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Review Article

# Pharmacological Approaches to Investigate the Potential Herbal Medicine (Decoction) in Treating COVID-19

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## Abstract

Since December 2019, COVID-19 infection is spreading rapidly throughout worldwide. Every virus has a unique structure, behavior and infectious agent to create infections. The ayurvedic herbal medicine that seem to work for other viral infections should be tested against COVID-19. Qingfei Paidu decoction, Shuanghuanglian oral liquid (SHL), Mahuang Gancao Ganjiang Decoction (MGGD) and licorice are remedies that officials in China have recommended against COVID-19. Simultaneously, an Ayush Ministry advisory suggested that drinking decoction (ginger, turmeric, tulsi leaves) as 'home remedies' to boost immune system against Covid-19 in India. Likewise, Barleria lupulina leaves decoction is also one of the potential candidates which may be helpful for the treatment of COVID-19.

**Keywords:** *COVID-19; Decoction; SARS; Immunity; Treatment*

## Graphical Abstract

## Introduction

Severe acute respiratory syndrome (SARS) - Coronavirus has a single stranded RNA (ssRNA) genome with positive sense, an enveloped, staples are round or oval, often polymorphic, with a diameter of 60 - 140 nm. The new coronavirus belonging to the family *Coronaviridae*, subfamily *Orthocoronavirinae*, subgenus *sarbecovirus* [1]. Now Coronaviruses are divided into four genera as α-CoV, β-CoV, γ-CoV, δ-CoV, out of these, α-CoV and β-CoV are the viruses which infect on mammals. Among coronavirus species, β-CoV, SARS-CoV and MERS-CoV are severe which led to potentially fatal respiratory tract infections [2].

Some traditional based medicines are promoted as a general prescription in the diagnosis and treatment plan of COVID-19. All scientist around the world are finding an alternative and effective treatments against COVID-19, to help those people who got sick with the respiratory infection problem caused by COVID-19. High-risk populations exposed to COVID-19 patients includes family members, medical personnel, other people (close contact with COVID-19 patients) and residents living in COVID-19 outbreak areas, would probably get benefit by taking Chinese herbal medicine [3,4]. It is not a novel idea to use herbal medicine for illness but many herbs like licorice, ginger, tulsi, giloy, bishalyakarani and ephedra etc. have been used to treat respiratory infections such as flu and pneumoniae etc. In an ancient time, people were dependent on herbal medicine for the any type of ailment, who claimed herbal medicines have kept them healthy or improved their health conditions [5]. Health experts don't have enough data to support the use of herbal remedies for COVID-19 who are working in this concern.

## History

SARS-CoV is infecting a number of mammals and birds. Scientists suggested that now it has jumped from animals or birds towards humans as host. So that the samples are in open markets in Guangdong. After studies it was confirmed that masked palm civets harbored variants of the SARS-CoV [6]. A number of civets were slaughtered, therefore studies failed to find out the infection (domestic or wild civets). During experiment infection of civets with human SARS-CoV strain made these animal ill, then civets become an unlikely candidate for the reservoir species. Such type of species would be expected to harbor SARS-CoV without symptoms and could efficiently spread the virus. Bats are reservoir hosts of various zoonotic viruses such as SARS-CoV, Hendra and Nipah viruses. Two groups of international scientists demonstrated independently that Chinese's horseshoe bats are the natural reservoir of SARS-like coronavirus in 2005. The genome of human and bat SARS-CoV are aligned together, it has been found that 92% nucleotides are identical [7]. The sequences of amino acid for tall proteins are 96 to 100% identical except receptor-binding spike proteins (SARS-CoV) mediates both host cell surface attachment and membrane of spike protein, the virus 'jumped' from bat (host cell) to humans. In 2019, several evidences have proved the SARS-CoV are transmitted directly to human from bat (eaten by China people) in Wuhan, China. The region of the SARS-CoV spike protein that binds to the host receptor, angiotensin-converting enzyme-2 (ACE2), forms a shallow pocket into which ACE2 rests. The region of the spike protein that makes this pocket is called the receptor binding domain (RBD). Out of 220 amino acids within the RBD, only four differ between civet and human. Two of these amino acids appear to be critical compared to the spike RBD in the SARS-CoV that caused the 2002 - 2003 epidemic, the civet spike has a serine (S) substituted for a threonine (T) at position 487 (T487S) and a lysine (K) at position 479 instead of asparagine (N), N479K. This causes a 1,000-fold decrease in the capacity of the virus to bind to human ACE2. Furthermore, the spike found in SARS-CoV isolated from patients in 2003 and 2004 also has a serine at position 487 as well as a proline (P) for leucine (L) substitution at position 472 (L472P). These amino acid substitutions could be responsible for the reduced virulence of the virus found in these more recent infections.

