

# Traditional Chinese medicine for combating COVID-19

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COVID-19 is an emerging, rapidly evolving pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Due to its distinctive features in etiology, epidemiology and pathology, this infectious disease poses considerable diagnostic and therapeutic challenge [1]. Patients with COVID-19 mainly receive supportive care and symptom management, since there is no specific antiviral treatment yet for COVID-19. In addition to the principles of early quarantine, early detection, and early treatment [2], the early inclusion of traditional Chinese medicine (TCM) to the Chinese protocol, i.e., the integration of TCM and Western medicine, also contributed to the rapid containment of COVID-19 in China. TCM not only has a long history against the epidemic diseases but also plays a significant role in combating COVID-19.

## Clinical practice

After the outbreak of COVID-19, the National Health Commission of China has issued seven editions of diagnosis and treatment protocols. Traditional Chinese medicine treatment was included in the protocol (3rd edition), which was later upgraded and modified to better adapt to the actual conditions. As of March 30, 2020, the TCM therapies were involved in 74 886 confirmed cases, 92% of the total confirmed cases. The early TCM intervention in China, with its advantages of well-documented clinical practice in preventive, individualized, and multi-target treatment of disease, improved symptoms in patients with COVID-19, sped up the patients' recovery, prevented mild or moderate cases from developing into severe ones, and helped alleviate the panic and anxiety of the public under the epidemic situation. The model of

makeshift cabin hospitals [3] has been used, first in China and later in many countries, to meet the treatment needs of COVID-19 patients. In the TCM-oriented makeshift hospital led by Zhang Boli, an academician of the Chinese Academy of Engineering, no patients developed into severe conditions after receiving comprehensive TCM therapies (Chinese herbal medicine, massage, Guasha-scraping, point application, and exercise of Taiji/Baduan-jin). The "Wuchang pattern" proposed by Tong Xiaolin, an academician of the Chinese Academy of Sciences and leader of the National TCM Expert Task Force has been proved effective in curbing the spread of the epidemic. This pattern used TCM to prevent and control the epidemic at a community level in the face of major public health emergencies, especially when medical resources are in short supply and no specific medicine is available. Such a pattern bought more time for patients to be treated and reduced mortality and severe illness. According to Huang Luqi, an academician of the Chinese Academy of Engineering and president of the Chinese Academy of Chinese Medical Sciences, three Chinese patent medicines and three herbal formulas have been screened for the COVID-19 treatment. The three Chinese patent medicines (approved by the National Medical Products Administration to list COVID-19 as an additional indication) are *Lianhua Qingwen Keli/Jiaonang* (Forsythiae and Honeysuckle Flower Pestilence-Clearing Granules/Capsules), *Jinhua Qinggan Keli* (Honeysuckle Flower Cold-Relieving Granules) and *Xuebijing* (Stasis-Resolving & Toxin-Removing) injection. The three herbal formulas are *Qingfei Paidu Fang* (Lung-Cleansing & Toxin-Removing Formula), *Huashi Baidu Fang* (Dampness-Transforming & Toxin-Removing Formula) and *Xuanfei Baidu Fang* (Lung-Dispersing and Toxin-Removing Formula). To date, *Lianhua Qingwen Zhiji* (Forsythiae and Honeysuckle Flower Pestilence-Clearing Preparations) have been registered in some countries like Thailand and Ecuador and are now waiting to be registered in more countries such as

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Russia and Spain.

According to available clinical data, TCM has shown four clinical advantages in COVID-19 treatment. First, for mild or moderate cases, it could significantly shorten the negative conversion time of SARS-CoV-2 nucleic acid, the median duration of fever, and the time to defervescence as well as reduce the occurrence of severe or critically ill conditions. Second, for severe or critically ill cases, Chinese medicine injection could stabilize the oxygen saturation, inhibit inflammatory reaction, decrease exudative lesions, block or contain cytokine storm, and reduce the use of supportive care and antibiotics. Third, for patients in the convalescent period, it could improve symptoms, speed up the recovery, alleviate pulmonary inflammation, decrease adhesion, and help with functional recovery of damaged organs. Lastly, it could substantially reduce the cost of treatment [1].

Ever since the outbreak of COVID-19, in addition to the frontline fight against COVID-19, TCM doctors and researchers have been actively engaged in clinical studies including randomized controlled trials [4]. The results of several published reports have suggested the beneficial effect of TCM in COVID-19 treatment [4–6]. However, there are still many limitations in the study design and quality, especially in the context of the epidemic. The Chinese version of *Guidance for Managing Ethical Issues in Infectious Disease Outbreaks* was officially released on February 19, 2020, translated by the Ethics Review Committee of the World Federation of Chinese Medicine Societies and published by the China Press of Traditional Chinese Medicine.

## Historical experience

Although COVID-19 is an emerging infectious disease, it is not accidental that TCM plays a role in its treatment. In ancient times, although there was no concept of virus in traditional Chinese medicine, the struggle against pestilence including viral infectious diseases had been going on for thousands of years. The understanding of pestilence has been documented throughout the history of traditional Chinese medicine. Effective measures and formulas have been recorded in many TCM classics, to name a few, *Huangdi Neijing* (Yellow Emperor's Internal Classic), *Shanghan Lun* (Treatise on Cold Damage), *Zhouhou Beiji Fang* (Emergency Formulas to Keep Up One's Sleeve), *Qianjin Yaofang* (Important Formulas Worth a Thousand Gold Pieces), *Wenyi Lun* (Treatise on Pestilence), *Shanghan Wenyi Taobian* (Systematic Differentiation of Cold Damage and Warm Epidemics), and *Wenbing Taobian* (Systematic Differentiation of Warm Diseases). The decoction, Chinese patent medicine, acupuncture, moxibustion and other therapies of TCM have been used

mainly based on syndrome differentiation against pestilence.

