

Review

Converging Paths: A Comprehensive Review of the Synergistic Approach between Complementary Medicines and Western Medicine in Addressing COVID-19 in 2020

Alexandra Moura ^{1,2,*} , Lara Lopes ^{1,2} , Luís Carlos Matos ^{2,3,4} , Jorge Machado ^{1,2} 
and Maria Begoña Criado ^{2,5} 

- ¹ ICBAS—Institute of Biomedical Sciences Abel Salazar, University of Porto, 4050-313 Porto, Portugal; ljlopes@icbas.up.pt (L.L.); jmachado@icbas.up.pt (J.M.)
 - ² CBSin—Center of BioSciences in Integrative Health, 4405-604 Vila Nova de Gaia, Portugal; lcmatos@fe.up.pt (L.C.M.); mbegona.criado@ipsn.cespu.pt (M.B.C.)
 - ³ Faculdade de Engenharia, Universidade do Porto, 4200-465 Porto, Portugal
 - ⁴ CTEC—Centro Transdisciplinar de Estudos da Consciência, Universidade Fernando Pessoa, 4249-004 Porto, Portugal
 - ⁵ 1H-TOXRUN—One Health Toxicology Research Unit, University Institute of Health Sciences (IUCS), CESPU, CRL, 4585-116 Gandra, Portugal
- * Correspondence: alexandramouramtc@gmail.com

Abstract: The rapid spread of the new coronavirus disease (COVID-19) caused by SARS-CoV-2 has become a global pandemic. Although specific vaccines are available and natural drugs are being researched, supportive care and specific treatments to alleviate symptoms and improve patient quality of life remain critical. Chinese medicine (CM) has been employed in China due to the similarities between the epidemiology, genomics, and pathogenesis of SARS-CoV-2 and SARS-CoV. Moreover, the integration of other traditional oriental medical systems into the broader framework of integrative medicine can offer a powerful approach to managing the disease. Additionally, it has been reported that integrated medicine has better effects and does not increase adverse drug reactions in the context of COVID-19. This article examines preventive measures, potential infection mechanisms, and immune responses in Western medicine (WM), as well as the pathophysiology based on principles of complementary medicine (CM). The convergence between WM and CM approaches, such as the importance of maintaining a strong immune system and promoting preventive care measures, is also addressed. Current treatment options, traditional therapies, and classical prescriptions based on empirical knowledge are also explored, with individual patient circumstances taken into account. An analysis of the potential benefits and challenges associated with the integration of complementary and Western medicine (WM) in the treatment of COVID-19 can provide valuable guidance, enrichment, and empowerment for future research endeavors.

Keywords: COVID-19; Western medicine; Chinese medicine; complementary medicine; integrative medicine; natural products



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1. Introduction

The etiology of novel coronavirus-infected pneumonia (NCIP) lies in a strain of the coronavirus family [1] that gained the ability to infect humans and subsequently spread from human to human, leading to a global pandemic. The first case was reported in Wuhan, China in December 2019, and on 11 February 2020, the World Health Organization (WHO) officially named the viral disease COVID-19 [2]. The scientific name of the virus is SARS-CoV-2 [3], which shares a sequence homology with SARS-CoV and other coronaviruses, including the recently identified RmYN02, which shares a 93.3% nucleotide identity with SARS-CoV-2 and a 97.2% identity with the 1ab gene. However, RmYN02 exhibits specific differences in the spike protein and receptor-binding domain [4]. In humans, all of these

viruses can cause symptoms ranging from the common cold to severe lung infections, including severe acute respiratory syndrome (SARS), Middle East respiratory syndrome (MERS), and COVID-19 [5].

Chinese medicine (CM) and Western medicine (WM) have different approaches, but they also share common points. Both believe that outbreaks of infectious diseases are associated with three interactive factors: the epidemic pathogens, the environment, and the host [6,7]. For more than two thousand years, CM, Ayurvedic medicine, and Unani Shidda (AYUSH) [8] have focused on developing methodologies to preserve and maintain health, giving importance to the balance among the organs. Whereas CM regulates the body in a very early phase, keeping the person harmonized, WM acts when the patient is already showing signs of an illness that is in advanced stages [9]. We now know that for the treatment of mild and moderate syndromes, multidisciplinary intervention reduces typical respiratory symptoms as well as lung exudation and prevents further development of the disease. Thus, an integrative approach could be the most effective strategy. This work aims to evaluate the differences in approaches to the treatment of COVID-19 between WM and complementary medical systems, as a guide to enrich and empower future health system research.