## Origin and transmission of SARS-CoV-2

Some studies assumed that the SARS-CoV-2 was mainly originated from a seafood market of Wuhan, China where an unknown acute respiratory tract infection was come into light on 12 December 2019 [8,9]. After recognition of this infection (SARS-CoV-2), it was confirmed by scientist that bats are main reservoir of this virus [10,11] because the genome sequence of COVID-19 is 96.2% identical to bat CoV RaTG13, as it shares 79.5% identity to SARS-CoV [12]. Transmission through the respiratory tract droplets and close contact is the main route of transmission. Prolonged exposure in a relatively closed environment means that there is a possibility of aerosol transmission in the case of high-concentration aerosols.

## Symptoms

On the basis of current epidemiological survey, the incubation period is 14 - 21 days, mostly 3 - 7 days. The main symptoms are fever, cough, fatigue, nasal congestion, runny nose, sore throat and difficulty in respiration.

## Treatments

A number of Traditional Chinese Medicine were described to prevent and treat SARS in 2003 (WHO, 2004). Besides herbal formulas are also used to prevent and treat such type of infectious ail-

ment [13]. On the basis of current epidemiology, Traditional Chinese Medicine and Indian herbal medicine an over-all symptoms of COVID-19 pneumonia patients, has advised to prescribe treatment that are likely to be an effective which are following below.

### Qingfei Paidu decoction

The National Administration of Traditional Chinese Medicine has been instantly launched the special project, "research on screening effective prescriptions of traditional Chinese medicine (TCM) for prevention and treatment of COVID-19" on 27 January 2020 in Wuhan, China. As the first pilot areas, Shanxi Province, Hebei Province, Heilongjiang Province and Shaanxi Province carried out clinical observation of Qingfei Paidu decoction in preventing and treating COVID-19. The basic formula of Qingfei Paidu decoction has been given in table 1. The decoction of Qingfei Paidu, as the official recommended emergency epidemic prevention prescription, has a high degree of participation in the prevention and treatment of patients with COVID-19 in Shanxi Province and it has better clinical efficacy in improving clinical symptoms and alleviating disease progression. According to the official report, the total effective rate of clinical treatment for 214 patients is more than 90%, Qingfei Paidu decoction has definite curative effect in preventing and improving the clinical symptoms of patients [14].

