

Progress of Traditional Chinese Medicine Treating COVID-19

Ming-Xue Li^a, Yue-Ying Yang^a, Yang Liu^a, Meng-Zhu Zheng^b, Jun Li^c, Li-Xia Chen^a, Hua Li^{a, b}

^aWuya College of Innovation, Key Laboratory of Structure-Based Drug Design and Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China, ^bSchool of Pharmacy, Tongji Medical College, Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China, ^cDepartment of Urology and Pharmacology, University of California, Irvine, Orange, CA 92868, USA

Abstract

The new coronavirus pneumonia (coronavirus disease 2019 [COVID-19]), caused by the new coronavirus (severe acute respiratory syndrome coronavirus 2 [SARS-CoV-2]), mainly manifests by fever, dry cough, and fatigue. The emergence of SARS-CoV-2 poses a huge threat to people's lives. Unfortunately, so far, there are no effective treatment drugs and vaccines. Traditional Chinese medicine (TCM) has played an important role and achieved good results for treating this epidemic. More than 85% of patients with SARS-CoV-2 infection in China have received TCM treatment. In this article, we describe the progress of TCM for the COVID-19 therapy.

Keywords: Chinese patent medicines, coronavirus disease 2019, decoctions, traditional Chinese medicine

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is an acute respiratory infectious disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection. Its main clinical manifestations are fever, cough, headache, fatigue, and dyspnea. Although the spread of the epidemic in China has been effectively controlled, it is still being accelerated in other parts of the world, involving >200 countries and regions. As of May 9, the global total of confirmed cases was >3.93 million, with >270,000 deaths. SARS-CoV-2 is an enveloped single-stranded RNA virus, belonging to β -coronavirus.^[1] The genome sequence homology of SARS-CoV-2 and SARS-CoV is 79.5%,^[2,3] while that of SARS-CoV-2 and MERS-CoV is only 50%.^[4] In addition, SARS-CoV-2 binds host cells to the same receptor as SARS-CoV, namely angiotensin-converting enzyme 2 (ACE2).^[2]

At present, there are no special drugs and vaccines for COVID-19 treatment. The popularity of COVID-19 has shown a huge impact on people's lives and social-economic development. Based on the experience of treating SARS or MERS, and the current clinical guidelines, the treatment of COVID-19 patients in China adopts natural medicine and traditional Chinese medicine (TCM) treatment.^[5-7] In the fight against the COVID-19 epidemic, TCMs have reported to play an important role and achieve good results, highlighting their

characteristics and advantages. TCM has accumulated rich experience through fighting against epidemics (named "Yi" diseases in TCM) for thousands of years, which recommends treatment plans usually based on the disease condition, local climate characteristics, and different physical conditions. By searching the websites of the Chinese Clinical Trial Registry to collect Chinese medicine therapy for COVID-19, we found that as of May 9, a total of 648 clinical trials have been registered, 90 of which are studies on TCM [Table 1]. Moreover, some articles on TCM treatment of COVID-19 have been published

Address for correspondence: Prof. Li-Xia Chen,

Wuya College of Innovation, Key Laboratory of Structure-Based Drug Design and Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China.
E-mail: syzyclx@163.com

Prof. Hua Li,

Wuya College of Innovation, Key Laboratory of Structure-Based Drug Design and Discovery, Ministry of Education, Shenyang Pharmaceutical University, Shenyang 110016, China.

Hubei Key Laboratory of Natural Medicinal Chemistry and Resource Evaluation, School of Pharmacy, Tongji Medical College, Huazhong University of Science and Technology, Wuhan 430030, China.
E-mail: li_hua@hust.edu.cn

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Received: 31-05-2020, **Accepted:** 03-07-2020, **Published:** 09-04-2021

How to cite this article: Li MX, Yang YY, Liu Y, Zheng MZ, Li J, Chen LX, et al. Progress of traditional Chinese medicine treating COVID-19. World J Tradit Chin Med 2021;7:167-83.

Access this article online

Quick Response Code:



Website: www.wjtcn.net

DOI: 10.4103/wjtcn.wjtcn_68_20

Table 1: 90 traditional Chinese medicines in clinical trials

| Registration number | Registration title |
|---------------------|---|
| ChiCTR2000029400 | Clinical controlled trial for TCM in the treatment of NCP (COVID-19) |
| ChiCTR2000029418 | Chinese herbal medicine for severe novel coronavirus pneumonia (COVID-19): A randomized controlled trial |
| ChiCTR2000029432 | A real world study for the efficacy and safety of large dose Tanreqing injection in the treatment of patients with NCP (COVID-19) |
| ChiCTR2000029433 | A randomized, open-label, blank-controlled trial for Lian-Hua Qing-Wen capsule/granule in the treatment of suspected NCP (COVID-19) |
| ChiCTR2000029434 | A randomized, open-label, blank-controlled trial for Lian-Hua Qing-Wen capsule/granule in the treatment of NCP (COVID-19) |
| ChiCTR2000029435 | Randomized controlled trial for TCM in the prevention of NCP (COVID-19) in high risk population |
| ChiCTR2000029436 | A single arm study for evaluation of integrated traditional Chinese and western medicine in the treatment of NCP (COVID-19) |
| ChiCTR2000029479 | Research for TCM technology prevention and control of 2019-nCoV pneumonia (NCP) in the community population |
| ChiCTR2000029487 | Clinical study for Gu-Biao Jie-Du-Ling in preventing of 2019-nCoV pneumonia (NCP) in children |
| ChiCTR2000029493 | TCM for pulmonary fibrosis, pulmonary function and quality of life in patients with 2019-nCoV pneumonia (NCP) in convalescent period: A randomized controlled trial |
| ChiCTR2000029517 | Chinese medicine prevention and treatment program for suspected 2019-nCoV pneumonia (NCP): A perspective, double-blind, placebo, randomised controlled trial |
| ChiCTR2000029518 | Chinese medicine prevention and treatment program for 2019-nCoV pneumonia (NCP): A perspective, double-blind, placebo, randomised controlled trial |
| ChiCTR2000029549 | Recommendations of integrated traditional Chinese and Western medicine for 2019-nCoV pneumonia (NCP) |
| ChiCTR2000029578 | Chinese medicine prevention and treatment program for 2019-nCoV pneumonia (NCP): A perspective, sing-arm trial |
| ChiCTR2000029589 | An open, prospective, multicenter clinical study for the efficacy and safety of Reduning injection in the treatment of 2019-nCoV pneumonia (NCP) |
| ChiCTR2000029605 | A randomized, open-label, blank-controlled, multicenter trial for Shuang-Huang-Lian oral solution in the treatment of 2019-nCoV pneumonia (NCP) |
| ChiCTR2000029624 | A real world study for TCM in the treatment of 2019-nCoV pneumonia (NCP) |
| ChiCTR2000029628 | A clinical observational study for Xin-Guan-2 formula in the treatment of suspected 2019-nCoV pneumonia (NCP) |
| ChiCTR2000029637 | An observational study for Xin-Guan-1 formula in the treatment of 2019-nCoV pneumonia (NCP) |
| ChiCTR2000029747 | Effect evaluation and prognosis of Chinese medicine based on NCP (COVID-19) |
| ChiCTR2000029755 | A randomized, open, parallel-controlled trial for the efficacy and safety of Jingyebaidu granules in treating NCP (COVID-19) |
| ChiCTR2000029756 | Clinical study of nebulized Xiyanping injection in the treatment of NCP (COVID-19) |
| ChiCTR2000029763 | The efficacy of TCM on NCP (COVID-19) patients treated in square cabin hospital: A prospective, randomized controlled trial |
| ChiCTR2000029769 | Babaodan capsule used for the adjuvant treatment of severe NCP (COVID-19) |
| ChiCTR2000029777 | A multicenter, randomized, controlled trial for integrated Chinese and western medicine in the treatment of NCP (COVID-19) based on the "Truncated Torsion" strategy |
| ChiCTR2000029778 | Clinical study for TCM combined with Western medicine in treatment of NCP (COVID-19) |
| ChiCTR2000029780 | A multicenter, randomized, open, controlled trial for the efficacy and safety of Shen-Qi Fu-Zheng injection in the treatment of NCP (COVID-19) |
| ChiCTR2000029788 | TCM cooperative therapy for patients with NCP (COVID-19): A randomized controlled trial |
| ChiCTR2000029789 | Randomized controlled trial for TCM syndrome differentiation treatment impacting quality of life of postdischarge patients with NCP (COVID-19) |
| ChiCTR2000029790 | Clinical study for the integration of traditional Chinese and Western medicine in the treatment of NCP (COVID-19) |
| ChiCTR2000029813 | Clinical trial for Tanreqing capsules in the treatment of NCP (COVID-19) |
| ChiCTR2000029814 | Clinical trial for integrated Chinese and Western medicine in the treatment of children with NCP (COVID-19) |
| ChiCTR2000029819 | Ba-Bao-Dan in the adjuvant therapy of NCP (COVID-19) patients |
| ChiCTR2000029822 | A randomized controlled trial for honeysuckle decoction in the treatment of patients with novel coronavirus (COVID-19) infection |
| ChiCTR2000029855 | A randomized, open and controlled clinical trial for TCM in the treatment of NCP (COVID-19) |
| ChiCTR2000029869 | A multicenter, randomized, controlled trial for integrated Chinese and Western medicine in the treatment of ordinary NCP (COVID-19) based on the 'Internal and External Relieving-Truncated Torsion' strategy |
| ChiCTR2000029896 | Evaluate the effectiveness of TCM in the treatment of NCP (COVID-19) |
| ChiCTR2000029941 | A randomized controlled trial for TCM in the treatment for NCP (COVID-19) |
| ChiCTR2000029947 | A randomized controlled trial for Qingyi number 4 compound in the treatment of convalescence patients of NCP (COVID-19) |
| ChiCTR2000029954 | Efficacy and safety of honeysuckle oral liquid in the treatment of NCP (COVID-19): A multicenter, randomized, controlled, open clinical trial |
| ChiCTR2000029956 | Chinese medicine promotes rehabilitation recommendations after 2019 novel coronavirus infection (COVID-19) |

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Table 1: Contd...

