Efficacy and mechanisms of Traditional Chinese Medicine prevention and treatment for respiratory viruses

Fan-Fan Yang¹, Jun Ren², Bin Xu³, Jian Xu⁴

¹School of Medical Technology and Information Engineering, Zhejiang Chinese Medical University, Hangzhou 310053, China. ²School of Humanities and Management, Zhejiang Chinese Medical University, Hangzhou 310053, China. ³Department of General Surgery, Sir Run Run Shaw Hospital, School of Medicine, Zhejiang University, Hangzhou 310016, China.

*Corresponding to: Jian Xu. School of Medical Technology and Information Engineering, Zhejiang Chinese Medical University, No. 548 Bin Wen Road, Hangzhou 310053, China. E-mail: 20061036@zcmu.edu.cn.

Abstract

Respiratory virus infection was the most common viral infection in clinical practice with the greatest impact, including the Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), posing a huge threat to the world's public health and human life safety. Commonly used antiviral drugs have obvious side effects and a narrow scope of application. Respiratory viruses are susceptible to infection, mutation, and prevalence, which also pose challenges to traditional antiviral drugs and vaccine development. Traditional Chinese Medicine (TCM) has a long history of treating infectious diseases, with many herbs and compounds. Its multi-component, multi-target and multi-path characteristics have made it have great advantages and potential in the development of new anti-respiratory virus drugs. This review summarized TCM for the prevention and treatment of common respiratory viruses, and provided new strategies for the research and development of new TCM antiviral drugs and for responding to infectious respiratory virus diseases.

Keywords: respiratory virus; Traditional Chinese Medicine; influenza viruses; respiratory syncytial virus; human rhinovirus; novel coronavirus

Author contributions

Fan-Fan Yang: Writing - original draft; Jun Ren: Conceptualization, design; Bin Xu, Jian Xu: Writing - review & editing. All authors read and approved the final manuscript.

Competing interests

The authors declare no conflicts of interest.

Peer review information

Infectious Diseases Research thanks Da-Qiang Wu, Hai-Jun Gao and other anonymous reviewers for their contribution to the peer review of this paper.

Abbreviations

SARS-CoV-2, Severe acute respiratory syndrome coronavirus 2; TCM, Traditional Chinese Medicine; RSV, Respiratory syncytial virus; LHQW, Lianhua Qingwen Capsules; IAV, Influenza A virus; ECMO, extracorporeal membrane oxygenation; QFPD, Qingfei Paidu Decoction; AV, Avian influenza viruses; MIWQH, Modified Jiu Wei Qiang Huo decoction; GGD, Ge Gen Decoction; LSW, Liu Shen Wan; FPYH, Fufang Yinhua Jiedu Granules; SJDD, Shu Feng Jie Du Capsule; GQQ, Gegen Qinlian Decoction; HLJDT, Huanglian JieDu Tang; DAP, didehydroandrographolide; LEBD, Lung endothelial barrier dysfunction; CYZH, Compound Yi-Zhi-Hao pellet; SHL, Shuang-Huang-Lian water extract; HKD, Huangliang Xiangru Decoction; LBO, Luofushan-Baicao Oil; YHPG, Yinhuapinggan granule; HMQG, Jin Hua Qing Gan Granule; JOL, Jinning oral liquid; HRV, Human rhinovirus; HKQQ, Huo Xiang Zheng Qi Decoction; ACEPQD, acute exacerbations of chronic obstructive pulmonary disease; HSV, Herpes simplex virus.

Citation

Tradition

The related TCM for the prevention and treatment of respiratory viruses were introduced.

The possible mechanisms of different TCM were described.

The action targets of different TCM were summarized.

Introduction

Respiratory diseases are common and frequent, affecting the trachea, bronchus, lung, and thorax [1]. In recent years, the incidence of respiratory diseases has increased significantly due to air pollution, smoking, physical and chemical factors, biological factors, and an aging population. Respiratory diseases seriously affect the health of people around the world. In addition to air quality factors, respiratory viruses have become public enemies that affect human life [2]. Respiratory viruses invade the respiratory tract, causing respiratory lesions or primarily causing diseases of tissues and organs outside the respiratory tract due to respiratory tract infection [3]. Examples of the former include Influenza virus, Rhinovirus, Respiratory syncytial virus (RSV), etc., while examples of the latter include measles virus, mumps virus, rubella virus, and others.