| Decoction name | Traditional medicinal plants name | Preparation dose | Target diseases | References |
|---|---|---|---|---|
| Qingfei Paidu decoction | Mahuang (Herba Ephedrae) | 9g | SARS-Covid-19 | [51] |
| | Zhigancao (Radix Glycyrrhizae) | 6g | | |
| | Xingren (Semen Armeniacae Amarum) | 9g | | |
| | Shengshigao (Gypsum Fibrosum) | 15g | | |
| | Guizhi (Ramulus Cinnamomi) | 9g | | |
| | Zexie (Rhizoma Alismatis) | 9g | | |
| | Zhuling (Polyporus Umbellatus) | 9g | | |
| | Baizhu (Rhizoma Atractylodis Macrocephalae | 9g | | |
| | Fuling (Poria) | 15g | | |
| | Chaihu (Radix Bupleuri) | 16g | | |
| | Huangqin (Radix Scutellariae) | 6g | | |
| | Jiangbanxia (Rhizome Pinelliae Preparata) | 9g | | |
| | Shengjiang (Rhizoma Zingiberis Recens) | 9g | | |
| | Ziyuan (Radix Asteris) | 9g | | |
| | Kuandonghua (Flos Farfarae) | 9g | | |
| | Shegan (Rhizoma Belamcandae) | 9g | | |
| | Xixin (Herba Asari) | 6g | | |
| | Shanyao (Rhizoma Dioscoreae) | 12g | | |
| | Zhishi (Fructus Aurantii Immaturus) | 6g | | |
| | Chenpi (Pericarpium Citri Reticulatae) | 6g | | |
| | Huoxiang (Herba Pogostemonis) | 9g | | |
| Sheganmahuang decoction | *Scutellaria baicalensis* | 20 mL once three times a day | Cough, cold, fever, sore throat SARS-Covid-19 | [12] |
| | Honeysuckle | | | |
| | Forsythia | | | |
| Mahuang gancao ganjiang decoction | Mahuang (Ephedra) | 20g | Exogenous cold stress, asthma, SARS-Covid-19 | [15] |
| | Gancao (Liquorice) | 30g | | |
| | Ganjiang (dried ginger) | 30g | | |
| Yupingfeng Powder | Radix astragali | 20g | Immunomodulating effects, prevent from pathogens | [52,53] |
| | *Aatractylodes macrocephala* | 15g | | |
| | Radix saposhnikoviae | 15g | | |

| | | | | |
|---|---|---|---|---|
| Fuzheng Kang-Ai decoction | Radix Pseudostellariae | 30g | Induces lung cancer cell apoptosis | [27] |
| | Rhizoma Atractylodis Macrocephalae | 15g | | |
| | Milkvetch Root | 30g | | |
| | *Hedyotis difusa* | 30g | | |
| | *Solanum nigrum* | 30g | | |
| | Chinese Sage Herb | 30g | | |
| | Indian Iphigenia Bulb | 30g | | |
| | Coix seed | 30g | | |
| | *Akebia trifoliata Koidz* | 30g | | |
| | Snake bubble ilicifolius | 30g | | |
| | *Curcuma zedoaria* | 15g | | |
| | Licorice | 10g | | |
| Yinqiao Powder | Forsythia | 15g | Act against SARS, antiviral, antibacterial, reduce fever, H1N1 influenza virus infection and improvement of the function of upper respiratory mucosal immune system | [22] |
| | Chinese bellflower | 6g | | |
| | Honeysuckle | 15g | | |
| | Mint | 6g | | |
| | Bamboo leaves | 6g | | |
| | Licorice | 3g | | |
| | Nepeta | 6g | | |
| | Burdock | 6g | | |
| | Light tempeh | 5g | | |
| Sangju yin | Mulberry leaf | 15g | Relief in severe cough, cold, flu (influenza), sore throat, mild thirst and fever | [29,30] |
| | Chrysanthemum | 10g | | |
| | Forsythia | 10g | | |
| | Almond | 9g | | |
| | Mint | 6g | | |
| | Chinese bellflower | 6g | | |
| | Reed root | 15g | | |
| | Licorice | 3g | | |
| Maxinshigan Decoction | Ephedra | 15g | Clear lung fever, reduce? phlegm inflammation, suppressing cytokine storm, alleviating pulmonary edema, regulating immune response and protecting pulmonary alveolar-capillary barrier | [28] |
| | Almond | 10g | | |
| | Plaster | 20g | | |
| | Licorice | 9g | | |

| | | | | |
|---|---|---|---|---|
| Baihegujin Decoction | Shudihuang | 15g | Invigorate the lung and expel the pathogens, reduce fever, transforms phlegm, stops cough, hot palms and soles, night sweat, dry and sore throat nourishes the blood and thereby supporting a healthy respiratory function etc. | [31] |
| | Dihuang | 15g | | |
| | Angelica | 15g | | |
| | White peony | 6g | | |
| | Xuanshen | 10g | | |
| | Chinese bellflower | 6g | | |
| | Ophiopogon | 6g | | |
| | Lily | 6g | | |
| | Beimu | 6g | | |
| | Licorice | 3g | | |

