y	Y	Y	Y	Y	U	Y	Y	U	U	U	7
Song et al., 2020 <sup>[9]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Xu et al., 2020 <sup>[10]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Li et al., 2020 <sup>[11]</sup>	Y	Y	Y	U	U	U	Y	Y	U	U	U	5
Li et al., 2020 <sup>[12]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Lin et al., 2020 <sup>[13]</sup>	Y	Y	Y	Y	Y	U	N	Y	N	Y	U	7
Pan and Hu 2020 <sup>[14]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Zheng et al., 2020 <sup>[15]</sup>	Y	Y	Y	Y	Y	U	Y	Y	U	U	U	7
Lu et al., 2020 <sup>[16]</sup>	Y	Y	U	U	Y	U	U	Y	U	U	U	4
Gao et al., 2020 <sup>[17]</sup>	Y	Y	Y	Y	Y	U	U	U	U	U	U	5
Huang et al., 2020 <sup>[18]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Xue et al., 2020 <sup>[19]</sup>	Y	Y	U	U	Y	U	U	Y	U	U	U	4
Gong et al., 2020 <sup>[20]</sup>	Y	Y	Y	Y	Y	Y	U	Y	U	Y	U	8
Yang et al., 2020 <sup>[21]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Yang et al., 2020 <sup>[22]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Yuan et al., 2020 <sup>[23]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Zhang et al., 2020 <sup>[24]</sup>	Y	Y	Y	Y	Y	Y	U	Y	U	U	U	7
Mao et al., 2020 <sup>[25]</sup>	Y	Y	N	U	Y	U	U	Y	U	U	U	4
Dong et al., 2020 <sup>[26]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Li et al., 2020 <sup>[27]</sup>	Y	Y	Y	Y	Y	U	U	U	U	U	U	5
Tian et al., 2020 <sup>[28]</sup>	Y	Y	Y	Y	Y	U	U	Y	U	U	U	6
Ran et al., 2020 <sup>[29]</sup>	Y	Y	Y	Y	Y	U	U	U	U	U	U	5

\*An item was scored '0' if the response was "NO" or "UNCLEAR;" if the response was "YES," then the item was scored "1." Article quality was assessed as follows: low quality=0-3, moderate quality=4-7, and high quality=8-11. Q1: Define the source of information (survey, record review); Q2: List inclusion and exclusion criteria for exposed and unexposed individuals (cases and controls) or refer to previous publications; Q3: Indicate the time period used for identifying patients; Q4: Indicate whether or not individuals were consecutive if not population-based; Q5: Indicate whether evaluators of subjective components of the study were masked to other aspects of the status of the participants; Q6: Describe any assessments undertaken for quality assurance purposes (e.g., test/retest of primary outcome measurements); Q7: Explain any patient exclusions from the analysis; Q8: Describe how confounding was assessed and/or controlled; Q9: If applicable, explain how missing data were handled in the analysis; Q10: Summarize patient response rates and completeness of data collection; Q11: Clarify the follow-up, if any, expected and the percentage of patients for which incomplete data or follow-up was obtained. Y: Yes, N: No, U: Unclear

**Table 2: Traditional Chinese medicine syndromes and the meta-analysis (patients ≥10 in one study)**

TCM syndrome	Studies	Patients (n)	Incidence (%)	95% CI	P	P <sup>2</sup> (%)
Damp-heat accumulation in the lung pattern	12	1973	45	0.32-0.58	0.000	98
Damp abundance due to spleen deficiency	1	98	48	0.38-0.58	0.000	NA
Epidemic toxin invading the lung pattern	4	178	47	0.10-0.85	0.010	97
Damp-toxin constraint in the lung pattern	9	1146	31	0.21-0.42	0.000	96
Heat-toxin constraint in the lung pattern	3	286	31	0.26-0.36	0.000	0
Deficiency of both qi and yin pattern	6	1587	28	0.10-0.45	0.002	99
Cold-damp constraint in the lung pattern	9	1741	28	0.17-0.39	0.000	97
Heat-damp invading the lung pattern	2	198	25	-0.18-0.69	0.250	99
Damp-toxin blocking the lung pattern	1	46	22	0.10-0.34	0.000	NA
Lung-spleen qi deficiency pattern	9	1958	14	0.07-0.21	0.000	96
Damp blocking lung and stomach pattern	2	565	12	0.06-0.17	0.000	49
Fluid consumption due to lung heat pattern	1	209	11	0.06-0.15	0.000	NA
Heat-toxin blocking the lung pattern	4	289	8	0.03-0.13	0.001	56
Epidemic toxin blocking the lung pattern	7	1605	8	0.03-0.13	0.001	90
Wind-heat invading lung pattern	2	565	7	0.03-0.11	0.002	27
Pathogen invading lung-defense phase pattern	1	209	5	0.02-0.08	0.000	NA
Internal blockage and external desertion pattern	2	551	2	0.01-0.04	0.000	0