| Registration number | Registration title |
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| ChiCTR2000029991 | A randomized, open-label, controlled trial for the safety and efficiency of Kesuting syrup and Keqing capsule in the treatment of mild and moderate NCP (COVID-19) |
| ChiCTR2000030003 | Optimization protocol of integrated traditional Chinese and Western medicine in the treatment for NCP (COVID-19) |
| ChiCTR2000030022 | A parallel, randomized controlled clinical trial for the efficacy and safety of pediatric Huatanzhike granules (containing ipecacuanha tincture) in the treatment of mild and moderate NCP (COVID-19) |
| ChiCTR2000030033 | A study for the intervention of Xiangxue antiviral oral solution and Wu-Zhi-Fang-Guan-Fang on close contacts of NCP (COVID-19) |
| ChiCTR2000030034 | TCM in the treatment of NCP (COVID-19): A multicentre, randomized controlled trial |
| ChiCTR2000030043 | Shen-Fu injection in the treatment of severe NCP (COVID-19): A multicenter, randomized, open-label, controlled trial |
| ChiCTR2000030117 | A multicenter, randomized, open, parallel controlled trial for the evaluation of the effectiveness and safety of Xiyanping injection in the treatment of common type NCP (COVID-19) |
| ChiCTR2000030166 | Randomized, parallel control, open trial for Qing-Wen Bai-Du-Yin combined with antiviral therapy in the treatment of NCP (COVID-19) |
| ChiCTR2000030188 | Clinical study on syndrome differentiation of TCM in treating severe and critical NCP (COVID-19) |
| ChiCTR2000030215 | Study for the efficacy of Kangguan number 1–3 prescription in the treatment of NCP (COVID-19) |
| ChiCTR2000030255 | Efficacy and safety of Jing-Yin granule in the treatment of NCP (COVID-19) wind-heat syndrome |
| ChiCTR2000030314 | TCM Ma-Xing-Shi-Gan-Tang and Sheng-Jiang-San in the treatment of children with NCP (COVID-19) |
| ChiCTR2000030388 | Efficacy and safety of Xue-Bi-Jing injection in the treatment of severe cases of NCP (COVID-19) |
| ChiCTR2000030469 | A randomized parallel controlled trial for Liushenwan in treatment of NCP (COVID-19) |
| ChiCTR2000030479 | Study for the effectiveness and safety of Yi-Qi Hua-shi Jie-Du-Fang in the treatment of the NCP (COVID-19) |
| ChiCTR2000030492 | Retrospective study for integrate Chinese and conventional medicine treatment of NCP (COVID-19) in Hu'nan province |
| ChiCTR2000030522 | Efficacy and safety of Ma-Xing-Gan-Shi decoction in the treatment of NCP (COVID-19) |
| ChiCTR2000030545 | Efficacy and safety of honeysuckle oral liquid in the treatment of NCP (COVID-19): A multicenter, randomized, controlled, open clinical trial |
| ChiCTR2000030619 | A medical records based real world study for the characteristics and correlation mechanism of TCM combined with Western medicine in the treatment of patients with NCP (COVID-19) |
| ChiCTR2000030704 | Observation of clinical efficacy and safety of Bufonis venenum injection in the treatment of severe NCP (COVID-19) |
| ChiCTR2000030719 | A retrospective cohort study for integrated traditional Chinese and Western medicine in the treatment of 1071 patients with NCP (COVID-19) in Wuhan |
| ChiCTR2000030747 | A prospective cohort study for comprehensive treatment of Chinese medicine in the treatment of convalescent patients of NCP (COVID-19) |
| ChiCTR2000030759 | Study for the therapeutic effect and mechanism of TCM in the treatment of NCP (COVID-19) |
| ChiCTR2000030804 | Exocarpium Citri Grandis relieves symptoms of novel coronavirus pneumonia (COVID-19): A randomized controlled clinical trial |
| ChiCTR2000030806 | Retrospective study for the efficacy of ulinastatin combined with “clear lung detoxification soup” in the treatment of NCP (COVID-19) |
| ChiCTR2000030810 | Clinical observation and evaluation of TCM in the treatment of NCP (COVID-19) in Hubei 672 orthopaedics hospital of integrated Chinese and Western medicine |
| ChiCTR2000030836 | NCP (COVID-19) combined with Chinese and Western medicine based on “Internal and External Relieving-Truncated Torsion” strategy |
| ChiCTR2000030864 | TCM for NCP (COVID-19) |
| ChiCTR2000030920 | Evaluation of the effect of taking <i>Tricholoma matsutake</i> , <i>Cannabis sativa</i> capsule and <i>Dendrobium candidum</i> to nutrition intervention of patients with NCP (COVID-19) during convalescence |
| ChiCTR2000030923 | The treatment and diagnosis plan of integrated traditional Chinese and Western medicine for NCP (COVID-19) |
| ChiCTR2000030936 | A real-world study for the Chinese medicines “Xinguan 2” and “Xinguan 3” in the treatment of NCP (COVID-19) |
| ChiCTR2000030937 | A randomized, open-label, controlled trial for Gu-Shen Ding-Chuan-Wan in the treatment of patients with NCP (COVID-19) at recovery phase with Fei-Pi-Qi-Xu Zhen |
| ChiCTR2000030962 | Clinical efficacy of TCM syndrome differentiation in the treatment of severe/critical type of NCP (COVID-19): A prospective, observational, one-arm clinical study |
| ChiCTR2000030988 | A randomized controlled trial for Hua-Shi Bai-Du granules in patients with NCP (COVID-19) |
| ChiCTR2000031089 | A medical records based study for Tou-Jie-Qu-Wen Granules in the treatment of mild and moderate patients with NCP (COVID-19) |
| ChiCTR2000031672 | Development and application of TCM body regulating protection scheme for the convalescent population of NCP (COVID-19) |
| ChiCTR2000031888 | A medical records based study for “Guangdong Pneumonia No.1” in the treatment of NCP (COVID-19) |
| ChiCTR2000031982 | Clinical observation for the effect of Ke-Gan-Li-Yan oral liquid on the relief of laryngeal symptoms of NCP (COVID-19) convalescence and suspected patients and other susceptible people |

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| Table 1: Contd... | |
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| Registration number | Registration title |
| ChiCTR2000032098 | Danggui Shaoyao powder in the synergistic treatment of NCP (COVID-19) |
| ChiCTR2000032135 | Efficacy and Safety of ulinastatin in the treatment of NCP (COVID-19) |
| ChiCTR2000032165 | A multicenter, randomized, double-blind, parallel-controlled trial for Qi-Mai-Fei-Luo-Ping mixture in the improvement of lung function of NCP (COVID-19) in the convalescent period |
| ChiCTR2000032205 | A multicenter randomized, double-blind, placebo-controlled trial for Sheng-Mai-Yin for improvement of the pulmonary heart function related symptoms of convalescence patients of new coronavirus pneumonia |
| ChiCTR2000032237 | A multicenter, randomized, double-blind, placebo-controlled trial for Xiang-Sha-Liu-Jun Pill in the treatment of NCP (COVID-19) decline in digestive function during convalescence |
| ChiCTR2000032313 | Study for efficacy and safety of Jie-Xing-Jun-Zi granules in the treatment of convalescent patients of novel coronavirus pneumonia (COVID-19) |
| ChiCTR2000032461 | A medical records based retrospective study for effect of applying individualized Chinese herbal medicine in treatment of patients with NCP (COVID-19) |
| ChiCTR2000032480 | Study on data management and diagnosis-treatment mode of TCM intervention for NCP (COVID-19) convalescence |
| ChiCTR2000032573 | A randomized, double-blind, controlled trial for Bu-Fei-Huo-Xue Capsule in the treatment of NCP (COVID-19) convalescence patient with “Fei-Pi-Qi-Xu zhen” |
| ChiCTR2000032717 | Efficacy and safety of high-dose Vitamin C combined with TCM in the treatment of moderate and severe NCP (COVID-19) |
| ChiCTR2000032767 | A medical records based study for clinical efficacy and safety of “clear lung detoxification soup” in the treatment of NCP (COVID-19) |

NCP: Novel coronavirus pneumonia, TCM: Traditional Chinese medicine

recently.^[8-11] Herein, based on the current research reports, we elaborate on the progress and future prospects of TCM in the treatment of COVID-19.

CHINESE PATENT MEDICINES

Since the outbreak of COVID-19, many TCMs have been promptly and comprehensively involved in the entire process of diagnosis and treatment. Integrated Chinese and Western medicine treatment has effectively reduced the incidence of mild-to-severe and critically ill patients and improves the cure rate. The diagnosis and treatment plan (Trial Version 3) for new coronavirus infectious disease first describe the relevant contents of the TCM treatment plan in detail. Until now, the Newest Trial Version 7 has been issued, and some Chinese patent medicines [Table 2] have been recommended for cases of medical observation period and severe and critical cases of the clinical treatment period (confirmed cases) in the Chinese medicine treatment section. According to the diagnosis and treatment plan for new coronavirus infectious disease published in various places in China, we also summarized the involved Chinese patent medicines herein [Table 3].

Lianhua Qingwen capsule has been included in the recommended medication of COVID-19 diagnosis and treatment plan in many countries and localities.^[12] Clinical studies have shown that Lianhua Qingwen has a significant effect on relieving the symptoms of fever, cough, sputum, and shortness of breath in COVID-19 patients. COVID-19 mainly manifests as fever, fatigue, and dry cough. Lianhua Qingwen, composed of 13 herbs, is derived from two TCM prescriptions: Maxing Shigan decoction and Yinqiaosan. Maxing Shigan decoction which was originally described in “Shang Han Lun,” can inhibit the entry of virus, which has been designated for the treatment of bronchitis, pneumonia, and early stage of measles.^[13] Yinqiaosan is mainly used to treat “warm disease”

characterized by fever, thirst, and headache. Lianhua Qingwen capsule has been widely used as an antiviral agent in clinical practice, especially for various respiratory viral infections. An experiment evaluating the efficacy and safety of Lianhua Qingwen capsule for the treatment of H1N1 influenza virus infection showed that Lianhua Qingwen capsule obviously relieved fever, cough, sore throat, and fatigue compared with oseltamivir.^[14,15] Another study showed that Lianhua Qingwen capsule exerts anti-influenza activity by inhibiting virus reproduction and affecting immune function.^[16] Lianhua Qingwen capsule was reported to have a broad-spectrum effects on a range of influenza viruses and specifically regulate the immune response to viral infections.^[16] In addition, the anti-influenza activity of Lianhua Qingwen in infected mice may depend on the regulation of cytokines, especially those associated with cytokine storms.^[16] Pathological studies have shown that the pathological features of COVID-19 are very similar to SARS and MERS.^[17-19] Previous studies have confirmed that Lianhua Qingwen can significantly inhibit SARS-CoV *in vitro* and also has a certain inhibitory effect on MERS-CoV. In short, Lianhua Qingwen could have a solid theoretical foundation for the treatment of COVID-19.