**Table 1:** Various decoction with their ingredients may use against COVID-19.

## Shuanghuanglian (SHL)

COVID-19 and their symptoms resolved after using the Chinese traditional patent medicine SHL (containing extracts of three Chinese herbs, such as *Scutellaria baicalensis*, honeysuckle and forsythia, generally used to treat cold, cough, and sore throat with fever) and rapidly recovered without obvious adverse effects. For a long time, SHL has been used in clinical practice due to its affordable cost with no side effect. Based on preliminary study findings it has been indicated that SHL can inhibit 2019-nCoV (http://www.cas.cn/yw/202001/t20200131_4733137.shtml, accessed on January 31, 2020).

## Mahuang Gancao Ganjiang decoction (MGGD)

MGGD can effectively alleviate the symptoms of the patients suffering from exogenous cold stress. It was found to be able to protect lymphocytes against cold-stress induced apoptosis, which are important for the immune response in mammals. Lymphocytes apoptosis may cause disorder of immune system in human body and cannot protect to invaded by viruses specially during flu or cold exposure. MGGD may regulate the immune response through inhibiting the lymphocytes apoptosis, fusion and fission of mitochondria, mediated by regulating the expression level of Mfn1, Mfn2 and Drp1in mice under cold stress [15].

## Decoction of licorice

Since 2002 the outbreak of SARS, there was numerous studies and research done to find a cure for the SARS Coronavirus by researchers from China, Hong Kong, Europe and the US. From ages, the root of *Glycyrrhiza glabra* (Licorice) are used in ancient Indian Ayurvedic medicine, Egyptian medicine and in traditional Chinese medicine. It's native to Europe and Asia. Licorice roots had already been known for its antiviral properties but researchers noticed that during the SARS outbreak in 2012, certain groups of people drinking concoctions of it during the SARS outbreak did not get infected with the virus despite having been exposed to it by having relatives in the same household who were infected [16]. It can potentially drug candidate for the SARS-Cov-2 coronavirus.

## Yupingfeng powder

Yupingfeng powder, a traditional Chinese complex prescription, contains three medicinal plants: *Radix astragali*, *Atractylodes macrocephala* and *Radix saposhnikoviae* (Table 1). Pharmacological studies have found that it possesses antiviral, anti-inflammatory, immunomodulating activities [17,18], which enhance innate immunity, stimulates cellular immune response, raise humoral and cellular immune function [19-21] and main ingredients for preventing SARS.

## Yinqiao powder

Yinqiao Powder contains Japonicae Flos (Jinyinhua) and Forsythiae Fructus (Lianqiao) core components, is a classical formula used to prevent respiratory infectious ailments. It has confirmed that Yinqiao Powder is effective in preventing upper respiratory tract infection as it contains antiviral, antibacterial properties which reduces the time to fever resolution in patients with the H1N1 influenza virus infection and improves the function of upper respiratory mucosal immune system [22,23].

## Fuzheng Kang-Ai (FZKA) decoction

12-herb containing Fuzheng Kang-Ai decoction, was firstly prescribed by Dr. Wanyin Wu. It has been used to cure non-small cell lung cancer (NSCLC) patients in Guangdong Provincial Hospital of Chinese Medicine. FZKA decoction combined with gefitinib showed positive results on longer progression-free survival with less tox-

icity than gefitinib [24] and enhanced the disease control rate as well as median survival time in NSCLC patients [25,26]. Wang., *et al*. [27] reported that FZKA decoction promotes lung cancer cell apoptosis through STAT3/Bcl-2/caspase-3 signaling pathways or control the growth of human lung cancer cells.