TCM: Traditional Chinese medicine, CI: Confidence interval, NA: Not available

Shen (*Adenophorae Radix*) (68.75%), Wu Wei Zi (56.25%),  
Tai Zi shen (*Pseudostellariae Radix*) (43.75%), Bai

Zhu (*Atractylodis macrocephalae Rhizoma*) (43.75%), and  
Chen Pi (43.75%).



**Table 3: Traditional Chinese medicine syndrome elements and the meta-analysis**

Syndrome elements	Studies included	Frequency	incidence (%)	95% CI	P	I <sup>2</sup> (%)
Dampness	21	3338	38	0.32-0.45	0.000	93
Heat	15	3020	34	0.27-0.41	0.000	95
Toxin	19	3168	22	0.16-0.28	0.000	96
Cold	8	1778	17	0.11-0.24	0.000	93
Plague	11	2596	9	0.05-0.13	0.000	95
Sputum	1	112	7	0.02-0.12	0.003	NA
Wind	2	914	4	0.03-0.05	0.000	0
Blood stasis	1	100	2	-0.01-0.05	0.15	NA
Warm	1	102	2	-0.01-0.05	0.15	NA

TCM: Traditional Chinese medicine, CI: Confidence interval, NA: Not available

### Cold-damp constraint in the lung

According to the recommended frequency, the top five rankings were Ma Huang (100%), Sheng Jiang (*Zingiberis Rhizoma recens*) (100%), Cang Zhu (*Atractylodis Rhizoma*) (90%), Huo Xiang (*Pogostemonis Herba*) (90%), and Chen Pi (90%).

### Damp constraint in the lung pattern

According to the recommended frequency, the top five rankings were Xing Ren (100%), Ma Huang (80%), Yi Yi Ren (*Coicis Semen*) (80%), Huang Qin (*Scutellariae Radix*) (80%), and Gan Cao (80%).

### Wind-heat invading lung pattern

According to the recommended frequency, the top seven rankings were Jin Yin Hua (*Lonicerae Japonicae Flos*) (100%), Lian Qiao (*Forsythiae Fructus*) (100%), Niu Bang Zi (*Arch Fructus*) (100%), Gan Cao (100%), Jie Geng (*Platycodonis Radix*) (66.67%), and Xing Ren (66.67%).

### Damp-heat accumulation in the lung

According to the recommended frequency, the top five rankings were Gan Cao (88.89%), Huang Qin (77.78%), Xing Ren (66.67%), Cao Guo (*Tsaoko Fructus*) (55.56%), Hou Po (*Magnoliae officinalis Cortex*) (55.56%), Cang Zhu (55.56%), and Lian Qiao (55.56%).

### Damp-toxin constraint in the lung

According to the recommended frequency, the top five rankings were Xing Ren (100%), Ma Huang (80%), Huang Qin (80%), Huo Xiang (6%), Fu Ling (60%), and Gan Cao (100%).

### Heat-toxin accumulation in the lung pattern

According to the recommended frequency, the top five rankings were Ma Huang (100%), Xing Ren (100%), Sheng Shi Gao (100%), Gan Cao (80%), Huang Qin (60%), and Da Huang (60%).

### Blazing of both qi and ying pattern

According to the recommended frequency, the top rankings were Sheng Shi Gao (100%), Zhi Mu (*Anemarrhenae Rhizoma*) (100%), Di Huang (*Rehmanniae Radix*) (100%), Shui Niu Jiao (*Bubali Cornu*) (100%), Chi Shao (*Paeoniae Radix rubra*) (100%), Xuan Shen (*Scrophulariae Radix*) (100%), Lian Qiao (100%), Dan Pi (*Moutan Cortex*) (100%), Huang Lian (*Coptidis Rhizoma*) (100%), Zhu Ye (*Phyllostachys*

*nigrae Folium*) (100%), Ting Li Zi (100%), and Gan Cao (100%).