A study pointed out that the Lianhua Qingwen combination can significantly relieve the main symptoms and slow down the progress of COVID-19.^[20] Recently, Runfeng *et al.* studied the antiviral activity of Lianhua Qingwen on SARS-CoV-2 and its potential role in regulating the host immune response.^[21] The results showed that Lianhua Qingwen significantly inhibited the replication of SARS-COV-2, affected the virus morphology, and significantly reduced the production of pro-inflammatory cytokines (tumor necrosis factor-alpha [TNF-α], interleukin [IL]-6, chemokine (C-C motif) ligand 2 CCL-2/monocyte chemoattractant protein [MCP-1], and CXCL-10/IP-10), exerting

Table 2: Chinese patent medicine recommended by “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7)”

| Disease stage | Symptom | Recommend Chinese patent medicine |
|---|--|--|
| Medical observation period | Fatigue with gastrointestinal discomfort | Huoxiang Zhengqi capsule (pill, liquid, oral liquid) |
| | Fatigue with fever | Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule) |
| Clinical treatment period (confirmed cases) | Mild, moderate, and severe cases | Qingfei Paidu decoction |
| | Severe cases (syndrome of flaring heat in Qifen and Yingfen) | Xiyanping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection |
| | Critical cases (syndrome of internal blockade and external collapse) | Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shengmai injection, Shenmai injection |

Table 3: Chinese patent medicines involved in the diagnosis and treatment plan for COVID-19 issued by local governments of China

| Province | Chinese patent medicine |
|--------------|---|
| Sichuan | Yinqiaosan, Angong Niu Huang Pill, Zixuesan |
| Beijing | Jinhua Qinggan granule, Lianhua Qingwen granule (capsule), Shuanghuanglian granule (oral liquid), Qingkailing capsule, Shema oral liquid, Tanreqing injection, Xuebijing injection, Reduning injection, Xinxue granule, Zixuedan, Shenmai injection, Shenfu injection, Angong Niu Huang pill, Suhexiang pill, Shengmai Yin |
| Guangdong | Lianhua Qingwen capsule, Tanreqing capsule, Jinhua Qinggan granule, Chaishi Tuire granule, antiviral oral liquid (Granule), Kegan Liyan oral liquid, Lanqin oral liquid, Shufeng Jiedu capsule, Fangfeng Tongsheng pill, Tanreqing injection, Xuebijing injection, Reduning injection, Xiyanping injection, Shenfu injection, Shengmai injection, Shengmai Yin, Shenling Baizhu San, Xiangsha Liu Jun pill, Buzhong Yiqi pill |
| Shanxi | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Fangfeng Tongsheng pill (granule), Xuebijing injection, Shexiang Niu Huang pill, Shenfu injection, Shengmai injection |
| Shanxi | Huoxiang Zhengqi San, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule, Fangfeng Tongsheng pill, Reyanning mixture, Siji antiviral mixture, Lanqin oral liquid, Yinqiao Jiedu pill, Yinling capsule, Shuanghuanglian oral liquid, Tanreqing injection, Xiyanping injection, Xuebijing injection, Suhexiang pill, Zhibaoan, Angong Niu Huang pill, Qingkailing injection, Xingnaojing injection, Shengpu agent, Shengmai oral liquid, Shengmai Yin, Shenmai injection, Shengmai injection |
| Hainan | Lianhua Qingwen granule, Pudilan anti-inflammatory tablets (liquid), Qingkailing oral liquid, Tong Xuan Lifei pill |
| Hunan | Huoxiang Zhengqi pill or oral liquid, Yin Huang Qingfei capsule, Qing Rejiedu granule |
| Hebei | Huoxiang Zhengqi soft capsule (pill, liquid, oral liquid), Lianhua Qingwen capsule (granule), Qingkailing soft capsule, Jinhua Qinggan granule, Shufeng Jiedu capsule (granule), Fangfeng Tongsheng pill (granule), Qingkailing injection, Xuebijing injection, Shenfu injection |
| Shandong | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Compound Xi Ling Jiedu capsule (tablet), Kugan granule, Qingwen Jiedu pill, Xiyanping injection, Reduning injection, Xuebijing injection, Xingnaojing injection, Shenfu injection, Shengmai injection |
| Liaoning | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Fangfeng Tongsheng pill (granule), Sanni tablet, Xiyanping injection, Xuebifeng injection, Tanreqing injection, Reduning injection, Qingkailing injection (capsule, granule, oral liquid), Angong Niu Huang pill, Zhibaoan, Zixuesan (granule, oral liquid, capsule), Shenfu injection, Shengmai injection (capsule, granule, oral liquid), Xiangsha Liu Junzi pill, Shengmai Yin |
| Heilongjiang | Tanreqing injection, Reduning injection, compound Jinyinhua granule, Shuanghuanglian oral liquid, Shuanghuanglian injection, Shuanghuanglian Powder injection, compound Quinlan oral liquid |
| Gansu | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Fangfeng Tongsheng pill (granule) |
| Qinghai | Jing Fang Baidu San, Jiuwei Qianghuo pill, Compound Yuxingcao tablet (mixture), Lianhua Qingwen capsule, Lanqin oral liquid, Xiyanping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shenmai injection |
| Jiangxi | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Shanla Meiye granule, Xiyanping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shengmai injection, Shenmai injection, Shenling Baizhu San, Xiangsha Liu Jun pill, Jin Shuibao capsule (tablet) |
| Ningxia | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Fangfeng Tongsheng pill (granule), Xiyanping injection, Xuebijing injection, Shenfu injection, Shengmai injection |
| Shanghai | Huoxiang Zhengqi capsule (pill, liquid, oral liquid), Jinhua Qinggan granule, Lianhua Qingwen capsule (granule), Shufeng Jiedu capsule (granule), Jing Yin granule, Liu Sheng pill, Xiao Qing Long oral liquid, Tanreqing capsule, Qingkailing soft capsule, Xiyanping injection, Xuebijing injection, Reduning injection, Tanreqing injection, Xingnaojing injection, Shenfu injection, Shengmai INJECTION, Shenmai injection |
| Tianjin | Xiyanping injection, Xuebifeng injection, Shenfu injection, Shengmai injection |

anti-inflammatory activity.^[21] Their research confirmed that Lianhua Qingwen possesses antiviral and anti-inflammatory activity against SARS-CoV-2 infection, further supporting the clinical application of Lianhua Qingwen in combination with existing therapies for COVID-19.^[21] Lianhua Qingwen can reduce inflammatory cytokines in patients with chronic obstructive pulmonary disease (COPD).^[22] Furthermore, it also inhibits the virus-induced activation of NF- κ B and reduces the expression levels of IL-6, IL-8, TNF- α , IP-10, and MCP-1.^[16] Lianhua Qingwen has a potential inhibitory effect on the arachidonic acid pathway, which may be an important target for the treatment of COVID-19. Therefore, Lianhua Qingwen can suppress inflammatory storms, reduce lung damage induced by SARS-CoV-2 infection, and improve lung function.

In summary, Lianhua Qingwen not only exhibits antiviral effect but also inhibits inflammatory response and regulates the function of immune system, demonstrating that Lianhua Qingwen can be used to treat COVID-19 due to its advantages of overall regulation and multi-target therapy.

Xuebijing injection plays a protective role against lung injury caused by paraquat by downregulating the expression of p38 MAPK in rats.^[23] It also showed anti-inflammatory effect on lung injury caused by dichlorvos poisoning and downregulated the expression of TLR4 and NF- κ B.^[24] Xuebijing can antagonize endotoxin and inhibit the excessive release of inflammatory mediators, such as interferon (IFN) and IL, thereby inhibiting inflammatory reactions and enhancing immunity. At present, Xuebijing injection has become the recommended medication for COVID-19, which promotes the elimination of inflammatory factors, and is mainly used for the early- and mid-term treatment of severe and critically ill patients. It can improve the cure rate and discharge rate and reduce the chance of conversion from severe to critically ill.

Jinhua Qinggan granules have anti-influenza effects^[25] and are safe and effective in treating influenza patients with wind-heat affecting Fei syndrome.^[26] Clinical studies have shown that Jinhua Qinggan granules can significantly reduce the levels of IFN gamma (IFN- γ) and C-reactive protein cytokines in the serum of influenza patients. Jinhua Qinggan granules exhibited a potential inhibitory effect on the arachidonic acid pathway, which may inhibit pneumonia caused by SARS-CoV-2 by relieving cytokine storms.^[27] Clinical studies have shown that Jinhua Qinggan granules have a definite effect on the therapy of COVID-19 light and normal patients, as well as can shorten the time of fever, increase the normalization rate of lymphocytes and white blood cells, and improve related immunological indicators.

Shenfu injection can alleviate endotoxin-induced acute lung injury (ALI) in rats by inhibiting the TNF- α -NF- κ B pathway.^[28] It can also reduce the levels of IL-6, IL-8, and TNF- α and increase the expression of IL-4 and IL-10.^[29] Shenfu injection can regulate the level of cytokines, enhance the body's immune function, and reduce immune dysfunction after recovery.^[29] Besides anti-inflammatory, anti-oxidant,

anti-shock, and immunomodulatory effects, Shenfu injection can also be used for viral pneumonia, viral myocarditis, *etc.* In the treatment of severe pneumonia in the elderly COVID-19 patients, Shenfu injection effectively eliminates inflammatory mediators.^[30] COVID-19 critically ill patients are often found multiple organ failure and the disease progresses quickly, and Shenfu injection can play a good role in rescuing critically ill patients.

Xingnaojing injection is used for cleaning heat toxicity, improving brain function, and promoting blood flow.^[31] Many studies have shown that Xingnaojing injection possesses good therapeutic effects on consciousness diseases, including stroke and various coma.^[32-34] Compared with traditional drug treatment, Xingnaojing injection exhibits obvious recovery advantages by improving neurological deficits and hemorheology and reducing the level of TNF- α in serum.^[33,35,36] The anti-inflammation, antioxidation, and immune regulation of Xingnaojing injection^[37] makes it currently be recommended as the therapy for severe and critically ill patients with COVID-19.

The predecessor of Jinye Baidu granule is a special anti-infective preparation developed by Tongji Hospital affiliated to Tongji Medical College of Huazhong University of Science and Technology, which was invented in 1970, and has 50 years of research and clinical application history until now. It is mainly made up of the classic anti-infection TCM formulas of *Lonicera japonica*, *Clerodendrum cyrtophyllum* Turcz., *Taraxacum mongolicum*, and *Houttuynia cordata* Thunb. It possesses antiviral, antipyretic, anti-inflammatory, antibacterial, endotoxin suppression, and immunity enhancement functions. Jinye Baidu granule has been used for the treatment of viral pneumonia, acute upper respiratory tract infection, influenza, and other viruses, as well as bacterial infectious diseases. During the 2003 SARS epidemic, Jinye Baidu granule was used in the prevention and treatment of SARS-CoV infection and has achieved good therapeutic results. Therefore, it is praised as "TONGJI COFFEE" by foreign friends. In this epidemic, Jinye Baidu granule once again played an important preventive and therapeutic role against SARS-CoV-2 infection. Jinye Baidu granule is listed as one of the prevention and treatment drugs of COVID-19.

CHINESE MEDICINE DECOCTIONS

We summarize the TCM decoctions involved in the trial of diagnosis and treatment program for COVID-19 issued by the National Health Commission [Table 4] and local governments [Table 5]. According to the Chinese patent medicines mentioned above, we have made a detailed overview on the composition and predicted active ingredients and action mechanism of the frequently used Chinese patent medicines and decoctions in clinic [Table 6].