### Maxinshigan decoction

Maxingshigan decoction (MXSGD) is combination of traditional Chinese medicine and modern medicine which is recommended and widely applied as a basic prescription in the clinical treatment of COVID-19. After taking MXSGD, some biological processes altered within the human body which were related to the regulation processes like chemokine production, acute inflammatory, response to oxygen radicals, oxidative stress-induced apoptosis, vascular permeability, T cell differentiation, tumor necrosis factor, immunomodulation, immunoglobulin secretion and against viral infection. The therapeutic effect of MXSGD may helpful in regulating the immune response, alleviating pulmonary edema, decreasing fever, reducing inflammation and protecting the pulmonary alveolar-capillary barrier etc. on COVID-19 [28].

### Sang Ju Yin

Sang Ju Yin is a traditional Chinese herbal medicine that acts against pathogenic factors. It is mostly used for the cough, cold, flu (influenza), sore throat, mild thirst and fever. Therefore, its applied for common cold or flu, whooping cough, tonsillitis and bronchitis [29]. In the spring season 2009, when swine flu outbreak occurred it was used as utmost important medicine by the Chinese health authorities for the treatment of swine flu (Sang Ju Yin). Several years back, it was also used with Yu Ping Feng San combination where it played its significant role SARS virus prevention [30].

### Baihegujin decoction

Baihegujin Decoction is also a famous Chinese herbal medicine that played its significant role in the eradication of various ailments such as moistens the lungs, reduce fever, transforms phlegm, stops cough, hot palms and soles, night sweat, dry and sore throat and nourishes the blood by supporting a healthy respiratory function etc [31].

### Decoction of *Barleria lupulina*

*Barleria lupulina* Lindl. (Family: Acanthaceae) is one of the promising medicinal plant natives to India which is widely present in Southern and Western mountains of India. It's an alternate medicine of hydroxychloroquine. Several studied found *B. lupulina* as immunomodulatory [32], radio protecting abilities and anticlastogenic effects [33], antimicrobial [34,35], anti-inflammatory [36-38], antidiabetic [39,40], antibacterial [41-44], anticancer, antioxidants [44], anti-arthritis [45], anti-viral [46] and anti-ulcer [40]. It is traditionally using of the plant as tonic and for treatment of common cold, cough, fever, dermatitis, sexual disorder, body ache, itches, eczema, and scabies [47], We can self-formulate according to need either fresh young leaves or dried (powder) of *B. lupulina* to fight against COVID-19 (SARS-coronavirus) in clinical test.

## Discussion

Traditional Chinese Medicine were used a lot of descriptions to prevent and treat SARS in 2003 [48,49]. National Administration of Traditional Chinese Medicine of China organized a program for the treatment of H1N1 viral infection9 in 2009. During the outbreak of COVID-19, Traditional Chinese Medicine works very well clinically against COVID-19. During the treatment of Covid-19 around the world, there is no effective treatment available yet for it. Based on experiences, we found that the intervention of traditional Chinese medicine can improve the patients health. The outbreak of COVID-19 has challenged the economic, medical and public health infrastructure. Therefore, based on the consideration of health prevention programs health economics and balance of risks and benefits. The therapy of Traditional Chinese Medicine might be useful for people all around the world [50]. Ministry of AYUSH had issued an advisory to drink herbal tea, decoction (kadha) to boost the immunity.

## Conclusion

Herbal medicine has anti-microbial, antiviral, anti-inflammatory anti-diabetic, anti-oxidants and immunoregulatory effects due to presence of bioactive compounds or alkaloids and easily available in pharmacies. It can used as alternative medicine in spite of synthetic drug. It acts on ailment site or suppress the microbial growth or infection and improve our immune system but due to health differences, we do not recommend that all people should take herbal medicine to prevent COVID-19.

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