Based on the analysis of 11 TCM syndromes of COVID-19, the Chinese medicines recommended to treat more than one type of TCM syndrome were Gan Cao (10/11), Xing Ren (9/11), Sheng Shi Gao (9/11), Fu Ling (8/11), Ban Xia (*Rhizoma Praeparatum*) (8/11), and Lian Qiao (8/11); followed by Ting Li Zi (7/11), Cang Zhu (7/11), Huo Xiang (7/11), Chen Pi (7/11), Huang Qin (7/11), Gan Lu Gen (*Phragmitis Rhizoma*) (7/11), and Yi Yi Ren (*Coicis Semen*) (7/11). The herbs suitable for more than 6 types of syndromes included Ma Huang (6/11), Cao Guo (6/11), Bing Lang (*Arecae Semen*) (6/11), Hou Po (6/11), Chi Shao (6/11), Jie Geng (6/11), and Chai Hu (*Bupleuri Radix*) (6/11).

### Recommended herb for different traditional Chinese medicine syndrome elements of COVID-19 based on each diagnosis and treatment protocol

By decomposing wind-heat invading lung, heat-toxin accumulation in the lung, DTL, DHL, damp constraint in the lung, CDL, and epidemic toxin blocking the lung into disease nature syndrome elements, the suitable herbs for these disease syndrome elements were identified as: (1) Gan Cao, Lian Qiao, Xing Ren, Jie Geng, and Huang Qin, which can be used as basic herbs when the disease syndrome elements of COVID-19 are wind, heat, toxin, dampness, cold, or plague; (2) Jin Yin Hua, Gan Lu Gen, Chai Hu, Sang Ye (*Mori Folium*), and Chan Tui (*Cicadae Periostracmu*), which are used to treat the disease syndrome elements of wind, heat, toxin, dampness, and plague; (3) Ma Huang, Sheng Shi Gao, Gua Lou (*Trichosanthis Fructus*), Chuan Bei Mu (*Fritillariae Cirrhosae Bulbus*), and Huo Xiang, which are used to treat the disease syndrome elements of heat, toxin, dampness, cold, or plague; (4) For different disease syndrome elements, the herbs, Lian Qiao, Gan Cao, Xing Ren, and Jie Geng, were found to be suitable for “wind.” Gan Cao, Xing Ren, Huang Qin, and Lian Qiao were suitable for “hot.” Xing Ren, Sheng Shi Gao, Ma Huang, and Ting Li Zi were suitable for “toxin.” Ma Huang, Xing Ren, Cang Zhu, Cao Guo, Huo Xiang, and Hou Po were suitable for “dampness.” Hou Po, Ma Huang, and Sheng Jiang were suitable for “cold.” Xing Ren, Sheng Shi Gao, Ma Huang, and Ting Li Zi were suitable for “plague [Table 5].”