Qingfei Paidu decoction was recommended for COVID-19 treatment in the new coronavirus pneumonia diagnosis and plan (Trial Version 6). Qingfei Paidu decoction is an optimized combination of classic prescriptions for treating

Table 4: The traditional Chinese medicine decoction involved in “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Versions 1-7)”

| File name | Decoctions |
|--|---|
| New coronavirus infection pneumonia diagnosis and treatment plan (Trial Version 3) | Maxing Yigan decoction, Sheng Jiang San, Dayuan yin, Maxing Shigan decoction, Yinqiaosan, Xuan Bai Cheng Qi decoction, Huang Lian Jiedu decoction, Jiedu Huoxue decoction, Sinijia Renshen decoction |
| New coronavirus infection pneumonia diagnosis and treatment plan (trial version 4) | Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. lancea</i> (Thunb.) DC, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g Recommended prescription: <i>A. communis</i> Vas 10 g, <i>Gypsum fibrosum</i> 30 g, <i>T. kirilowii</i> Maxim. 30 g, <i>R. palmatum</i> L. 6 g, <i>E. sinica</i> Stapf. 6 g, <i>D. nemorosa</i> 10 g, <i>P. semen</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>A. catechu</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g Recommended prescription: <i>R. pinelliae</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>C. pilosula</i> (Franch.) Nannf. 15 g, <i>A. propinquus</i> Schischkin 30 g, <i>W. cocos</i> 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. villosum</i> Lour. 6 g |
| New coronavirus infection pneumonia diagnosis and treatment plan (trial version 5) | Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g Recommended prescription: <i>A. communis</i> Vas 10 g, <i>Gypsum fibrosum</i> 30 g, <i>T. kirilowii</i> Maxim. 30 g, <i>R. palmatum</i> L. 6 g, <i>E. sinica</i> Stapf 6 g, <i>D. nemorosa</i> 10 g, <i>P. semen</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>A. catechu</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g Recommended prescription: <i>R. pinelliae</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>C. pilosula</i> (Franch.) Nannf. 15 g, <i>A. propinquus</i> Schischkin 30 g, <i>W. cocos</i> 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. villosum</i> Lour. 6 g |
| New coronavirus infection pneumonia diagnosis and treatment plan (trial version 6) | Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>Gypsum fibrosum</i> 15 g, <i>A. communis</i> Vas 9 g, <i>N. incisum</i> Ting ex H. T. Chang 15 g, <i>D. nemorosa</i> 15 g, <i>D. setosa</i> 9 g, <i>Lumbricus</i> 15 g, <i>C. paniculatum</i> (Bunge) Kitagawa 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 15 g, <i>E. fortune</i> 9 g, <i>A. lancea</i> (Thunb.) DC. 15 g, <i>W. cocos</i> 45 g, <i>A. macrocephala</i> Koidz. 30 g, Jiao San Xian 9 g, <i>M. officinalis</i> Rehd. et Wils. 15 g, <i>A. catechu</i> 9 g, <i>A. tsaoko</i> Crevost et Lemarie 9 g, <i>Z. officinale</i> Roscoe 15 g Recommended prescription: <i>A. catechu</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. asphodeloides</i> 10 g, <i>S. baicalensis</i> Georgi 10 g, <i>B. chinense</i> 10 g, <i>P. radix</i> Rubra 10 g, <i>F. suspense</i> 15 g, <i>A. carvifolia</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>C. cyrtophyllum</i> Turcz. 10 g, <i>G. uralensis</i> Fisch. 5 g Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>Armeniacae Amarum Semen</i> 15 g, <i>Gypsum fibrosum</i> 30 g, <i>S. coicis</i> 30 g, (Thunb.) DC. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 15 g, <i>A. carvifolia</i> 12 g, <i>R. japonica</i> Houtt. 20 g, <i>V. officinalis</i> L. 30 g, <i>R. phragmitis</i> 30 g, <i>D. nemorosa</i> 15 g, <i>Citri Grandis Exocarpium</i> 15 g, <i>G. uralensis</i> Fisch. 10 g Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>A. communis</i> Vas 9 g, <i>Gypsum Fibrosum</i> 15 g, <i>G. uralensis</i> Fisch. 3 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. lancea</i> (Thunb.) DC. 15 g, <i>A. tsaoko</i> Crevost et Lemarie 10 g, <i>R. pinelliae</i> 9 g, <i>W. cocos</i> 15 g, <i>R. palmatum</i> L. 5 g, <i>A. mongholicus</i> Bunge 10 g, <i>D. nemorosa</i> 10 g, <i>P. radix</i> Rubra 10 g Recommended prescription: <i>Gypsum fibrosum</i> 30–60 g, <i>A. asphodeloides</i> 30 g, <i>R. glutinosa</i> Libosch 30–60 g, <i>Cornu bubali</i> 30 g, <i>P. radix</i> Rubra 30 g, <i>S. ningpoensis</i> Hemsl. 30 g, <i>F. suspense</i> 15 g, <i>Cortex Moutan radialis</i> 15 g, <i>C. chinensis</i> Franch. 6 g, <i>Lophatheri herba</i> 12 g, <i>D. nemorosa</i> 15 g, <i>G. uralensis</i> Fisch. 6 g Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g |
| New coronavirus infection pneumonia diagnosis and treatment plan (trial version 7) | Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>Gypsum Fibrosum</i> 15 g, <i>A. communis</i> Vas 9 g, <i>N. incisum</i> Ting ex H. T. Chang 15 g, <i>D. nemorosa</i> 15 g, <i>D. setosa</i> 9 g, <i>Lumbricus</i> 15 g, <i>C. paniculatum</i> (Bunge) Kitagawa 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 15 g, <i>E. fortune</i> 9 g, <i>A. lancea</i> (Thunb.) DC. 15 g, <i>W. cocos</i> 45 g, <i>A. macrocephala</i> Koidz. 30 g, Jiao San Xian 9 g, <i>M. officinalis</i> Rehd. et Wils. 15 g, <i>A. catechu</i> 9 g, <i>A. tsaoko</i> Crevost et Lemarie 9 g, <i>Z. officinale</i> Roscoe 15 g Recommended prescription: <i>A. catechu</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. asphodeloides</i> 10 g, <i>S. baicalensis</i> Georgi 10 g, <i>B. chinense</i> 10 g, <i>P. radix</i> Rubra 10 g, <i>F. suspense</i> 15 g, <i>A. carvifolia</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>C. cyrtophyllum</i> Turcz. 10 g, <i>G. uralensis</i> Fisch. 5 g Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>Armeniacae Amarum Semen</i> 15 g, <i>Gypsum Fibrosum</i> 30 g, <i>S. coicis</i> 30 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 15 g, <i>A. carvifolia</i> 12 g, <i>R. japonica</i> Houtt. 20 g, <i>V. officinalis</i> L. 30 g, <i>R. phragmitis</i> 30 g, <i>D. nemorosa</i> 15 g, <i>Citri Grandis Exocarpium</i> 15 g, <i>G. uralensis</i> Fisch. 10 g Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g Huashi Baidufang |

Contd...

Table 4: Contd...

| File name | Decoctions |
|-----------|--|
| | Recommended prescription: <i>Gypsum Fibrosum</i> 30~60 g, <i>A. asphodeloides</i> 30 g, <i>R. glutinosa</i> Libosch 30~60 g, <i>Cornu Bubali</i> 30 g, <i>P. radix Rubra</i> 30 g, <i>S. ningpoensis</i> Hemsl. 30 g, <i>F. suspense</i> 15 g, <i>Cortex Moutan Radicis</i> 15 g, <i>C. chinensis</i> Franch. 6 g, <i>Lophatheri Herba</i> 12 g, <i>D. nemorosa</i> 15 g, <i>G. uralensis</i> Fisch. 6 g |
| | Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g |
| | <i>A. lancea</i> : <i>Atractylodes lancea</i> , <i>M. officinalis</i> : <i>Magnolia officinalis</i> , <i>A. rugosa</i> : <i>Agastache rugosa</i> , <i>A. tsaoko</i> : <i>Amomum tsaoko</i> , <i>E. sinica</i> : <i>Ephedra sinica</i> , <i>N. incisum</i> : <i>Notopterygium incisum</i> , <i>Z. officinale</i> : <i>Zingiber officinale</i> , <i>A. catechu</i> : <i>Areca catechu</i> , <i>A. communis</i> : <i>Amygdalus communis</i> , <i>T. kirilowii</i> : <i>Trichosanthes kirilowii</i> , <i>R. palmatum</i> : <i>Rheum palmatum</i> , <i>D. nemorosa</i> : <i>Draba nemorosa</i> , <i>P. semen</i> : <i>Persicaria semen</i> , <i>P. ginseng</i> : <i>Panax ginseng</i> , <i>A. carmichaeli</i> : <i>Aconitum carmichaeli</i> , <i>C. officinalis</i> : <i>Cornus officinalis</i> , <i>R. pinelliae</i> : <i>Rhizoma pinelliae</i> , <i>C. pilosula</i> : <i>Codonopsis pilosula</i> , <i>A. propinquus</i> : <i>Astragalus propinquus</i> , <i>W. cocos</i> : <i>Wolfiporia cocos</i> , <i>A. villosus</i> : <i>Amomum villosus</i> , <i>D. setosa</i> : <i>Dryopteris setosa</i> , <i>C. paniculatum</i> : <i>Cynanchum paniculatum</i> , <i>E. fortune</i> : <i>Eupatorium fortune</i> , <i>A. macrocephala</i> : <i>Atractylodes macrocephala</i> , <i>A. asphodeloides</i> : <i>Anemarrhena asphodeloides</i> , <i>S. baicalensis</i> : <i>Scutellaria baicalensis</i> , <i>B. chinense</i> : <i>Bupleurum chinense</i> , <i>P. radix</i> : <i>Paeoniae radix</i> , <i>F. suspense</i> : <i>Forsythia suspense</i> , <i>A. carvifolia</i> : <i>Artemisia carvifolia</i> , <i>C. cyrtophyllum</i> : <i>Clerodendrum cyrtophyllum</i> , <i>G. uralensis</i> : <i>Glycyrrhiza uralensis</i> , <i>S. coicis</i> : <i>Semen coicis</i> , <i>R. japonica</i> : <i>Reynoutria japonica</i> , <i>V. officinalis</i> : <i>Verbena officinalis</i> , <i>R. phragmitis</i> : <i>Rhizoma phragmitis</i> , <i>A. mongholicus</i> : <i>Astragalus mongholicus</i> , <i>R. glutinosa</i> : <i>Rehmannia glutinosa</i> , <i>S. ningpoensis</i> : <i>Scrophularia ningpoensis</i> , <i>C. chinensis</i> : <i>Coptis chinensis</i> |

exogenous fever caused by cold evils in “Treatise on Febrile and Miscellaneous Diseases” by Zhang Zhongjing in the Han Dynasty. For this prescription, >300 chemical components and >200 blood components have been identified, and >790 potential targets have been initially predicted, confirming its therapeutic effect through acting on multi-components and multi-targets. Network pharmacology results showed that Qingfei Paidu decoction produced a multi-directional intervention on the occurrence and development of COVID-19.^[38] It may interfere with COVID-19 through multiple components targeting at a variety of signaling pathways.^[39] After long-term clinical observation in COVID-19 therapy, Qingfei Paidu decoction can block the development of light and ordinary types to heavy and critical types and effectively rescue heavy and critical patients.

Huashi Baidufang and Xuanfei Baidufang are effective prescriptions based on clinical observations of the academician teams of Huang Luqi and Zhang Boli in the treatment frontline of Wuhan, respectively. They showed good effects in blocking the development of disease and relieving symptoms, especially in shortening the course of the disease.