The 1918 pandemic remains the worst outbreak of infectious disease in history. In 2002, the SARS epidemic swept 29 countries [4], and in December 2019, pneumonia of unknown etiology occurred in some medical institutions [5]. On January 27, 2020, a novel variant of the SARS coronavirus was detected in a laboratory. It was later named COVID-19 [6]. The virus has a long incubation period, and people can be infected by droplets when they sneeze or cough. Initially, the novel coronavirus was less well understood than ordinary influenza viruses due to its unique characteristics, and it spread rapidly in China and around the world. As of February 17, 2022, there have been 418,170,548 confirmed cases and 5,869,034 deaths worldwide.

Although COVID-19 patients occasionally appeared in different cities in China in 2021, they did not cause large-scale infections due to the effective isolation and control policies of the Chinese government. With TCM intervention, most infected people showed mild symptoms and recovered quickly. The number of deaths and hospitalizations of COVID-19 patients in China is far below the global average. Although vaccination may not prevent infection with the mutant virus, it may reduce the risk of severe pneumonia. Mild patients can also recover quickly with TCM.

TCM has a long history of fighting epidemics. The Yellow Emperor’s Internal Classic, which dates back to the Qin and Han dynasties, recorded “that the five diseases are easy to infect, regardless of size and similar symptoms.” In 2003, Traditional Chinese Medicine was shown to be effective in treating and preventing severe respiratory diseases, and good clinical results were achieved by using Lianhuaxingwencapsules (LHFW) to treat Influenza A virus (IAV). At the onset of COVID-19, Favilavir and Remdesivir were the primary treatments used by most people [7]. However, after the outbreaks of H5N1, H1N1 and H7N9, which caused huge losses of life and property, antiviral drugs such as oseltamivir were stockpiled in large quantities, placing a heavy burden on government budgets. Long-term hyperthermia and severe lung failure are mainly treated with corticosteroids and extracorporeal membrane oxygenation (ECMO). Hormone therapy is known to cause osteoporosis, and ECMO treatment is limited and expensive, placing a heavy burden on government budgets. Despite being an early site of infection with the novel coronavirus, China has a lower case fatality rate of 4.06%, compared to 12.8% in Italy and 10.5% in Spain [7]. This is due to the use of TCM, including Qingfeipaidudecocation (QPFD), LHFW, and other herbs, which play a role in fighting respiratory viruses through different mechanisms of action. This review provides an overview of TCM’s prevention and treatment of respiratory viruses.

Prevention and treatment of Orthomyxoviridae with TCM (Figure 1)

The Orthomyxoviridae family includes influenza viruses and avian influenza viruses (AIV). AIV causes severe systemic disease in birds, while Influenza viruses primarily infect humans and cause acute respiratory infections. Influenza A, B, and C viruses are responsible for most human infections, IAV has a high mutation, which makes it difficult to develop targeted preventive vaccination. At present, there is no effective therapeutic method for IAV, mainly treatment according to symptoms and guard against secondary bacterial infection. As a multi-target compound drug, TCM is difficult to produce influenza virus drug resistance, which makes TCM has evident superiority in the cure of influenza virus.

LHQW inhibits influenza-inductive adherence of bacteria through lower molecule of adhesion and shows a tendency to improve severe pneumonia. It can also treat H1N1 infection by affecting arachidonic acid metabolism in a mouse model. In addition, LHQW can synergize with oseltamivir against Influenza B virus, which can improve inflammatory factors in influenza patients [8-12]. Clinical research has shown that LHQW can remarkably reduce the severity of the disease, shorten the duration of symptoms, and improve clinical symptoms caused by influenza [13, 14].

Modified JiuiWenQiangRenDecocation (M/QWD) upgrades metabolomics of dysfunction through amino acid, fatty acid, and arachidonic acid pathways, pathologies, and profiles in Influenza A pneumonia-infected mice [15], Ge Gen Decocton (GGD) can decrease TNF-α expression, improve Th1/Th2 immune balance and reduce inordinate immune response in mice infected with H1N1 [16]. LiuShenWan (LSW) downregulates the expression of inflammatory cytokines induced by influenza virus by regulating the activity of the TLR4/NF-kB signaling routing [17]. The anti-influenza virus effect of FufangYhuaJieduGranules (FFYH) may be attributed to the inhibition of the expression of inflammatory cytokines by regulating the TLR7/MyD88/NF-kB signaling passage in vivo, providing evidence for the clinical treatment of IAV infection by FFYH [18]. Clinical research shows that FFYH is secure and efficacious in treating influenza with wind-heat syndrome [19].