Table 4: Recommended herb frequency for different Traditional Chinese medicine syndromes of COVID-19 (Top 30)											
Herb	Wind-heat invading lung pattern	Heat-toxin accumulation in the lung pattern	Blazing of both qi and ying pattern	Damp-toxin constraint in the lung pattern	Damp constraint in the lung pattern	Cold-damp constraint in the lung pattern	Lung-spleen qi deficiency pattern	Deficiency of both qi and yin pattern	Internal blockage and external desertion pattern	Epidemic toxin blocking the lung pattern	n
Gan Cao ( <i>Glycyrrhizae radix</i> )	3	4	4	3	4	2	4	13	0	13	10
Xing Ren ( <i>Armeniacae semen</i> )	2	5	0	5	5	4	0	3	1	22	9
Ma Huang ( <i>Ephedrae herba</i> )	0	5	0	4	4	10	0	0	0	19	6
Sheng Shi Gao ( <i>Gypsum fibrosum</i> )	0	5	4	2	1	1	0	5	1	22	9
Fu Ling ( <i>Poria</i> )	0	1	0	3	4	3	15	6	0	4	8
Huo Xiang ( <i>Pogostemonis Herba</i> )	0	1	0	3	2	9	13	0	0	6	7
Chen Pi ( <i>Citri reticulatae Pericarpium</i> )	1	0	0	1	2	9	14	7	0	0	7
Ban Xia ( <i>Rhizoma Praeparatum</i> )	0	1	0	2	2	3	14	5	0	6	8
Ting Li Zi ( <i>Lepidii/ Descurainiae semen</i> )	0	1	4	2	0	2	0	0	1	20	7
Cang Zhu ( <i>Atractylodis Rhizoma</i> )	0	1	0	1	2	9	0	0	1	12	7
Cao Guo ( <i>Isaoko Fructus</i> )	0	1	0	1	3	8	0	0	0	10	6
Huang Qin ( <i>Scutellariae Radix</i> )	1	3	0	4	4	1	0	0	0	7	7
Huang Qi ( <i>Astragali Radix</i> )	0	0	0	1	0	0	14	6	1	4	5
Bing Lang ( <i>Arecace Semen</i> )	0	1	0	1	4	7	0	0	0	9	6
Hou Po ( <i>Magnoliae officinalis Cortex</i> )	0	1	0	2	5	8	0	0	0	5	6
Chi Shao ( <i>Paeoniae Radix rubra</i> )	0	1	4	1	2	0	0	2	0	12	6
Ren Shen ( <i>Ginseng Radix</i> )	0	0	0	0	0	0	1	1	20	0	3
Lian Qiao ( <i>Forsythiae Fructus</i> )	3	2	4	1	5	3	0	0	0	2	8
Da Huang ( <i>Rhei Radix et Rhizoma</i> )	0	3	0	0	0	0	0	0	0	18	2

Contd...

Table 4: Contd...											
Herb	Wind-heat invading lung pattern	Heat-toxin accumulation in the lung pattern	Blazing of both qi and ying pattern	Damp-toxin constraint in the lung pattern	Damp-heat accumulation in the lung pattern	Damp constraint in the lung pattern	Cold-damp constraint in the lung pattern	Lung-spleen qi deficiency pattern	Deficiency of both qi and yin pattern	Internal blockage and external desertion pattern	Epidemic toxin blocking the lung pattern
Gua Lou ( <i>Trichosanthis Fructus</i> )	0	2	0	1	2	0	1	0	0	0	15
Hei Shun Pian ( <i>Aconiti Radix lateralis praeparata</i> )	0	0	0	0	0	0	0	0	0	21	0
Shan Zhu Yu ( <i>Corni Fructus</i> )	0	0	0	0	0	0	0	0	0	20	0
Mai Dong ( <i>Ophiopogonis Radix</i> )	0	0	0	0	0	0	0	0	15	4	1
Bai Zhu ( <i>Atractylodis macrocephalae Rhizoma</i> )	0	0	0	1	0	3	2	5	7	0	0
Gan Lu Gen ( <i>Phragmitis Rhizoma</i> )	1	1	0	2	4	1	0	0	5	0	3
Yi Yi Ren ( <i>Coicis Semen</i> )	0	2	0	2	4	4	0	1	1	0	2
Tao Ren ( <i>Persicae Semen</i> )	0	0	0	2	1	0	0	0	0	0	13
Sha Ren ( <i>AmomiFructus</i> )	0	0	0	0	0	0	0	15	1	0	0
Dang Shen ( <i>Codonopsis Radix</i> )	0	0	0	0	0	0	0	13	2	0	0
Sheng Jiang ( <i>Zingiberis Rhizoma recens</i> )	0	0	0	1	1	2	10	0	0	0	0

**Table 5: Recommended herb frequency for different Traditional Chinese medicine syndrome elements of COVID-19 (Top 30)**