Shashen Maidong decoction can improve the immune function of rats with radiation pneumonitis by increasing the concentration of IFN- γ and decreasing the concentration of IL-4. It regulates the body's immune function and restores the stability of the internal environment possibly by increasing the relative ratio of IFN- γ /IL-4 to regulate Th1/Th2 immune imbalance.^[40] In the treatment of COVID-19, Shashen Maidong decoction is the recommended medication for patients in recovery stage.

SINGLE TRADITIONAL CHINESE MEDICINE AND ITS ACTIVE INGREDIENTS

Based on the recently announced diagnosis and treatment plan on COVID-19, we summarize the recommended TCMs and ingredients in the plan and screen out the commonly used medicinal materials to describe in detail [Table 7]. We hope to provide a reference for combating the epidemic and help the development of TCM. Moreover, the active ingredients

commonly used in the treatment of COVID and their mechanisms of action are listed in Table 8. Since the screening of active ingredients is very important for the development of TCM, many methods and technologies have been applied for the screening of active ingredients, such as the screening based on bioassay-guided fractionation, the screening based on serum pharmacochimistry and serum pharmacology, the screening based on metabonomics, the screening based on molecular recognition technology, and the screening based on computer virtual technology. The potential active components against SARS-CoV-2 mentioned in this paper are screened by molecular docking method, and their binding patterns and affinity were predicted.

Antipyretic and anti-inflammation

Bupleurum chinense

Bupleurum chinense has a long history of application in China. Studies have reported that the chemical constituents of *B. chinense* mainly include triterpene saponins, volatile oils, flavonoids, lignins, and phenylpropanol derivatives.^[41] The crude extracts and pure compounds obtained from *B. chinense* show various biological activities, such as anti-inflammatory, anti-viral, anticancer, antipyretic, antimicrobial, hepatoprotective, immunomodulatory, and neuroprotective effects.^[42] Saikosaponin A shows anti-inflammatory role by inhibiting the NF- κ B and NLRP3 signaling pathways and protective effect on ALI induced by LPS.^[43] Saikosaponin A can inhibit H1N1 virus replication, downregulate NF- κ B expression, and reduce caspase-3-dependent viral ribonucleoprotein nuclear export, showing strong anti-influenza virus activity.^[44] Saikosaponin C inhibits the synthesis of hepatitis B virus (HBV) pgRNA by targeting HNF1 α and HNF4 α .^[45] An *in vitro* experiment showed that Saikosaponins can inhibit human coronavirus 229E.^[46] Saikosaponin C also exhibits inhibitory activity against HBV.^[47] Saikosaponin b2 can effectively inhibit the entry of HCV.^[48] *B. chinense* volatile oil also exhibits obvious antipyretic and anti-inflammatory effects. Therefore, *B. chinense* and its constituents may be potential therapeutic drugs for COVID-19.

Table 5: Chinese herbal medicine decoctions for treating COVID-19 in various places of China

| Province | Decoctions |
|--------------|--|
| Hebei | Maxing Shigan decoction, Xiao Chaihu decoction, Wulingsan, Shegan Mahuang decoction, Xuanbai Cheng Qi decoction, Huang Lian Jiedu decoction, Jiedu Huoxue decoction, Sinijia Renshen decoction, Wang Shi Qing Shu Yiqi decoction, Erchen decoction |
| Shandong | Dayuan Yin, Maxing Shigan decoction, Liu Junzi Decoction, Shenfu decoction |
| Liaoning | Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>A. communis</i> Vas 10 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g Recommended prescription: <i>A. communis</i> Vas 10 g, <i>Gypsum Fibrosum</i> 30 g, <i>T. kirilowii</i> Maxim. 30 g, <i>R. palmatum</i> L. 6 g, <i>E. sinica</i> Stapf 6 g, <i>D. nemorosa</i> 10 g, <i>P. semen</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>A. catechu</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g Recommended prescription: <i>R. pinelliae</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>C. pilosula</i> (Franch.) Nannf. 15 g, <i>A. propinquus</i> Schischkin 30 g, <i>W. cocos</i> 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. villosum</i> Lour. 6 g Recommended prescription: <i>A. propinquus</i> Schischkin 15 g, <i>Radix Pseudostellariae</i> 15 g, <i>Lophatheri Herba</i> 15 g, <i>A. stricta</i> Miq. 15 g, <i>O. japonicus</i> (Linn. f.) Ker-Gawl. 15 g, <i>R. phragmitis</i> 20 g, <i>Trichosanthis Radix</i> 9 g, <i>P. odoratum</i> (Mill.) Druce 6 g, <i>I. cylindrica</i> 20 g, <i>G. uralensis</i> Fisch. 10 g |
| Heilongjiang | Sanren decoction, Huopu Xia Ling decoction, Maxing Shigan decoction, Qingqi Huatan decoction, Qingwen Baidu Yin, Jiedu Huoxue decoction, Zhuye Shigao decoction, Qing Zao Jiufei decoction |
| Jilin | Maxing Yigan decoction, Sheng Jiang San, Dayuan Yin, Maxing Shigan decoction, Xiao Chaihu decoction, Xuanbai Chengqi decoction, Huang Lian Jiedu decoction, Jiedu Huoxue decoction, Sinijia Renshen decoction |
| Gansu | Maxing Yigan decoction, Sheng Jiang San, Dayuanyin, Qianghuo Shengshi decoction, Maxing Shigan decoction, Yinqiaosan, Xuanbai Chengqi decoction, Huang Lian Jiedu decoction, Xi Jiao Dihuang decoction, Sinijia Renshen decoction, Buzhong Yiqi decoction, Chaihu Shugan San |
| Qinghai | Maxing Yigan decoction, Sheng Jiang San, Dayuanyin, Sang Xing decoction, Qingzao Jiufei decoction, Shashen Maidong decoction |
| Jiangxi | Qingfei Paidu decoction, Wen Fei Hua Xian decoction |
| Guangdong | Dayuanyin, Yinqiaosan, Sanren decoction, Maxing Shigan decoction, Qianjin Weijin decoction, Xiao Xian Xiong decoction, Shenfu decoction, Wangshi Qingshu Yiqi decoction, Shenling Baizhu San |
| Yunnan | Maxing Yigan Decoction, Sheng Jiang San, Dayuanyin, Maxing Shigan Decoction, Yinqiaosan, Xuanbai Chengqi Decoction, Huang Lian Jiedu Decoction, Jiedu Huoxue Decoction, Sinijia Renshen Decoction |
| Hunan | Sang Juyin, Yinqiaosan, Sang Bei Zhibu San, Wangshi Lianpu Yin, Huopu Xialing decoction, Maxing Shigan decoction, Sangbeisan, Xuanbai Chengqi decoction, Sheng Maisan, Sanshi decoction, Shenfu Longmu decoction, Shashen Maidong decoction, Huangqi Liu Junzi decoction |
| Hainan | Yinqiaosan, Qingwen Baidu Yin, Huopu Xialing decoction, Maxing Yigan decoction |
| Shanxi | Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>A. communis</i> Vas 9 g, <i>S. coicis</i> 18 g, <i>Alpinia kinensis</i> Gagnep 9 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 9 g, <i>M. officinalis</i> Rehd. et Wils. 12 g, <i>Pinelliae Rhizoma Praeparatum Cum Alumine</i> 9 g, <i>W. cocos</i> 12 g, polyporus 9 g, <i>S. baicalensis</i> Georgi 9 g, <i>F. suspense</i> 12 g, <i>G. uralensis</i> Fisch. 6 g Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 9 g, <i>Pinelliae Rhizoma Praeparatum Cum Alumine</i> 9 g, <i>M. officinalis</i> Rehd. et Wils. 9 g, <i>E. sinica</i> Stapf 6 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 9 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>N. incisum</i> Ting ex H. T. Chang 9 g, <i>C. chinensis</i> Franch. 6 g, <i>Z. officinale</i> Roscoe 9 g Recommended prescription: <i>E. sinica</i> Stapf 9–12 g, <i>A. communis</i> Vas 9 g, <i>Gypsum Fibrosum</i> 30 g, <i>T. kirilowii</i> Maxim. 30 g, <i>S. baicalensis</i> Georgi 12 g, <i>M. alba</i> 30 g, <i>Bulbus Fritillariae Thunbergii</i> 9 g, <i>E. japonica</i> Thunb. 9 g, <i>A. stricta</i> Miq. 12 g, <i>Cicadae Periostracum</i> 6 g Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>A. communis</i> Vas 9 g, <i>Gypsum Fibrosum</i> 30 g, <i>D. nemorosa</i> 9 g, <i>T. kirilowii</i> Maxim. 30 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>A. catechu</i> 12 g, <i>A. lancea</i> (Thunb.) DC. 9 g, <i>P. semen</i> 9 g, <i>R. palmatum</i> L. 6 g Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g Recommended prescription: <i>C. pilosula</i> (Franch.) Nannf. 15 g, <i>A. propinquus</i> Schischkin 30 g, <i>W. cocos</i> 15 g, <i>R. pinelliae</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 9 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 9 g, <i>A. villosum</i> Lour. 6 g Recommended prescription: <i>C. pilosula</i> (Franch.) Nannf. 15 g, <i>A. propinquus</i> Schischkin 30 g, <i>W. cocos</i> 15 g, <i>R. pinelliae</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 9 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 9 g, <i>A. villosum</i> Lour. 6 g |
| Sichuan | Yinqiaosan, Huopu Xialing decoction, Jing Fang Baidu San, Maxing Yigan decoction, Sheng Jiang San, Dayuanyin, Qingqi Huatan decoction, Maxing Shigan decoction, Xuanbai Chengqi decoction, Huang Lian Jiedu decoction, Jiedu Huoxue decoction, Sinijia Renshen Decoction, Zhuye Shigao decoction, Si Junzi decoction |
| Ningxia | Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g Recommended prescription: <i>A. communis</i> Vas 10 g, <i>Gypsum Fibrosum</i> 30 g, <i>T. kirilowii</i> Maxim. 30 g, <i>R. palmatum</i> L. 6 g, <i>E. sinica</i> Stapf 6 g, <i>D. nemorosa</i> 10 g, <i>P. semen</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>A. catechu</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g Recommended prescription: <i>P. ternate</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>C. pilosula</i> (Franch.) Nannf. 15 g, <i>A. propinquus</i> Schischkin 30 g, <i>W. cocos</i> 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. villosum</i> Lour. 6 g |
| Shanxi | Huoxiang Zhengqi San, Ginseng Baidu San, Yinqiaosan, Maxing Ganshi decoction, Daqing Long decoction, Qianjin Wei Jing Decoction, Xuanbai Chengqi Decoction, Shenfu decoction, Zhuye Shigao decoction, Maiwei Buzhong Yiqi decoction |

Contd...