Polyphylla saponin I has antiviral activity against IAV both in vivo and in vitro [20]. ShufengJieDuCapsule (SFJD) can improve upper respiratory tract infection through the ERK pathway and, when combined with oseltamivir, can significantly reduce IAV-induced airway inflammation and lung virus titers. It has been extensively used in the treatment of infections of upper respiratory tract [21-23]. One trial showed that after three days of treatment, SFJD combined with acyclovir had a higher probability of fever resolution than acyclovir alone [24].

After influenza virus infection, the host inflammatory response may be balanced by GegenQidanDecotion (GGD) by downregulating factor expression in the TLR signaling pathway [25]. Neumaminidase on the IAV membrane may be inhibited by Panonia delavayi Extracts and HuangLianJieduTang (HJTJ) [26, 27]. Research has shown that 14-deoxy-11,12-dihydroandrographolide (DAP), a main component of Andrographis paniculata, mainly acts on caspase-9 to exert anti-IAV activity [28]. Evidence suggests that Panula can shorten the duration of cough and sore throat and the time of sick leave/remission compared to routine nursing [29].

MusaHerbflavonoids can alleviate IAV-induced pulmonary endothelial barrier dysfunction by inhibiting NOX4/NF-kB/MLCK channel, may be a potential drug to prevent lung endothelial barrier dysfunction (LEBD) and IAV (30). Compound Yi-Zhi-Hao pellet (CYPH) inhibits IAV replication in vitro, in part by activating Nrf2/HO1 pathway expression [31, 32]. Baicalin, sweroside, arachidonic acid, forsythoside A, and phillyrin are the anti-flu substances of Shuang-Huan-Lian water extract (SHL), which downregulate TNA-α, IL-1β and IL-6 and inhibited the let out of IFN-β [33, 34]. Children's SHL combined with oseltamivir phosphate has a remarkable influence on the treatment of children with moderate and mild influenza. It can better improve the immune function of patients, quickly alleviate clinical symptoms, and meet safety requirements [35].
Influenza virus