Herb	Wind	Hot	Toxin	Dampness	Cold	Plague	n
Gan Cao ( <i>Glycyrrhizae radix</i> )	3	15	20	17	2	13	6
Lian Qiao ( <i>Forsythiae Fructus</i> )	3	10	5	10	1	2	6
Xing Ren ( <i>Armeniacae semen</i> )	2	13	32	20	4	22	6
Jie Geng ( <i>Platycodonis Radix</i> )	2	3	3	3	1	3	6
Huang Qin ( <i>Scutellariae Radix</i> )	1	11	14	16	1	7	6
Chen Pi ( <i>Citri reticulatae Pericarpium</i> )	1	3	1	14	9	0	5
Jin Yin Hua ( <i>Lonicerae Japonicae Flos</i> )	3	7	3	2	0	1	5
Gan Lu Gen ( <i>Phragmitis Rhizoma</i> )	1	6	6	7	0	3	5
Chai Hu ( <i>Bupleuri Radix</i> )	1	3	3	5	0	1	5
Sang Ye ( <i>Mori Folium</i> )	1	2	2	2	0	1	5
Chan Tui ( <i>Cicadae Periostracmu</i> )	1	2	1	1	0	1	5
Ma Huang ( <i>Ephedrae herba</i> )	0	8	29	21	10	20	5
Sheng Shi Gao ( <i>Gypsum fibrosum</i> )	0	7	29	6	1	22	5
Gua Lou ( <i>Trichosanthis Fructus</i> )	0	4	18	4	1	15	5
Chuan Bei Mu ( <i>Fritillariae Cirrhosae Bulbus</i> )	0	2	7	5	3	4	5
Huo Xiang ( <i>Pogostemonis Herba</i> )	0	4	10	17	9	6	5
Ban Xia ( <i>Rhizoma Praeparatum</i> )	0	3	3	15	3	6	5
Ting Li Zi ( <i>Lepidii/ Descurainiae semen</i> )	0	3	23	6	2	20	5
Cang Zhu ( <i>Atractylodis Rhizoma</i> )	0	6	14	17	9	12	5
Cao Guo ( <i>Tsaoko Fructus</i> )	0	6	12	17	8	10	5
Bing Lang ( <i>Arecae Semen</i> )	0	5	11	15	7	9	5
Dou Kou ( <i>Amomi Fructus Rotundus</i> )	0	5	4	7	1	2	5
Zi Su ( <i>Perillae Fructus</i> )	0	1	3	2	1	1	5
Di Long ( <i>Pheretima</i> )	0	1	3	2	1	3	5
Jiang Can ( <i>Bombyx Batryticatus</i> )	1	1	1	0	0	1	4
Jiang Huang ( <i>Curcuma Longae Rhizoma</i> )	1	1	1	0	0	1	4
Yi Yi Ren ( <i>Coicis Semen</i> )	0	6	6	10	0	2	4
Fu Ling ( <i>Poria</i> )	0	5	8	10	0	4	4
Hou Po ( <i>Magnoliae officinalis Cortex</i> )	0	6	8	17	13	0	4
Chi Shao ( <i>Paeoniae Radix rubra</i> )	0	3	14	3	0	12	4



## Comparison of high-frequency recommended herbs for COVID-19 traditional Chinese medicine syndromes and syndrome elements based on diagnosis and treatment protocols and clinical practice

(1) Among the herbs suitable for six or more TCM syndromes and five or more syndrome elements, Gan Cao, Sheng Shi Gao, Huo Xiang, Xing Ren, Ma Huang, Ban Xia, Chen Pi, Huang Qin, and Chai Hu appeared in QPD. In addition, Fu Ling was identified as a suitable herb for six or more TCM syndromes. (2) Among the herbs suitable for six or more TCM syndromes and five or more syndrome elements, Gan Cao, Sheng Shi Gao, Huo Xiang, Xing Ren, Ma Huang, Ting Li Zi, Cang Zhu, and Gan Lu Gen appeared in XBF. In addition, Yi Yi Ren was identified as a suitable herb for six or more TCM syndromes. (3) Among the herbs suitable for six or more TCM syndromes and five or more syndrome elements, Gan Cao, Sheng Shi Gao, Huo Xiang, Ma Huang, Xing Ren, Ban Xia, Ting Li Zi, Cang Zhu, and Cao Guo appeared in HBF. In addition, Fu Ling, Hou Po, and Chi Shao were identified as suitable herbs for six or more TCM syndromes. (4) Among the herbs suitable for six or more TCM syndromes and five or more syndrome elements, Gan Cao, Sheng Shi Gao, Huo Xiang, Xing Ren, Ban Xia, Huang Qin, Chai Hu, Cang Zhu, Gan Lu Gen, Jie Geng, and Lian Qiao appeared as high-frequency herbs used in single-case clinical studies (patient use rate above 15%). In addition, Fu Ling and Hou Po were identified as suitable herbs for six or more TCM syndromes, while Jin Yin Hua and Chuan Bei Mu were identified as suitable herbs for five or more syndrome elements. (5) Gan Cao, Sheng Shi Gao, Huo Xiang, Ma Huang, Xing Ren, Ban Xia, Chen Pi, Huang Qin, Chai Hu, Ting Li Zi, Cang Zhu, Gan Lu Gen, Dou Kou (*Amomi Fructus Rotundus*), Cao Guo, Bing Lang, Jie Geng, and Lian Qiao were identified as other suitable herbs for six or more TCM syndromes and five or more syndrome elements. (6) For herbs used in QPD, Gan Cao, Sheng Shi Gao, Huo Xiang, Xing Ren, Ban Xia, Huang Qin, Chai Hu, Fu Ling, Gui Zhi (*Cinnamomi Ramulus*), Bai Zhu, and Zhi Shi (*Aurantii Fructus immaturus*) appeared as high-frequency herbs used in single-case clinical studies. For herbs used in XBF, Gan Cao, Sheng Shi Gao, Huo Xiang, Xing Ren, Cang Zhu, Gan Lu Gen, and Qing Hao (*Artemisiae Annuae Herba*) appeared as high-frequency herbs used in single-case clinical studies. For herbs used in HBF, Gan Cao, Sheng Shi Gao, Huo Xiang, Xing Ren, Ban Xia, Cang Zhu, Fu Ling, and Hou Po appeared as high-frequency herbs used in single-case clinical studies. (7) The herbs used in QPD, XBF, and HBF that are suitable for six or more TCM syndromes and five or more syndrome elements and were also identified as high-frequency herbs used in single-case clinical studies were Huo Xiang, Xing Ren, Sheng Shi Gao, and Gan Cao [Table 6].