Table 5: Contd...

| Province | Decoctions |
|----------|---|
| Beijing | <p>Recommended prescription: <i>A. mongholicus</i> Bunge 15 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>A. macrocephala</i> Koidz. 10 g, <i>S. divaricate</i> (Trucz.) Schischk. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>L. japonica</i> 15 g, <i>G. uralensis</i> Fisch. 10 g, <i>M. alba</i> 9 g, <i>S. baicalensis</i> Georgi 12 g</p> <p>Recommended prescription: <i>E. sinica</i> Stapf 10 g, <i>A. communis</i> Vas 9 g, <i>S. baicalensis</i> Georgi 15 g, <i>A. asphodeloides</i> 10 g, <i>Alpinia tonkinensis</i> Gagnep 6 g, <i>S. coicis</i> 30 g, <i>M. alba</i> 15 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>L. japonica</i> 15 g, <i>F. suspense</i> 15 g</p> <p>Recommended prescription: <i>Gypsum Fibrosum</i> 45 g, <i>E. sinica</i> Stapf 10 g, <i>A. communis</i> Vas 10 g, <i>L. japonica</i> 15 g, <i>A. asphodeloides</i> 10 g, <i>Cornu Bubali</i> 30 g, <i>Bulbus Fritillariae Thunbergii</i> 10 g, <i>T. kirilowii</i> Maxim. 30 g, <i>Lumbricus</i> 20 g, <i>D. nemorosa</i> 20 g, <i>P. radix</i> Rubra 20 g, <i>A. mongholicus</i> Bunge 20 g, <i>R. glutinosa</i> Libosch 30 g, <i>Cortex Moutan Radicis</i> 15 g</p> <p>Recommended prescription: <i>Radix Ginseng</i> 30 g, <i>A. mongholicus</i> Bunge 30 g, <i>A. carmichaeli</i> Debx. 15 g, <i>S. miltiorrhiza</i> Bunge 30 g, <i>O. japonicus</i> (Linn. f.) Ker-Gawl. 30 g, X. X. Chen 10 g, <i>Lumbricus</i> 15 g, <i>Panax notoginseng</i> (Burkill) F. H. Chen ex C. H. 9 g, <i>D. nemorosa</i> 15 g, <i>Bombyx mori</i> L. 15 g <i>Curcuma sichuanensis</i>, <i>A. lancea</i> (Thunb.) DC. 15 g, <i>polyporus</i> 30 g</p> |
| Shanghai | <p>Qingfei Paidu decoction</p> <p>Recommended prescription: <i>L. japonica</i> 15 g, <i>F. suspense</i> 15 g, <i>S. divaricate</i> (Trucz.) Schischk. 9 g, <i>S. baicalensis</i> Georgi 15 g, <i>Fructus arctii</i> 9 g, <i>P. grandiflorus</i> 9 g, <i>R. phragmitis</i> 18 g, <i>B. chinense</i> 9 g, <i>Citri Reticulatae Pericarpium</i> 9 g, <i>G. uralensis</i> Fisch. 6 g</p> <p>Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>Gypsum Fibrosum</i> 15 g, <i>A. communis</i> Vas 9 g, <i>N. incisum</i> Ting ex H. T. Chang 15 g, <i>D. nemorosa</i> 15 g, <i>D. setosa</i> 9 g, <i>Lumbricus</i> 15 g, <i>C. paniculatum</i> (Bunge) Kitagawa 15 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 15 g, <i>E. fortune</i> 9 g, <i>A. lancea</i> (Thunb.) DC. 15 g, <i>W. cocos</i> 45 g, <i>A. macrocephala</i> Koidz. 30 g, Jiao San Xian 9 g, <i>M. officinalis</i> Rehd. et Wils. 15 g, <i>A. catechu</i> 9 g, <i>A. tsaoko</i> Crevost et Lemarie 9 g, <i>Z. officinale</i> Roscoe 15 g</p> <p>Recommended prescription: <i>A. catechu</i> 10 g, <i>A. tsaoko</i> Crevost et Lemarie 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. asphodeloides</i> 10 g, <i>S. baicalensis</i> Georgi 10 g, <i>B. chinense</i> 10 g, <i>P. radix</i> Rubra 10 g, <i>F. suspense</i> 15 g, <i>A. carvifolia</i> 10 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>C. cyrtophyllum</i> Turcz. 10 g, <i>G. uralensis</i> Fisch. 5 g</p> <p>Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>Armeniacae Amarum Semen</i> 15 g, <i>Gypsum Fibrosum</i> 30 g, <i>S. coicis</i> 30 g, <i>A. lancea</i> (Thunb.) DC. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 15 g, <i>A. carvifolia</i> 12 g, <i>R. japonica</i> Houtt. 20 g, <i>V. officinalis</i> L. 30 g, <i>R. phragmitis</i> 30 g, <i>D. nemorosa</i> 15 g, <i>Citri Grandis Exocarpium</i> 15 g, <i>G. uralensis</i> Fisch. 10 g</p> <p>Recommended prescription: <i>A. lancea</i> (Thunb.) DC. 15 g, <i>Citri Reticulatae Pericarpium</i> 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>A. tsaoko</i> Crevost et Lemarie 6 g, <i>E. sinica</i> Stapf 6 g, <i>N. incisum</i> Ting ex H. T. Chang 10 g, <i>Z. officinale</i> Roscoe 10 g, <i>A. catechu</i> 10 g</p> <p>Recommended prescription: <i>E. sinica</i> Stapf 6 g, <i>A. communis</i> Vas 9 g, <i>Gypsum Fibrosum</i> 15 g, <i>G. uralensis</i> Fisch. 3 g, <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. 10 g, <i>M. officinalis</i> Rehd. et Wils. 10 g, <i>A. lancea</i> (Thunb.) DC. 15 g, <i>A. tsaoko</i> Crevost et Lemarie 10 g, <i>R. pinelliae</i> 9 g, <i>W. cocos</i> 15 g, <i>R. palmatum</i> L. 5 g, <i>A. mongholicus</i> Bunge 10 g, <i>D. nemorosa</i> 10 g, <i>P. radix</i> Rubra 10 g</p> <p>Recommended prescription: <i>Gypsum fibrosum</i> 30–60 g, <i>A. asphodeloides</i> 30 g, <i>R. glutinosa</i> Libosch 30–60 g, <i>Cornu Bubali</i> 30 g, <i>P. radix</i> Rubra 30 g, <i>S. ningpoensis</i> Hemsl. 30 g, <i>F. suspense</i> 15 g, <i>Cortex Moutan Radicis</i> 15 g, <i>C. chinensis</i> Franch. 6 g, <i>Lophatheri Herba</i> 12 g, <i>D. nemorosa</i> 15 g, <i>G. uralensis</i> Fisch. 6 g</p> <p>Recommended prescription: <i>P. ginseng</i> C. A. Mey 15 g, <i>A. carmichaeli</i> Debx. 10 g, <i>C. officinalis</i> Sieb. et Zucc. 15 g</p> |
| Tianjin | <p>Qingwen Baiduyin, Dayuanyin, Huopu Xialing decoction, Sheng Jiang San, Moxing Ganshi decoction, Xuanbai Chengqi decoction, Baihu decoction, Qing Ying decoction, Xiangsha Liu Junzi Decoction, Si Junzi decoction</p> |
| Guizhou | <p>Maxing Yigan decoction, Dayuan Yin, Sheng Jiang San, Xiang Ru Yin, Sanren decoction, Chaihu Dayuan Yin, Moxing Shigan decoction, Chuwen Huadu decoction, Xuanbai Chengqi Decoction, Sanxiaoyin, Huopu Xialing decoction, Qianjin Wei Jing decoction, Sanzi Yang Qin decoction, Sheng Yang Yiwei decoction, Xiangsha Liu junzi decoction, Shensu Longqi decoction, Poge Jiuxin decoction, Gua Louxie Baibanxia decoction, Danshenyin, Liu junzi decoction, Lizhong decoction, Maimen Dong decoction, Chaihu Qingzao decoction</p> |

A. stricta: *Adenophora stricta*, *O. japonicus*: *Ophiopogon japonicus*, *P. odoratum*: *Polygonatum odoratum*, *I. cylindrica*: *Imperata cylindrical*, *M. alba*: *Morus alba*, *E. japonica*: *Eriobotrya japonica*, *P. ternate*: *Pinellia ternate*, *S. divaricate*: *Saposhnikovia divaricate*, *P. grandiflorus*: *Platycodon grandiflorus*, *A. lancea*: *Atractylodes lancea*, *M. officinalis*: *Magnolia officinalis*, *A. rugosa*: *Agastache rugosa*, *A. tsaoko*: *Amomum tsaoko*, *E. sinica*: *Ephedra sinica*, *N. incisum*: *Notopterygium incisum*, *Z. officinale*: *Zingiber officinale*, *A. catechu*: *Areca catechu*, *A. communis*: *Amygdalus communis*, *T. kirilowii*: *Trichosanthes kirilowii*, *R. palmatum*: *Rheum palmatum*, *D. nemorosa*: *Draba nemorosa*, *P. semen*: *Persicaria semen*, *P. ginseng*: *Panax ginseng*, *A. carmichaeli*: *Aconitum carmichaeli*, *C. officinalis*: *Cornus officinalis*, *R. pinelliae*: *Rhizoma pinelliae*, *C. pilosula*: *Codonopsis pilosula*, *A. propinquus*: *Astragalus propinquus*, *W. cocos*: *Wolfiporia cocos*, *A. villosus*: *Amomum villosus*, *D. setosa*: *Dryopteris setosa*, *C. paniculatum*: *Cynanchum paniculatum*, *E. fortune*: *Eupatorium fortune*, *A. macrocephala*: *Atractylodes macrocephala*, *A. asphodeloides*: *Anemarrhena asphodeloides*, *S. baicalensis*: *Scutellaria baicalensis*, *B. chinense*: *Bupleurum chinense*, *P. radix*: *Paeoniae radix*, *F. suspense*: *Forsythia suspense*, *A. carvifolia*: *Artemisia carvifolia*, *C. cyrtophyllum*: *Clerodendrum cyrtophyllum*, *G. uralensis*: *Glycyrrhiza uralensis*, *S. coicis*: *Semen coicis*, *R. japonica*: *Reynoutria japonica*, *V. officinalis*: *Verbena officinalis*, *R. phragmitis*: *Rhizoma phragmitis*, *A. mongholicus*: *Astragalus mongholicus*, *R. glutinosa*: *Rehmannia glutinosa*, *S. ningpoensis*: *Scrophularia ningpoensis*, *C. chinensis*: *Coptis chinensis*, *L. japonica*: *Lonicera japonica*, *S. miltiorrhiza*: *Salvia miltiorrhiza*

Scutellaria baicalensis Georgi.