Table 1 TCM for Influenza virus

<table>
<thead>
<tr>
<th>virus</th>
<th>Clinical symptoms</th>
<th>proprietary Chinese medicine</th>
<th>Active ingredient</th>
<th>target</th>
<th>pathway</th>
<th>references</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHQW</td>
<td>Generally acute onset, with fatigue symptoms in the prodromal stage, and systemic poisoning symptoms such as high fever, chills, chill, headache, aches and pains in muscles and joints of the whole body will soon appear.</td>
<td>chlorogenic acid, phyllrin, foersythioside A</td>
<td>IL-6, COX-2, IL-8, ICAM-1, TNF-α</td>
<td>Arachidonic acid metabolic, NF-κ B, JAK-STATS, p38-MAPks</td>
<td>[8, 11, 12]</td>
<td></td>
</tr>
<tr>
<td>SFJD</td>
<td></td>
<td>Phyllrin, emodin, verbenalin</td>
<td>P-ERK, IL-1β, IL-18</td>
<td>ERK, NLRP3</td>
<td>[21, 22, 95]</td>
<td></td>
</tr>
<tr>
<td>MJWQH</td>
<td></td>
<td></td>
<td>prostaglandin E2, phospholipase A2</td>
<td>fatty acid, amino acid, arachidonic acid metabolism</td>
<td>[15]</td>
<td></td>
</tr>
<tr>
<td>GGD</td>
<td></td>
<td></td>
<td>TNF-α</td>
<td>the toll-like receptor 7</td>
<td>[16]</td>
<td></td>
</tr>
<tr>
<td>LSW</td>
<td></td>
<td></td>
<td>IL-1β, TLR4, NF-κ B, TNF-α, IFN-γ, IL-6, p65, IκBα</td>
<td>TLR4, NF-κ B</td>
<td>[17]</td>
<td></td>
</tr>
<tr>
<td>FFYH</td>
<td></td>
<td></td>
<td>TNF-α, IL-6, IL-10, IFN-γ, IP10, IL-1β</td>
<td>TLR7, MyD88, NF-κ B</td>
<td>[18]</td>
<td></td>
</tr>
<tr>
<td>GQD</td>
<td></td>
<td></td>
<td>TLR7, NF-κ B p65, MyD88,</td>
<td>TLR</td>
<td>[25]</td>
<td></td>
</tr>
<tr>
<td>HLJDT</td>
<td>With or without local symptoms such as dry cough, nasal obstruction, runny nose, sore throat, retrosternal discomfort, facial flushing, and conjunctival congestion and so on.</td>
<td>baikalein, berberine, coptisine</td>
<td></td>
<td>NA-1</td>
<td>[27]</td>
<td></td>
</tr>
<tr>
<td>CYZH</td>
<td></td>
<td></td>
<td>HO-1, Nrf2, NF-κ B</td>
<td>Nrf2/HO-1, Nrf2/ARE</td>
<td>[31]</td>
<td></td>
</tr>
<tr>
<td>SHL</td>
<td></td>
<td></td>
<td>TNF-α, IL-1β, GSH, IL-6, IFN-β</td>
<td>TFN</td>
<td>[33, 34]</td>
<td></td>
</tr>
<tr>
<td>HXD</td>
<td></td>
<td></td>
<td>IL-6, TNF-α, IFN-γ, NO, IL-2, SOD, TLR3, TLR7, MyD88, NF-κ B p65</td>
<td>TLR</td>
<td>[36]</td>
<td></td>
</tr>
<tr>
<td>LBO</td>
<td></td>
<td></td>
<td>IL-1β, TRAF, IL-6, IFN-β, p65, IRF3</td>
<td></td>
<td>[40]</td>
<td></td>
</tr>
<tr>
<td>YHPG</td>
<td></td>
<td></td>
<td>IFN-β, IFN, IL-6, TNF-α, STAT1, TLR4, MyD88, TRAF6, NF-κ B p65, IL-2, IL-4</td>
<td>PRRs, TLR4-MyD88-TRAF6</td>
<td>[41]</td>
<td></td>
</tr>
</tbody>
</table>

Submit a manuscript: https://www.tmrjournals.com/idr
After the host is infected with IAV, Huangliang Xiangru Decoction (HXD) plays an anti-influenza effect through the TLRs pathway to enhance antioxidant capacity and immune function [36]. Secoiridoid analogs from Ligustrum lucidum fruit and furanocoumarins isolated from Angelica dahurica inhibit IAV activity [37, 38]. Aqueous extracts from dandelion, Luofushan-Baicao Oil (LBO), and Yinhuaopinggan granule (YHPG) can all be developed as alternative therapeutic agents for the prevention of IAV [39–41]. Clinical experiments have shown that Jin Hua Qing Gan Granule (JHGG) can shorten the antipyretic time of patients and has a high overall curative effect [42]. Ban Lan Gen combined with oseltamivir can reduce the risk of cough and sore throat and shorten hospital stay [43].

Prevention and treatment of Paramyxoviridae with TCM (Figure 2) (Table 2)