2. The Outbreak of COVID-19: Perspectives from Chinese Medicine and Western Medicine

2.1. Western Medicine Perspective

The coronavirus infection can be explained by its attachment to the lung epithelium via spike proteins that bind to the ACE2 receptor. This receptor is present in various organs, such as the lungs, blood vessels, heart, kidneys, and gut, potentially leading to the manifestation of the disease in these areas. It was previously thought that the symptoms of COVID-19 developed slowly over a 14-day incubation period, but recent studies have shown that the duration of the viable virus peak occurs within the first week of the illness, despite prolonged SARS-CoV-2 RNA discharge in respiratory and stool samples [10]. Distinguishing SARS-CoV-2 from other respiratory viral infections is difficult due to the absence of specific symptoms and overlapping clinical features, including febrile illness with a cough that lasts for several days before potentially progressing to acute pneumonia. Additionally, patients may exhibit atypical or minimal symptoms, and co-infections with bacteria or other viruses in upper respiratory tract tissues have been identified, further complicating the diagnosis of COVID-19. As the viral load in the respiratory tract increases, SARS-CoV-2 produces the enzyme 3CL protease, which inhibits the host's innate immune response and enables the virus to spread to surrounding cells, forming lesions. The mechanism of SARS-CoV-2 in host cells is similar to SARS-CoV, although with increased virulence, an accelerated spreading rate, and higher contagiousness [11,12]. Three evolutionary stages of SARS-CoV-2 infection have been identified, including early infection, the pulmonary phase, and systemic hyperinflammation, each characterized by specific clinical signs and symptoms [13].

From the WM point of view, several predisposing factors for the COVID-19 pandemic have been noted, namely, geographic factors, social dynamics, governmental policies, global connectivity, and medical factors. Some works have pointed to the association between optimal temperature and humidity, especially in cities, affecting COVID-19 proliferation [13,14]. Other works have suggested that an increase in serum 25-Hydroxy-VitaminD level could improve clinical outcomes in COVID-19 patients [15]. Men seem to be more prone to infection than women [15], and obesity, especially in men, as well as higher levels of smoking and alcohol intake seem to significantly increase the risk of developing severe pneumonia in COVID-19 patients. On the other hand, women have proven to be more responsible concerning the measures of preventive care such as frequent handwashing, wearing a face mask, and staying at home [15].

In addition, serum lipid levels in COVID-19 patients, especially total cholesterol, HDL-cholesterol, and LDL-cholesterol, were found to be significantly lower than in healthy

controls. It was reported that the first clinical laboratorial profile in COVID-19 patients after their admission showed lower neutrophils and lymphocyte levels than healthy controls and an increased monocyte/HDL-cholesterol ratio. Compared with female patients, male patients have higher levels of monocytes and lactate dehydrogenase [16]. Older patients (>65 years) with comorbidities and acute respiratory distress syndrome seem to be at higher risk of death [17]. Alterations in the microbiome are associated with fecal levels of SARS-CoV-2 and also with the severity of the COVID-19 disease [18,19].

2.2. Chinese Medicine Perspective

According to CM, COVID-19 is one of the “five epidemic diseases,” all with similar symptoms and easily spreading infection through the air, independently of a person’s age [20]. The immune system becomes weaker and more susceptible to a similar epidemic miasma, which, following the classic book of CM, *Huangdi Neijing*, occurs mainly during the winter–spring period, being highly infectious. In this scenario, a clear recommendation from ancient Chinese medical doctors was to avoid staying in crowded places to prevent infection. The *Huangdi Neijing* book explains that normal lung functions can be drastically affected by any epidemic disease through the nose from contaminated air, causing coughs, wheezing, and fever. At the time of its publication, *Huangdi Neijing* did not propose any specific diagnosis or adequate treatment. Only later, in the Ming (1360–1644) and Qing (1644–1912) dynasties, medical specialists in febrile diseases found many ways to diagnose and treat epidemics, which are still relevant nowadays. They mainly proposed reinforcing the internal Qi (or immunity) and preventive care. For example, Wu Youke, a specialist in epidemics in the Ming dynasty, advised people to wear face masks and to quarantine patients suffering from febrile diseases [21].

In CM, it is generally accepted that the pathogenesis of COVID-19 is based on the interactions of dampness, toxins, heat, and stasis [22].

According to CM, cold tends to invade through the superficial to the interior of the body until it damages the internal organs, namely, the heart and kidneys. Dampness tends to affect the spleen and stomach, which reflects the effect of the virus on the gastrointestinal tract. Over time, the pathogen may also affect the heart [21]. The fullness of the Earth element may lead to heat in the stomach and spleen, which, combined with dampness, generate blockages (stasis) [23]. A blocked stomach, in terms of WM, can be comparable to blocked vagal functions. In airway diseases, a lack of control of the surfaces is also involved, e.g., the mucous membranes. The pulmonary orb, along with the large intestine and stomach, collectively governs these surfaces. When dampness moves into the lungs, phlegm comes up, triggering a cough. Treating dampness involves removing the blockages and dissipating the pathological substances.

3. Prevention and Treatment of COVID-19

3.1. Prevention and Conventional Treatment of COVID-19 in Western Medicine

The eyes, nose, and mouth are the main entry points for droplets carrying SARS-CoV-2 into the body. Before reaching the lungs, the virus gains access to the throat region, where it can stay for several hours. The fatty coating of the virus initially adheres to the mucosal lining, allowing it to enter cells by binding to specific receptors. Isolation, hygiene precautions, and social distancing are essential for preventing COVID-19 infection [24]. Table 1 presents preventive measures for COVID-19 mentioned in the literature.