Flavonoids and their glycosides are the main active ingredients of *Scutellaria baicalensis* Georgi. Baicalin exerts antipyretic and anti-inflammatory effects by inhibiting the N-methyl-D-aspartate receptor-dependent hydroxyl radical pathway in the hypothalamus and reducing TNF- α .^[49] Baicalin

can also increase the expression of caspase-3 in the pancreas of severe acute pancreatitis rats and inhibit the expression of TNF- α mRNA and P-selectin protein.^[50] Baicalein inhibits cyclooxygenase-2 (COX-2) gene expression by inhibiting C/EBP-beta DNA binding activity, thereby playing a role in inhibiting inflammation.^[51] Baicalin shows anti-inflammatory, antioxidant, and antiadipogenic effects in atherosclerosis in

Table 6: Composition, predicted active ingredients, and action mechanism of the frequently used Chinese patent medicines and decoctions

| Chinese medicine | Composition | Predicted active ingredient | Action mechanism |
|-----------------------------------|---|---|---|
| Lianhua Qingwen capsule (granule) | 13 herbs, including <i>L. japonica</i> Flos, <i>Ephedrae Herba</i> , <i>Isatidis Radix</i> , <i>Armeniacae Semen Amarum</i> , and <i>Rhei Radix et Rhizoma</i> , etc. | Quercetin, luteolin, rutin, wogonin, kaempferol, naringenin, lonicerin, salidroside, etc. | Inhibiting the virus infection and replication |
| Huoxiang Zhengqi capsule | 11 herbs, including <i>Poria</i> , <i>Pogostemonis Herba</i> , <i>Arecae Pericarpium</i> , etc. | Quercetin, wogonin, stigmasterol, robinin, licorice glycoside E, kaempferol, etc. | Inhibiting the virus invasion and replication |
| Xue Bijing injection | 5 herbs, including <i>C. tinctorius</i> L., <i>Paeoniae</i> , <i>L. chuanxiong</i> hort, <i>S. miltiorrhiza</i> Bunge, <i>Angelica sinensis</i> | Hydroxysafflor yellow A, chlorogenic acid and salvianolic acid B, quercetin, rutin, kaempferol, etc. | Inhibiting the virus replication by PI3K-Akt signal pathway |
| Jinhua Qinggan granule | 12 herbs, including <i>Ephedrae Herba</i> , <i>L. japonica</i> Flos, <i>Gypsum Fibrosum</i> , <i>Armeniacae Semen Amarum</i> , etc. | Lonicerin, baicalein, quercetin, naringenin, wogonin, coptisine, isorhamnetin, kaempferol, licochalcone A, etc. | inhibiting the virus invasion |
| Qingfei Paidu Decoction | 21 herbs, including <i>Glycyrrhizae Radix et Rhizoma</i> , <i>Ephedrae Herba</i> , <i>Scutellariae Radix</i> , <i>Pogostemonis Herba</i> , <i>Armeniacae Semen Amarum</i> , <i>Asteris Radix et Rhizoma</i> , and <i>Polyporus</i> , etc. | Luteolin, quercetin, patchouli alcohol, baicalein, kaempferol, naringenin, shionone, isorhamnetin, glycyrrhizic acid, tussilagone, etc. | Inhibiting the virus replication |
| Huashi Baidu Decoction | 14 herbs, including <i>Ephedrae Herba</i> , <i>Glycyrrhizae Radix et Rhizoma</i> , <i>Armeniacae Semen Amarum</i> , <i>Pogostemonis Herba</i> , etc. | Licorice phenol, baicalein, etc. | Inhibiting the virus replication |

L. japonica: *Lonicera japonica*, *C. tinctorius*: *Carthamus tinctorius*, *L. chuanxiong*: *Ligusticum chuanxiong*, *S. miltiorrhiza*: *Salvia miltiorrhiza*

Table 7: Frequency of single Chinese medicine used at present

| Chinese medicine | Frequency |
|--|-----------|
| <i>A. rugosa</i> (Fisch. et Mey.) O. Ktze. | 44 |
| <i>A. tsaoko</i> Crevost et Lemarie | 43 |
| <i>A. communis</i> Vas | 38 |
| <i>D. nemorosa</i> | 37 |
| <i>G. uralensis</i> Fisch. | 34 |
| <i>A. lancea</i> (Thunb.) DC. | 28 |
| <i>E. sinica</i> Stapf | 27 |
| <i>F. suspense</i> | 20 |
| <i>W. cocos</i> | 18 |
| <i>P. ginseng</i> C. A. Mey | 18 |
| <i>A. catechu</i> | 18 |
| <i>M. officinalis</i> Rehd. et Wils. | 17 |
| <i>B. chinense</i> | 16 |
| <i>R. palmatum</i> L. | 15 |
| <i>T. kirilowii</i> Maxim. | 15 |
| <i>Citri Reticulatae Pericarpium</i> | 14 |
| <i>A. propinquus</i> Schischkin | 10 |
| <i>S. baicalensis</i> Georgi | 8 |
| <i>L. japonica</i> | 4 |

A. rugosa: *Agastache rugosa*, *A. tsaoko*: *Amomum tsaoko*, *A. communis*: *Amygdalus communis*, *D. nemorosa*: *Draba nemorosa*, *G. uralensis*: *Glycyrrhiza uralensis*, *A. lancea*: *Atractylodes lancea*, *E. sinica*: *Ephedra sinica*, *F. suspense*: *Forsythia suspense*, *W. cocos*: *Wolfiporia cocos*, *P. ginseng*: *Panax ginseng*, *A. catechu*: *Areca catechu*, *M. officinalis*: *Magnolia officinalis*, *B. chinense*: *Bupleurum chinense*, *R. palmatum*: *Rheum palmatum*, *T. kirilowii*: *Trichosanthes kirilowii*, *A. propinquus*: *Astragalus propinquus*, *S. baicalensis*: *Scutellaria baicalensis*, *L. japonica*: *Lonicera japonica*

a dose-dependent manner by inhibiting the NF- κ B and p38 MAPK signaling pathways.^[52] Dinda *et al.* described in detail

the antioxidant and anti-inflammatory effects of baicalin and baicalein and the molecular mechanisms of chemoprophylaxis and chemotherapy in the treatment of inflammation-related diseases.^[53] Moreover, baicalin shows low toxicity and high efficacy against Chikungunya virus (CHIKV), suggesting its potential as an antiviral agent for CHIKV infection.^[54] For human immunodeficiency virus type 1 (HIV-1),^[55,56] H1N1 virus,^[57] coxsackievirus B3,^[58] human T-cell leukemia virus type I,^[59] chronic HBV,^[60] enterovirus 71 (EV71),^[61] Duck hepatitis A virus type 1,^[62] respiratory syncytial virus,^[63] Newcastle disease virus,^[64] dengue virus (DENV),^[65] and Zika virus (ZIKV),^[66] baicalein exhibits relatively good inhibitory effect on all of these viruses. Recently, researchers found that the ethanolic extract of *S. baicalensis* Georgi. can inhibit the activity of SARS-CoV-2 3CLpro *in vitro*.^[67] Besides, in Vero cells, it also inhibited the replication of SARS-CoV-2 with an EC₅₀ of 0.74 μ g/mL.^[67] Furthermore, they also found that baicalein intensively inhibited the activity of SARS-CoV-2 3CLpro activity with an IC₅₀ of 0.39 μ M.^[67] In another study, baicalin and baicalein were determined to the first class of noncovalent and nonpeptidomimetic inhibitors of SARS-CoV-2 3CLpro, which showed strong antiviral activity in cell-based systems.^[68] It is worth noting that the binding pattern of baicalein and SARS-CoV-2 3CLpro determined by X-ray protein crystallography is significantly different from those of known inhibitors.^[68] Baicalein is secured to the core of the substrate-binding pocket by interacting with two catalytic residues (the critical S1/S2 subsite and the oxyanion loop), thereby preventing the peptide substrate from approaching the active site.^[68] These studies highlight the great potential of *S. baicalensis* Georgi. and baicalein as anticoronavirus drugs. Baicalin is shown to have a high binding affinity for

Table 8: The potential active components and mechanism of the representative COVID-19 treatment

| The common potential active components | Mechanism of action | Molecular modeling study |
|--|---|--------------------------|
| Baicalin | Inhibition of 3CLpro | Molecular docking |
| Luteolin | It has a good affinity with NSP15 | |
| Glycyrrhizin | Inhibition of virus replication, adsorption, and infiltration | Molecular docking |
| Quercetin | Inhibition of 3CLpro | Molecular docking |
| Hesperidin | Inhibition of 3CLpro | Molecular docking |
| Emodin | It inhibits the 3a protein to reduce the release of the virus | Molecular docking |
| Andrographolide | Inhibition of 3CLpro | Molecular docking |
| Tanshinone | Inhibition of 3CLpro and PLpro | Molecular docking |
| Shikonin | Inhibition of 3CLpro | Molecular docking |
| Kaempferol | Inhibition of 3CLpro and PLpro | Molecular docking |
| Naringenin | It is acting on MAPK1 | Molecular docking |
| Lonicerin | Its target is RELA | Molecular docking |
| Licorice glycoside E | Its target is IL4 | Molecular docking |
| Rutin | Its target is LTA4H | Molecular docking |

Papain-like proteinase (PLpro) protein, indicating its potential utility in treating SARS-CoV-2 infection.^[69]

Ephedra sinica Stapf.

Ephedra sinica Stapf. has been used for the treatment of asthma, antipyretics, and rheumatoid arthritis and mainly contains six ephedrine alkaloids as its pharmacologically active ingredients: (-)-ephedrine, (+)-pseudoephedrine, (-)-N-methylephedrine, (+)-N-methylpseudoephedrine, (-)-norephedrine, and (+)-norpseudoephedrine.^[70] *E. sinica* extract can downregulate the phosphorylation of Raf/MEK1/2/ERK1/2, thereby inhibiting the expression of COX-2 and matrix metalloproteinase-1 (MMP-1) induced by ultraviolet B.^[71] COX-2 and MMP-1 are the representative signs of skin inflammation and photoaging, respectively.^[71] *Ephedra* A and B from *E. sinica* roots can inhibit the activation of NF-κB in RAW 264.7 macrophages, thereby inhibiting LPS-induced inflammatory mediators.^[72] *E. sinica* Stapf. has an inhibitory effect on the growth of influenza A/PR/8 virus in the MDCK cells.^[73] *E. sinica* Stapf. is one of the core drugs of Chinese medicine-mediated *Mycoplasma pneumoniae* pneumonia treatment.^[74] The type A proanthocyanidins in *E. sinica* stems have antibacterial activity.^[75] *Ephedra* polysaccharides offer a potential treatment for COPD by modulating inflammatory cytokines and TGF-β1/Smad2 pathway to reduce airway and lung inflammation.^[76]

Citri Reticulatae Pericarpium/Citri Grandis Exocarpium

Citri Reticulatae Pericarpium and *Citri Grandis Exocarpium* are one of the main medicinal materials recommended by the Chinese medicine section of the “Diagnosis and Treatment Protocol for Novel Coronavirus Pneumonia (Trial Version 7).” Their peels are rich in flavonoids, such as hesperidin and hesperetin. Study has shown that hesperidin targets the binding interface between S protein and ACE2.^[69] Hesperidin may disrupt the interaction between ACE2 and RBD.^[69] Hesperetin, as the main *in vivo* metabolite of hesperidin, can inhibit SARS-CoV 3CLpro cleavage activity in a dose-dependent

manner in a cell-based assay, with an IC₅₀ of 8.3 μM.^[77] Molecular docking studies also showed that hesperidin possessed very high binding affinity with 3CLpro,^[78,79] S protein RBD, and ACE2.^[78] Furthermore, hesperidin can firmly bind to SARS-CoV-2 Mpro.^[80,81] These studies have explained to a certain extent the mechanism by which *Citri Reticulatae Pericarpium* and *Citri Grandis Exocarpium* display a potent efficiency in the prevention and treatment of COVID-19.