## DISCUSSION

COVID-19 is an acute respiratory infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Fever, dry cough, and fatigue are the main clinical manifestations of COVID-19. Most patients with this

disease have mild clinical symptoms and a good prognosis. However, some patients with severe disease rapidly progress to acute respiratory distress syndrome and experience septic shock.<sup>[30]</sup> Similar to SARS-CoV, SARS-CoV-2 uses angiotensin-converting enzyme II (ACE2) as its receptor. ACE2 is widely distributed in the lung, heart, kidney, gastrointestinal tract, and other organs.<sup>[33,34]</sup> TCM is composed of closely linked technical and cultural levels.<sup>[35]</sup> As there is no clear evidence to support the key therapeutic role of a specific drug, TCM allows doctors to exploit previous diagnosis and treatment experience for the treatment of new acute infectious diseases, thereby aligning with the clinical practice of modern medicine. Modern medicine summarizes the norms and principles of compassionate use. For example, compassionate use, as stipulated by the U.S. Food and Drug Administration, refers to scenarios where patients suffering from serious or life-threatening diseases utilize unlicensed test drugs outside clinical trials when they cannot be treated using existing drugs or those selected for clinical trials.<sup>[36]</sup> Importantly, doctors, especially experienced doctors, can write a prescription based on previous “fragmentary” knowledge or evidence. This prescription not only aims to target the main pathogenic changes in patients but also considers non-symptomatic factors, such as age, region, and constitution in patients.<sup>[37]</sup>

Many types of meta-analyses based on cross-sectional study without control dichotomy data are available. These meta-analyses include single rate meta-analysis, which is commonly used to determine prevalence rate, detection rate, awareness rate, mortality rate, and infection rate.<sup>[38]</sup> In this study, this approach was applied to analyze the frequency of COVID-19 syndromes. Consequently, DHL, DSD, and ETL were identified as frequent TCM syndromes of the disease. The frequency of the first two syndromes was approximately 50%. The lung was identified as the disease location, and dampness, heat, and toxin were identified as the disease syndrome elements.

TCM is used as a treatment according to syndrome differentiation and is not a good choice of treatment based on disease (modern medicine) differentiation. However, it is difficult to carry out individual syndrome differentiation and treatment for all individuals with sudden infectious diseases. Thus, achieving high-level disease differentiation and treatment is of great significance with respect to the characteristics and advantages of comprehensive syndrome differentiation and treatment. Syndrome elements are less than syndromes by unit; however, if diseases are classified by syndrome elements, they are greater than syndromes. Therefore, based on decomposition of COVID-19 syndromes into syndrome elements, this study formed a new unit of disease syndrome elements to guide the classification of COVID-19 in “a group of people treated with one prescription.”