RSV belongs to the genus Paramyxoviridae pulmonary virus and mainly causes lower respiratory tract infections in infants worldwide. Currently, there are no mature vaccines or drugs available to combat RSV. Pneumonia caused by RSV causes many infant deaths every year. TCM has unique advantages in fighting viruses. Houttuynia cordata Thumb exerts antiviral effects by regulating TNF, MAPK, VEGF and other signaling pathways [44]. Coumarins, quinic acid derivatives, flavonoids, alkaloids, and lignans isolated from five species of the Erycibe genus have anti-RSV activity [45]. Rhein inhibits the activation of NLRP3 inflammatory corpuses through NF-κB pathway, thus inhibiting RSV-induced lung inflammatory injury in mice [46]. The antiviral benzofuran, arestia A and B from Eupatorium chinense and the antiviral phloroglucinol-terpenoid adducts from arestia capitii have anti-RSV effects [47, 48]. Rhodomentosones A and B are two enantiomeric phloroglucinol trimers from Rhodomyrtus tomentosa whose asymmetric biomimetic synthesis shows promise against RSV [49]. Caffeic acid oligomers from Mesona chinensis exhibit significant antiviral activity against RSV in vitro [50]. Terpenoids from the stems of Celastrus hindii had anti-RSV activities [51]. A new meroterpenoid, tomentodione E (1), along with four known ones (2–5), were separated from the leaves of Rhodomyrtus tomentosa, and their antiviral activity against RSV was evaluated, with two showing potent anti-RSV effects in vitro [52]. There are three new biflavonols extracted from Fructus Aurantii Immaturus, which have antiviral effects on RSV A2 strain [53]. The ethanol extract of M. piperita L. leaves has anti-RSV effect and can inhibit the production of TNF-α, IL-6, NO and PGE2. Anti-inflammatory activity may be conductive in the fight against RSV infection [54]. The use of TCM in the treatment of children with RSV pneumonia has a significant effect. It can quickly relieve clinical symptoms, shorten the course of treatment, and has the advantages of fewer adverse reactions and improved quality of life. Jinxin oral liquid (JOL) has anti-inflammatory and therapeutic effects on RSV-associated pneumonia by improving the related lipid metabolism disorder and reducing the release of inflammatory factors in serum and lung homogenates in RSV-infected mice [55–57]. GGD, ShengMa GoGen Tung, and water extract from Paeonia lactiflora pallas have therapeutic effects against RSV [58–61].

![Figure 2 TCM for RSV](image)

### Table 2 TCM for RSV

<table>
<thead>
<tr>
<th>Virus</th>
<th>Clinical symptoms</th>
<th>Proprietary Chinese medicine</th>
<th>Active ingredient</th>
<th>Target</th>
<th>Pathway</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory syncytial</td>
<td>Early patients are mostly confined to the upper respiratory tract, and clinical manifestations are symptoms of irritation of the upper respiratory tract, such as nasal congestion, runny nose, cough, hoarseness, sore throat and itching of the throat. Some patients have upper respiratory tract infection symptoms for 2-4 days and can develop into lower respiratory tract infection, mainly manifested as bronchiolitis, pneumonia, such as cough, wheezing, shortness of breath, labored breathing, etc.</td>
<td>JOL</td>
<td>IL-1β, IL-3, NLRP3, ASC</td>
<td>Caspase recruitment domain, (ASC)/Caspase-1, TLR3, lipid metabolism</td>
<td>[55-57]</td>
<td></td>
</tr>
</tbody>
</table>

Submit a manuscript: https://www.tmrjournals.com/idr
Prevention and treatment of Human rhinovirus with TCM

Human rhinovirus (HRV) is the most common cause of serious respiratory diseases such as common cold, asthma and exacerbation of chronic obstructive pulmonary disease. Currently, there are no vaccines or antiviral agents available for the prevention or treatment of HRV infections. Although the disease is self-limiting and the prognosis is generally good, it is crucial to seek medical attention quickly to avoid exacerbating the disease.

In TCM, the lung is believed to be connected to the nose and is a delicate organ. Children may have insufficient lung qi and are therefore more susceptible to external pathogens. Rhinovirus enters the body through the mouth and nose and initially attacks the lungs. Lung imbalance is the leading cause of rhinopathy. TCM medicated baths act directly on the skin without gastrointestinal damage and have the advantages of quick efficacy, comfort, and no side effects. In addition, volatile components of TCM inhaled through the nose can inhibit some pathogenic microorganisms in the respiratory tract, reducing and alleviating the occurrence of upper respiratory tract infections.

Resveratrol has been shown to exert antiviral effects against various DNA and RNA viruses, making it a potential therapeutic approach for reducing HRV replication and virus-induced cytokine/chemokine production [62]. Quercetin 7-glucoside (QTG) and Oroch 7-O-d-glucoside (O7G) extracted from Lagenostroemia speciosa have shown anti-HRV2 effects by inhibiting virus replication in the early stages [63, 64]. Studies have also shown that the antiviral activity of Quercetin-type flavonoids distinctly reduce the death rate and average viral load of infected animals [65]. Raoullic acid derived from Raoulilia australis has broad-spectrum antiviral activity against six HRVs [66]. Iota-Carrageenan, a sulphated polysaccharide derived from red seaweed, is an effective anti-rhinovirus substance, which can reduce the growth of HRV and inhibit the cytopathic effect of the virus on infected HeLa cells [67]. Treatment of HRV-infected cells with Echinacea extracts may reduce TF levels to low levels [68]. A meta-analysis has suggested that utoonormal Echinacea extracts are effective in preventing common cold symptoms after a placebo-related clinical vaccine [69].