In TCM, the essential principles for epidemic prevention and treatment are to reinforce healthy (anti-pathogenic) qi and remove pathogenic factors. To reinforce healthy qi means to regulate the body functions, achieve homeostasis, and maximize the body's self-defending ability to alleviate organ damage and speed up recovery. To remove pathogenic factors means to improve symptoms rapidly and prevent disease deterioration. Some examples of great creativity became the inspiration of modern medical breakthroughs, such as variolation for the eradication of smallpox, and the discovery of artemisinin for malaria. TCM has shown remarkable efficacies for the SARS outbreak in 2003: it could significantly improve recovery and reduce mortality and complications.

The recommended formulas in the Chinese protocol for the diagnosis and treatment of COVID-19 have all been proven effective in the long history of combating infectious diseases. These formulas have survived the passage of time and are still regarded as having great relevance in today's environment. The safety and efficacy of some formulas have been proven by evidence-based clinical trials, for example, *Ma Xing Shi Gan Tang* (Ephedra, Apricot Kernel, Gypsum and Licorice Decoction) — *Yin Qiao San* (Lonicera and Forsythia Powder) for H1N1 [7].

## Pharmacological studies

As a highly pathogenic coronavirus, SARS-CoV-2 is not only associated with its biological features, but also with the overwhelming inflammatory responses of the host. The network pharmacology studies and virtual screening of Chinese medicine/active natural products were performed on potential targets such as 3CL protease, papain-like protease (PLpro), RNA polymerase (RdRp) and spike glycoprotein (Spike) of SARS-CoV-2. The numerous Chinese materia medica (such as *Huang Qin* (Radix Scutellariae), *Sang Ye* (Folium Mori), *He Zi* (Flos Chrysanthemi), *Ju Hua* (Flos Chrysanthemi), *Tou Hua Liao* (Polygonum Capitatum), *Jin Yin Hua* (Flos Lonicerae Japonicae), *Sheng Jiang* (Radix et Rhizoma Rhei), and *Da Huang* (Radix et Rhizoma Rhei)) and their components were found to possess anti-SARS-CoV-2 activity or anti-inflammatory actions [8]. Natural products used in TCM remain to be a wealthy source for the identification of novel therapeutic compounds against SARS-CoV-2. For example, the research teams of Academician Rao Zihe and Academician Jiang Hualiang [9] have successfully analyzed the high spatial resolution structure of main protease (Mpro, a key protein in the virus' life cycle) and identified six lead drugs using virtual

and high-throughput screening on more than 10 000 conventional drugs, clinical drugs, and active natural products. It has been reported that some of the key compounds including scutellarein show potential for the treatment of coronavirus in humans. These findings provided new lead compounds, targets, and research strategies for further *in vivo* and *in vitro* studies on anti-SARS-CoV-2 drugs [10]. Some Chinese medicines have been tested at the cellular level in P3 laboratories, for example, the research team of Academician Zhong Nanshan has found that *Lianhua Qingwen* preparations can inhibit SARS-CoV-2 replication, repair cell injuries and inflammation caused by the virus, and prevent the virus attack [11].

## Future directions

TCM have evolved over time and played a significant role in epidemic control. It can blend in beneficial harmony with Western medicine, taking advantage of the best features of each system and compensating for certain weakness in each as well. Integrated TCM and Western medicine can better contain epidemic and reduce the health and social costs. Although COVID-19 has been contained in China, SARS-CoV-2 may not go away on its own, and we may still face the big challenge of a potential second wave of COVID-19. It is, therefore, important to learn from the clinical practice, study on how TCM works for COVID-19.

In TCM, COVID-19 falls under the category of pestilence. Early intervention is crucial to prevent its deterioration. TCM has two features that distinguish itself from allopathic medicine: one is holistic view and the other is pattern identification. The clinical value of TCM should be evaluated on the basis of TCM theory-based method as well as of evidence-based medicine. To respond to the concern of international medical community toward its safety and efficacy [12], it is more urgent than ever to provide compelling high-quality evidence.

To date, multidisciplinary approach, applied information science, systems biology, and complexity science have all been used to uncover the mysteries of life and diseases. These new approaches and theories can help us better understand the multiple component formulas, quality control, and multi-target effects of TCM. The answers to these key issues may promote further inheritance and innovation of TCM.

Biomedicine today is now moving into holistic or systems medicine, and traditional medicine is moving from regional toward global. In May 2019, a chapter of traditional medicine was included in the 11th revision of the World Health Organization's (WHO) International Statistical Classification of Diseases (ICD-11). In the spirit

of optimism, COVID-19 turns a big challenge into a good opportunity for China to further develop the age-old TCM and make new contributions to human health.

## Compliance with ethics guidelines

Kaixian Chen and Hongzhuan Chen declare no conflict of interests. This manuscript does not involve a research protocol requiring approval by the relevant institutional review board or ethics committee.

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