In this study, the laws embodied in the specific clinical practices could not control or predict diagnosis and treatment compared to the scientific nature of the syndrome and

**Table 6: Comparison of the high-frequency recommended herbs for COVID-19 Traditional Chinese medicine syndromes and syndrome elements based on diagnosis and treatment protocols and clinical practice**

Herb	Herbs that suitable for 6 or more TCM syndromes	Herbs that suitable for 5 or more syndrome elements	Qingfei Paidu Decoction <sup>[30]</sup>	Xuanfei Baidu Formula <sup>[31]</sup>	Huashi Baidu Formula <sup>[32]</sup>	high-frequency herbs used in single-case clinical studies
Gan Cao ( <i>Glycyrrhizae radix</i> )	√	√	√	√	√	√
Sheng Shi Gao ( <i>Gypsum fibrosum</i> )	√	√	√	√	√	√
Huo Xiang ( <i>Pogostemonis Herba</i> )	√	√	√	√	√	√
Ma Huang ( <i>Ephedrae herba</i> )	√	√	√	√	√	×
Xing Ren ( <i>Armeniacae semen</i> )	√	√	√	√	√	√
Ban Xia ( <i>Rhizoma Praeparatum</i> )	√	√	√	×	√	√
Chen Pi ( <i>Citri reticulatae Pericarpium</i> )	√	√	√	×	×	×
Huang Qin ( <i>Scutellariae Radix</i> )	√	√	√	×	×	√
Chai Hu ( <i>Bupleuri Radix</i> )	√	√	√	×	×	√
Ting Li Zi ( <i>Lepidii/Descurainiae semen</i> )	√	√	×	√	√	×
Cang Zhu ( <i>Atractylodis Rhizoma</i> )	√	√	×	√	√	√
Gan Lu Gen ( <i>Phragmitis Rhizoma</i> )	√	√	×	√	×	√
Dou Kou ( <i>Amomi Fructus Rotundus</i> )	√	√	×	×	×	×
Cao Guo ( <i>Tsaoko Fructus</i> )	√	√	×	×	√	×
Bing Lang ( <i>Arecae Semen</i> )	√	√	×	×	×	×
Jie Geng ( <i>Platycodonis Radix</i> )	√	√	×	×	×	√
Lian Qiao ( <i>Forsythiae Fructus</i> )	√	√	×	×	×	√
Fu Ling ( <i>Poria</i> )	√	×	√	×	√	√
Yi Yi Ren ( <i>Coicis Semen</i> )	√	×	×	√	×	×
Hou Po ( <i>Magnoliae officinalis Cortex</i> )	√	×	×	×	√	√
Chi Shao ( <i>Paeoniae Radix rubra</i> )	√	×	×	×	√	×
Jin Yin Hua ( <i>Lonicerae Japonicae Flos</i> )	×	√	×	×	×	√
Sang Ye ( <i>Mori Folium</i> )	×	√	×	×	×	×
Chan Tui ( <i>Cicadae Periostracmu</i> )	×	√	×	×	×	×
Gua Lou ( <i>Trichosanthis Fructus</i> )	×	√	×	×	×	×
Chuan Bei Mu ( <i>Fritillariae Cirrhosae Bulbus</i> )	×	√	×	×	×	√
Zi Su ( <i>Perillae Fructus</i> )	×	√	×	×	×	×
Di Long ( <i>Pheretima</i> )	×	√	×	×	×	×
Qing Hao ( <i>Artemisiae Annuae Herba</i> )	×	×	×	√	×	√
Hu Zhang ( <i>Polygoni Cuspidati Rhizoma Et Radix</i> )	×	×	×	√	×	×

Contd...