Camellia sinensis (L.) O. Ktze.

Camellia sinensis (L.) O. Ktze. has been used in China for thousands of years. For a long time, it is not only a daily drink for people but also as a classic prescription in TCMs for clearing heat and detoxifying. (-)-Epigallocatechin gallate (EGCG), belonging to catechins, is the main component of *C. sinensis* (L.) O. Ktze. EGCG has antioxidation, antiviral, anticancer, and antiradiation damage activities. EGCG is currently reported to have an inhibitory effect on human papillomavirus,^[82] herpes simplex virus (HSV),^[83-86] adenovirus,^[87] HBV,^[88] HCV,^[89-91] ZIKV,^[92-95] HIV,^[96-98] Ebola virus,^[99] influenza virus,^[100-103] SARS-CoV,^[104] etc., Through computer screening, Wu *et al.* found for the first time that EGCG showed a strong interaction with SARS-CoV-2 PLpro.^[69] Moreover, EGCG and ACE2 also have a good affinity.^[69] Later, they discovered that EGCG and furin have a strong interaction.^[105] EGCG and epigallocatechin (EGC) were found to have good enzyme inhibitory activity against SARS-CoV 3CLpro, and molecular docking showed that EGC can produce hydrogen-binding interactions with multiple amino acid residues in the active pocket of 3CLpro.^[104] Researchers recently found that EGCG can bind to the SARS-CoV-2 spike protein, preventing the Spike protein from binding to the ACE2 receptor, thereby preventing the virus from entering the host cells.^[106] In addition, EGCG has the effect of promoting the dissociation of the spike protein that has bound to ACE2.^[106] It has been used as a clinical adjuvant therapy in patients with SARS-CoV-2 infection in Kunming Third Hospital.^[106] Moreover, two studies have also found that EGCG has a good binding affinity with 3CLpro and PLpro.^[107,108] These results

indicate that EGCG may prevent viral protein maturation and RNA replication by targeting one or more key enzymes of SARS-CoV-2, thereby displaying antiviral effect. In addition, it may also act on human ACE2 or furin to prevent SARS-CoV-2 from entering the host cells. The above findings have laid a theoretical foundation for the in-depth study of EGCG as a potential COVID-19 therapeutic drug.

Lonicera japonica

Lonicera japonica is one of the components in Jinye Baidu granule, Lianhua Qingwen capsule, and Jinhua Qinggan granule. Researchers discovered an atypical miRNA in *L. japonica*: MIR2911, which has broad-spectrum targeting anti-influenza virus activity. The results show that MIR2911 can target the mRNA of influenza viruses (H1N1, H5N1, and H7N9), thereby inhibiting virus replication.^[109] Luteolin, a flavonoid, is a major constituent of *L. japonica*, with a variety of pharmacological activities. Luteolin is mainly used for the treatment of cough, expectoration, and infectious diseases. Many studies have shown that it can inhibit influenza A virus, HIV, human herpes virus, and Japanese encephalitis virus.^[110-113] Luteolin was also reported to inhibit the replication of DENV by inhibiting furin.^[114] Study has found that luteolin has a good affinity with NSP15 (mfScore = -57.11, Score = -33.55),^[69] suggesting that luteolin is a potential drug candidate against SARS-CoV-2. Moreover, some studies have pointed out that the binding ability of luteolin to ACE2 is higher than that of lopinavir, ritonavir, and ribavirin, and its binding ability to Mpro is similar to the above three antiviral drugs.^[21] Luteolin was also speculated to inhibit SARS-CoV-2 replication by inhibiting furin,^[114] a new target for the treatment of SARS-CoV-2.^[105] Luteolin could cross the blood-brain barrier,^[113] suggesting that it may also have a therapeutic effect on the central nervous system infections caused by SARS-CoV-2. *L. japonica* also contains other antiviral active ingredients, such as chlorogenic acid and kaempferol-3-O-rutinoside, the latter of which has a good affinity with PLpro and may be a potential anti-SARS-CoV-2 drug candidate.^[69]

Immunoregulation

Astragalus mongholicus Bunge

Astragalus mongholicus Bunge is a TCM with immunomodulating effect. There is evidence that *Astragalus mongholicus* Bunge can change the response of LPS-stimulated macrophages and has an immunomodulatory effect, reducing the production of TNF- α , IL-6, IL-10, and IL-12 in a dose-dependent manner.^[115] *Astragalus mongholicus* Bunge extract can increase macrophage migration and release of immune response medium through heparanase (HPA), thereby activating the immune response of macrophages.^[116] The most important active ingredients of *Astragalus mongholicus* Bunge in regulating immune function have been reported to include *Astragalus* polysaccharides (APS), astragalosides, and *Astragalus* flavones. APS showed strong immunomodulatory activity by stimulating macrophages and could be used as an immunotherapy adjuvant.^[117] (1) APS strongly inhibits the

activation of NF- κ B and downregulates the phosphorylation of ERK and JNK in LPS-stimulated macrophages, an important signaling pathway involved in the production of TNF- α and IL-1 β , indicating that APS can inhibit the activation of NF- κ B and phosphorylation of ERK and JNK, and thereby reduce the production of TNF- α and IL-1 β .^[118] APS can also reduce the replication of H9N2 avian influenza virus (H9N2 AIV) and promote early humoral immunity in young chickens.^[119] APS inhibits porcine circovirus type 2 replication by inhibiting oxidative stress and blocking the NF- κ B pathway.^[120] Through the analysis of the currently released diagnosis and treatment plan, it is found that *Astragalus mongholicus* Bunge is one of the frequently used TCMs. In this fight against COVID-19, *Astragalus mongholicus* Bunge shows a potent effect on enhancing immunity and respiratory resistance.

Glycyrrhiza uralensis Fisch.

Glycyrrhiza uralensis Fisch. and its main active ingredients including glycyrrhizin, glycyrrhizic acid, glycyrrhetic acid, and glycyrrhizin polysaccharide show potent immunomodulatory effects. Glycyrrhizin shows multiple immunomodulatory activities and interferes with the immune response by targeting dendritic cells (DCs). Studies have shown that glycyrrhizin can upregulate the expression of CD80, CD86, and MHCII on the surface of DCs and increase the production of IL-12.^[121] In addition, glycyrrhizin also enhanced the proliferation of allogeneic T-cells, increased the expression of IFN- γ and IL-10, reduced the production of IL-4, and thereby regulated the Th1-type immune response.^[121] Glycyrrhizin is also a promoter of late signal transduction of IL-2 production by T-lymphocytes.^[122] IL-12 plays an important role in the development of Th1 cell-mediated immune response, and glycyrrhizin can enhance the production of IL-12 in peritoneal macrophages.^[123] Glycyrrhizin can also enhance the production of IL-10 by liver DCs in hepatitis mice.^[124] Other studies have also shown that glycyrrhizin can enhance the activity of NK cells/NKT cells.^[125] The antiviral activity of glycyrrhizin has also been confirmed.^[126] Glycyrrhizin and its modified compounds exhibit inhibitory activity against HIV-1 and HSV-1.^[127] A study evaluated the antiviral potential of 6-azauridine, ribavirin, mycophenolic acid, pyrazolin, and glycyrrhizin against two clinical isolates of coronaviruses (FFM-1 and FFM-2) in SARS patients.^[128] The results showed that among all compounds, glycyrrhizin possessed obvious inhibition on SARS-associated viruses.^[128] Furthermore, one study indicates that glycyrrhizin could bind to ACE2.^[129] Luo *et al.* discussed the potential of glycyrrhizin in the treatment of COVID-19 from the perspective of pharmacological effects, including downregulation of pro-inflammatory cytokines, binding to ACE2, inhibition of thrombin, inhibition of intracellular reactive oxygen species accumulation, and suppression of excessive production of airway exudate.^[130] Recently, Zhu *et al.* found that in Vero E6 cells, liquiritin significantly inhibited the replication of SARS-CoV-2 with an EC₅₀ of 2.39 μ M.^[131] They pointed out that liquiritin could mimic type I interferon, thereby exerting antiviral functions.^[131]

CONCLUSION

Since the outbreak of COVID-19, scientists have made their efforts to do a lot of research and have gained great progress in the research of new drugs and vaccines. Small molecule drugs such as remdesivir and chloroquine have entered clinical research. However, the law of new drug development determines that the discovery of new anti-SARS-CoV-2 drugs needs more patients. In the fight against COVID-19, TCM has played an important role and shown many advantages in intervening sudden infectious diseases such as viral pneumonia. Lianhua Qingwen capsule shows good efficacy in treating light and ordinary patients and obvious curative effect in relieving fever, cough, and fatigue. Xuebijing injection can promote the elimination of inflammatory factors and is mainly used for the early and mid-term treatment of severe and critically ill patients. Qingfei Paidu decoction plays an important role in preventing the development of patients from light and normal type to severe and critical type. At the same time, it also shows obvious effects on the rescue process of heavy and critical patients. In the diagnosis and treatment plan, *B. chinense*, *S. baicalensis* Georgi., *Astragalus mongholicus* Bunge, etc., also have a high frequency of use and important clinical value. TCM can not only be used to prevent and block the course of disease but also restore the body's resistance and promote rehabilitation. Then, TCM contains a variety of active ingredients, which has multi-target effects and is not easy to develop drug resistance. More importantly, many kinds of TCMs also have powerful anti-inflammatory and immune regulatory effects in their traditional use. Therefore, it is an important strategy to making full use of the advantages of TCM and combine with Western medicine for disease therapy. In the treatment of COVID-19 at critical phases, integrating TCM and Western medicine makes it easier and faster to control the disease, suppress cytokine storms, and reduce the mortality of critical patients. Therefore, it is necessary to give full play to TCM in the treatment of pneumonia caused by new coronavirus, strengthen the integration of TCM and Western medicine, and carry out scientific and standardized prevention and treatment by using TCM.

Although TCM has achieved good clinical results, some issues still deserve attention. The most important point is that the composition of TCM is relatively complex, and its efficacy and mechanism of action also need to be further clarified by clinical trials and in-depth pharmacological research. With the development of computer-aided drug discovery, scientists can screen effective small molecules from TCM based on the protein structures of disease targets, so as to provide clear evidence for the study on efficacy of prescriptions and the optimization of prescriptions in the clinic. In short, the multi-component and multi-target characteristics of TCM make it have great advantages and high clinical value in the treatment of COVID-19.

Acknowledgments

Nil.

Financial support and sponsorship

This work was financially supported by National

Mega-project for Innovative Drugs (grant number 2019ZX09721001-004-007), National Natural Science Foundation of China (NSFC) (NOs. 81773594, U1803122, U1703111, 81473254, and 81773637), the Fundamental Research Fund for the Central Universities (HUST COVID-19 Rapid Response Call, No. 2020kfyXGYJ037, China), and Liaoning Revitalization Talents Program (NO. XLYC1807182).

Conflicts of interest

There are no conflicts of interest.

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