Prevention and treatment of Coronavirus with TCM (Figure 3) (Table 3)

The role of TCM in the prevention and treatment of Severe Acute Respiratory Syndrome (SARS) was gradually recognized in 2002. With the continuous global spread of the novel coronavirus, a dialectical treatment plan for COVID-19 has been proposed, drawing on previous experiences in China, using TCM.

LHQW is a Chinese patent medicine that exerts antiviral activity by regulating immune function. Its main function is to clear toxins, detoxify, and relieve heat in the lungs. COVID-19 diagnosis and treatment guidelines recommend LHQW as a preventive measure during the medical observation. LHQW has been found to be effective in blocking the early stage of viral infection, inhibiting virus-induced NF-kB activation, and has a broad-spectrum effect on a range of influenza viruses. Moreover, it can regulate the immune response to viral infection [70–72].

The results of relevant clinical studies show that the combination of routine treatment and LHQW can significantly relieve clinical symptoms such as fever, cough, anticipation, and shortness of breath. Although there is no statistical difference in the time it takes for fever to disappear, on average, it is 1.5 days shorter than the control group, which also shows that the medicine has clinical advantages in improving fever symptoms [73, 74].

Huo Xiang Zheng Qi Decotion (HXZQ) is suitable for dampness and heat accumulation, internal obstruction leading to Qi stagnation, and can improve intestinal function. Research has shown that HXZQ can regulate the PI3K/AKT signaling pathway with active ingredients such as Liquorice, Tangerine peel, and Platycodon grandiflorum, playing the role of “Strengthening Qi and Exorcism,” and exerting antiviral activity [75]. COVID-19 diagnosis and treatment guidelines recommend the use of HXZQ for patients with clinical asthma and gastrointestinal discomfort.

A randomized clinical trial has revealed that combining Western medicine and HXZQ can improve the clinical symptoms and prognosis of COVID-19 patients. It also reduced the use of anti-infective drugs. HXZQ is expected to be a novel agonist for distal airway HCO(3)/(-) secretion, which has certain therapeutic significance [76]. In addition, the combined use of HXZQ and JHQQ can effectively protect community residents from respiratory diseases such as colds.

JHQQ is a prescription formulated by Chinese and Western medicine experts organized by the Beijing Administration of Traditional Chinese Medicine during the 2009 H1N1 epidemic. It was used for fever caused by exogenous pathogens, mild or non-severe colds, and is now recommended for the treatment of patients during the COVID-19 medical observation period. Clinical tests have shown [77, 78] that JHQQ can significantly promote the absorption of inflammatory exudate from pneumonia, reduce fever, cough, fatigue, and anticipation, and alleviate mentality nervous in patients with novel coronavirus pneumonia. In addition, JHQQ can also be used to treat wind-heat affecting Fei syndrome (WHAFS) [79].

The main function of SFJD is to relieve wind, clear heat, detoxify, and promote pharynx. As a complementary and alternative medicine for influenza prevention, SFJD can relieve clinical symptoms in patients with acute exacerbations of chronic obstructive pulmonary disease (AECOPD) [80]. Research has found that SFJD can inhibit H1N1, Parainfluenza virus, RSV, Herpes Simplex virus-1 (HSV-1), HSV-2, Coxackievirus-B4 (COX-B4) and COX-B5. The best inhibitory effect was on Parainfluenza virus, and the Therapeutic Index (TI) reached 15.93. It is evident that SFJD has a spectrum antiviral effect in vitro.

Xiao et al. treated mild COVID-19 patients with SFJD combined with Abidal and found that it can significantly improve the percentage of routine blood leukocytes and lymphocytes in patients, resulting in clear absorption of the CT infection focus in the chest, and fewer adverse reactions. SFJD therapy was more effective in the first 8 days after symptom onset [81].

QFPD plays an effective antiviral role by regulating cytokine expression in integrative TCM and Western medicine for COVID-19 patients. It should be used rationally according to the patient’s condition. For severe and critical patients, a combination of TCM injections (such as Xi Yan Ping Injection, Xue Bi Jing Injection, Re Du Ning Injection, Shen Fu Injection, etc.) and TCM decoction is recommended.