**Table 6: Contd...**

Herb	Herbs that suitable for 6 or more TCM syndromes	Herbs that suitable for 5 or more syndrome elements	Qingfei Paidu Decoction <sup>[90]</sup>	Xuanfei Baidu Formula <sup>[31]</sup>	Huashi Baidu Formula <sup>[32]</sup>	high-frequency herbs used in single-case clinical studies
Ma Bian Cao ( <i>Verbenae Herba</i> )	×	×	×	√	×	×
Hua Ju Hong ( <i>Citri grandis Exocarpium rubrum</i> )	×	×	×	√	×	×
Gui Zhi ( <i>Cinnamomi Ramulus</i> )	×	×	√	×	×	√
Ze Xie ( <i>Alismatis Rhizoma</i> )	×	×	√	×	×	×
Zhu Ling ( <i>Polyporus</i> )	×	×	√	×	×	×
Bai Zhu ( <i>Atractylodis macrocephalae Rhizoma</i> )	×	×	√	×	×	√
Sheng Jiang ( <i>Zingiberis Rhizoma recens</i> )	×	×	√	×	×	×
Zi Wan ( <i>Asteris Radix</i> )	×	×	√	×	×	×
Kuan Dong Hua ( <i>Farfarae Flos</i> )	×	×	√	×	×	×
She Gan ( <i>Belamcandae Rhizoma</i> )	×	×	√	×	×	×
Xi Xin ( <i>Asari Radix et Rhizoma</i> )	×	×	√	×	×	×
Shan Yao ( <i>Dioscoreae Rhizoma</i> )	×	×	√	×	×	×
Zhi Shi ( <i>Aurantii Fructus immaturus</i> )	×	×	√	×	×	√
Da Huang ( <i>Rhei Radix et Rhizoma</i> )	×	×	×	×	√	×
Huang Qi ( <i>Astragali Radix</i> )	×	×	×	×	√	×

treatment laws conveyed by the diagnosis and treatment standards, generalized and controlled by experts. Currently, well-designed clinical trials recommend fixed medication. In contrast, case reports record the patient's condition and specific prescription medication, which reflects the characteristics of syndrome differentiation and treatment with TCM. Similarly, COVID-19 TCM "Three Drugs and Three Prescriptions" featured a wide range of applications that are effective and representative of numerous clinical trials and basic studies. Therefore, in this single-case analysis, we employed the "three prescriptions" in the "three drugs and three prescriptions" of TCM as a control to verify whether the results obtained through the analysis of syndrome types and syndrome element coverage rate have a clinical value, and whether it provides a reference for the corresponding research on COVID-19 "Syndrome Types-Syndrome Elements-Diseases-Prescriptions" to integrate traditional Chinese and Western medicine. High-frequency medication, suitable for >6 syndromes and 5 syndrome elements, was found to be consistent with the study on single-case analysis and "three prescriptions" in the "Three Drugs Three Prescriptions" of TCM. These strategies also overlap with the main drugs targeting pathogenesis of COVID-19. Therefore,

the "special prescription" for COVID-19 can be preliminarily screened through syndrome types or the coverage rate of syndrome elements. However, whether the relatively simple syndrome differentiation can be used as a bridge between TCM and Western medicine remains to be investigated.

Herein, we mainly studied the guidelines issued by the National and Local Health committees. Further, the conclusions drawn must be validated using specific clinical and experimental data. Based on the characteristics of the disease, the medication of TCM syndrome elements does not consider the patient's constitution and prescription. Only the medication analysis of different disease syndrome elements of COVID-19 with lung disease location syndrome elements was included in the present study. Concurrent consideration of other disease location syndrome elements and the performance of synthesis are problems that must be further addressed. Of note, this method only considered the existing symptoms and signs of the patient. Thus, neither the symptoms and signs of the patient nor the etiology and pathogenesis of the disease, based on a combination of the symptoms and signs that the patient should not have and does not have, were considered. However, the latter is crucial to clinical syndrome differentiation and should be considered in specific clinical symptoms.

Some prior studies evaluated the efficacy and safety of TCM for the treatment of COVID-19; however, the included studies were basically randomized, controlled clinical trials or studies specifically targeting a certain Chinese patent medicine. Currently, a report that combines the analysis of the TCM DTP, a case report based on a single patient, and “three prescriptions and three drugs” has not been published; this is the entry point of this study.

## CONCLUSION

(1) The term “epidemic disease” in TCM for COVID-19 has a variety of meanings. In clinical treatment, in addition to syndrome differentiation and treatment corresponding to “one prescription for one person,” the establishment of a treatment scheme based on the classification of disease syndrome elements should be considered for sudden infectious diseases, such as COVID-19, to promote the rapid response and linkage between TCM and Western medicine. (2) Although there are numerous COVID-19 drugs, Sheng Shi Gao, Huo Xiang, Xing Ren, and Gan Cao, followed by Ma Huang and Ban Xia (*Pinellinae Rhizoma Praeparatum*), are the commonly used drugs.

## Authors' contributions

Gao Z wrote the manuscript, and GZ and Liu YY systemically revised the manuscript for important content. All authors read and approved the final manuscript.

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## Conflicts of interest

There are no conflicts of interest.

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