There are good synergistic effects and different emphases between the combined prescriptions. QFPD can relieve fibrosis, reducing COVID-19 patients mortality. When combined with antibiotics, QFPD can treat bacterial pneumonia in children [82]. Zhang et al. used QFPD according to the requirements of the sixth and seventh editions of the guidelines and found that this decoction can cause diarrhea symptoms for patients with Spleen Yang deficiency, epigastralgia, nausea, vomiting, and other symptoms for patients with stomach Yin deficiency, and excessive sweating, palpitation, elevated blood pressure, insomnia, and other discomfort for patients sensitive to ephedra.

In summary, QFPD as a general prescription for COVID-19 TCM treatment has great clinical value, and early treatment with QFPD may serve as an effective strategy to control the epidemic [83]. Appropriate adjustments should be made to individual differences in patients during treatment to achieve a better clinical effect. In addition, Jiawei Yuyingfang Decotion, a Chinese herbal medicine widely used in the treatment of respiratory diseases [84], regulates immune function by acting on estrogen receptor, PPAR, MAPK, PI3K/AKT, JNK signaling pathways, IL-17, lipid metabolism, and plays a preventive and therapeutic role [85–87]. In the treatment of COVID-19, Western medicine 5-O-methylisovanilmin, astragaloside IV, and 5-O-methylisovanilmin (hydroxylation) are vital constituents of YPF that target RELA, TNF, IL-6, MAPK14, MAPK8 [88]. Cangma Huadu granules is a novel drug
with the potential to treat coronavirus and influenza, which plays a role through anti-inflammatory and immunomodulation [89].

Figure 3 TCM for Coronavirus

<table>
<thead>
<tr>
<th>virus</th>
<th>Clinical symptoms</th>
<th>proprietary Chinese medicine</th>
<th>target</th>
<th>pathway</th>
<th>references</th>
</tr>
</thead>
<tbody>
<tr>
<td>LHQW</td>
<td>It mainly causes upper respiratory tract infection, which can be accompanied by fever, chills, headache, runny nose, congestion, sore throat, dry cough, nausea, vomiting, diarrhea, etc. Severe patients can have hypoxia, cyanosis, shortness of breath and dyspnea, and more severe patients can cause respiratory failure or even death.</td>
<td>AGE-RAGE, Kaposi, AKT1, MAPK1, IL6, HSP90AA1, TNF, SOCS3, CCL2, ACE2, 3CLPro, NO, GM</td>
<td>AE2, 3CLPro, TF, HNF4α, PPARγ, PTGS2, hsp90ab1, BCL2, CASP3, ncoa2</td>
<td>NF-κB, IL-17, NOD-like receptor, Toll-like receptor, Arachidonic acid metabolism</td>
<td>[96–105]</td>
</tr>
<tr>
<td>HXZQ</td>
<td></td>
<td></td>
<td>HCO(3)(-)</td>
<td>ACE2, 3CLPro, GM</td>
<td>[106–108]</td>
</tr>
<tr>
<td>JHQG</td>
<td></td>
<td></td>
<td></td>
<td>RELA, MAPK1, MAPK14, CASP3, CASP8, IL6, TNF, IL-10, IL-2, STAT1, CCL26, AR, PRSS1, NCOA2, PPARγ, PTGS2, HSP90AA1, IFN-γ, NOS2, PIM1, ESRI, ESRI, TP53, AKT1, NCOA1, 2OFZ,EGFR, PRKCA, ANXA1, CTNNB1, 1SSK, NCOA2, RELA, FO5,</td>
<td>[70, 98, 109]</td>
</tr>
<tr>
<td>SFJD</td>
<td></td>
<td></td>
<td></td>
<td>TP53, AKT1, NFKB1, rela, nfkbia, TNF-α, IL-1β, IL-8, PI3K, AKT, CASP8, INF-α, PTGS2, NOS2, PPARγ, MAPK14, PTGS1,3CLpro, ACE2, tp53, RELA, NFKBIA, AGTR1, FURIN, CASP3, CASP6,PP4,PP10,PILOD1, CYPs1A,2A6,2C8,2C9,2C19,2D6,2E1, CYP3A, CXC4, ICAM1, CXCL8, CXCL10, IL2, IL4, IFNG, IL-18</td>
<td>NF-κB, MAPK, Toll-like receptors, TNF, NOD, PI3K/AKT,</td>
</tr>
<tr>
<td>QFPDT</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Discussion

China’s TCM has a long history and played an important role in the management of the COVID-19 epidemic, contributing to saving lives and alleviating symptoms [90, 91]. China has sent medical teams to Italy, Venezuela and other countries, and shared Chinese medicine used in anti-epidemic activities with other countries after effectively controlling the epidemic. In addition, Chinese acupuncture and moxibustion treatment have been added to the latest “Diagnosis and Treatment Plan of Novel Coronavirus Pneumonia” [92].

COVID-19 belongs to the category of “pestilence” in TCM, and TCM’s experience in preventing and treating COVID-19 patients is worth learning from. “The Diagnosis and Treatment Plan for Novel Coronavirus Pneumonia” states that TCM should be used to treat patients dialectically according to their condition, local climate characteristics, and different physical conditions. On January 27, 2020, the State Administration of Traditional Chinese Medicine launched QFPD to treat COVID-19 patients in Shanxi, Hebei, Heilongjiang, and Shaanxi provinces [93].

In view of the novel coronavirus, the National Health Commission and the State Administration of Traditional Chinese Medicine jointly issued “Notice on the Use of QFPD in the Treatment of Pneumonia with Novel Coronavirus Infection in Integrative Medicine” on February 6, 2020. Up to March 1st, 2020, China has initiated 303 clinical trials to evaluate the efficacy and safety of COVID-19 patients. Among them, 50 trials (16.5%) involved the use of traditional Chinese medicine, and 14 of them (4.6%) were treated with integrated traditional Chinese and western medicine [94].

At present, COVID-19 has been effectively controlled in China, but it cannot be taken lightly. Western medicine has no specific treatment for the disease. Although vaccination efforts in China are progressing in an orderly manner, they can only play a preventive role. As a traditional medicine with thousands of years of cultural history, TCM has played a pivotal role in the fight against COVID-19. However, the mechanism for preventing and treating COVID-19 through TCM is still not well understood and requires further study.

Most TCM is formulated with Chinese herbal medicines, and the components of these medicines are very complex. TCM’s compatibility and mechanism against novel coronavirus differ from Western medicine. Currently, the main components of the role cannot be determined, and TCM does not rely on a single drug. In addition, the preparation process of Chinese herbal medicine also varies, with decoction, crushed pills, or granules being used as dosage forms for TCM.

With the rapid spread of the novel coronavirus around the world, it is believed that with the continuous accumulation of TCM experience in the treatment of COVID-19, TCM will certainly contribute to the improvement of the epidemic situation worldwide.

Conclusion

The thousands of years of experience accumulated by TCM in treating epidemics is worth learning from. Our overview showed that these TCM drugs may inhibit respiratory viruses, block infection, regulate immune responses, and inhibit inflammation by acting on multiple targets and pathways, which may provide meaningful and useful information for the development and progress of drug therapy for respiratory viral infectious diseases.

In the special period of epidemic outbreaks in recent years, TCM has played an important role in the prevention and control of epidemics and the treatment of patients, and has been recognized and trusted by more people. At the same time, with increasing attention to health and the gradual recognition of the concept of TCM, the process of internationalization of TCM is also accelerating. More and more countries and regions are beginning to pay attention to learning the concept of TCM culture, which provides opportunities for the promotion and popularization of traditional Chinese medicine in the world.

Paper context

Respiratory diseases seriously affect the health of the people around the world. In December 2019, pneumonia of unknown etiology occurred in some medical institutions. TCM has a long history of fighting epidemics and has the advantages of macroscopic overall dialectical treatment. Although herbs play a role in fighting respiratory viruses, their mechanisms of action are different. This review aims to provide an overview of TCM’s prevention and treatment of the respiratory viruses.

References


Li JH, Yang XY, Huang LF. Anti-Influenza Virus Activity and Constituents. Characterization of Paonia delavayi Extracts. Molecules 2016;21(9):1133. Available at: http://dx.doi.org/10.3390/molecules21091133


96. Xia QD, Xun Y, Lu JL, et al. Network pharmacology and