Table 1. Measures of preventive care for COVID-19.

Measures of Preventive Care	Reference
Isolation and social distancing	[15,18]
Washing the hands frequently using an alcohol-based hand sanitizer	[3,5,24]
Avoiding touching eyes, nose, and mouth when outside	[5]
Wearing face masks	[3]
Covering coughs and sneezes	[5]
Avoiding crowded places	[5]
Avoiding traveling	[3,5,24]
Avoiding public transportation	[3,5,24]
Opening windows for ventilation in shared areas such as toilets and kitchens and having well-ventilated single rooms	[3]
Using of povidone-iodine nasal spray and mouthwash to reduce cross infection and protect healthcare workers	[25,26]
Using a humidifier, as higher air humidity reduces virus survival for other viruses and may decrease transmission	[3]
Remaining updated and well-informed about the virus	[5,27]
Practicing good respiratory hygiene	[28]
Isolating vulnerable populations such as elderly people, pregnant women, and people with co-morbid conditions such as hypertension and diabetes mellitus	[28]
Women with infants are encouraged to breastfeed their babies to enhance their immunity	[5]
Stress-relieving measures are equally important to follow	[28]
Monitoring personal health daily	[3,20]

Since 2020, several clinical trials have been performed to find an efficient and safe treatment for COVID-19, but until now, no therapy has been approved for COVID-19 pneumonia. From the WM point of view, there are some therapeutic strategies that have been used from the beginning of the pandemic; these are summarized in Table 2. We will discuss some of them below.

The main treatment strategy in WM for COVID-19 infection is supportive care based on symptom-based therapies, which are supplemented by the combination of broad-spectrum antibiotics, antivirals, corticosteroids, and convalescent plasma [27,29]. Hypoxemia is common in patients who are hospitalized with COVID-19 disease, and oxygen therapy is the preferred treatment for these patients. Convalescent plasma therapy has been applied in the prevention and treatment of many infectious diseases for a long time and was successfully and safely used in the treatment of MERS, SARS, and the H1N1 pandemic [3,20,27].

The patient's immune response to viral components involves the production of type I interferons and proinflammatory cytokines [30]. Therefore, it is not surprising that IFN β 1 and interferon IFN- α 2b are used to treat COVID-19 disease in the early stages of infection. These reduce the levels of inflammatory markers such as IL-6 in the blood produced by the nuclear factor κ B (NF-KB). In this sense, it is important to point out that Artemisinin (*Artemisia annua*) and artesunate are considered effective treatments for COVID-19 because of their anti-NF-KB effect and chloroquine-like endocytosis inhibition mechanism [31]. IL-6 plays a central role in mediating and amplifying cytokine release syndrome (CRS), which is associated with acute viral infections including coronaviruses and SARS-CoV-2 infection, and high levels of IL-6 are observed. The use of IL-6 blockers seems promising for managing the cytokine storm occurring in the most aggressive patterns of SARS-CoV-2 infection. Monoclonal antibody drugs such as tocilizumab, sarilumab, and siltuximab are IL-6 receptor antagonists, so it is easy to understand their use in patients with COVID-19 [32].

Early in 2020, some studies reported that both chloroquine and hydroxychloroquine could inhibit SARS-CoV-2 *in vitro* [25,33] by intervening in the effective adhesion of the spike protein to the host cell, reducing the glycosylation of ACE2. Thus, they were considered an effective treatment for COVID-19 infection [34]. Gautret et al. evaluated nasal swabs from patients who received 600 mg of hydroxychloroquine daily and, depending on the clinical presentation, azithromycin was added to the treatment. In some cases, a significant reduction in viral transport was also shown. When added to hydroxychloroquine, azithromycin seemed to be significantly more efficient for SARS-CoV-2 elimination [35]. However, on July 4, the WHO, based on the recommendation from the Solidarity Trial's International Steering Committee, advised discontinuing the hydroxychloroquine as well as the lopinavir/ritonavir trials, once the results showed that they produced little or no reduction in the mortality of hospitalized COVID-19 patients when compared to standard care [33,36].

According to Kadioglu et al. [37], antiretroviral drugs have been shown to be effective against several enveloped (–) ssRNA viruses, such as remdesivir against the Ebola virus and Marburg virus, oseltamivir against influenza A and B viruses, and lopinavir and ritonavir against HIV1 and HIV-2. Therefore, it has been suggested that anti-HCV drugs may also be useful in combating SARS-CoV-2. Lopinavir/ritonavir has been found to prevent the formation of viral proteins by disrupting the proteolytic processing that mimics the structure of the peptide cleaved by HIV protease [37]. In fact, lopinavir/ritonavir has been recommended for the treatment of COVID-19 disease by the National Health Commission of China [38]. Another study has shown that early triple antiviral therapy with IFN β 1, lopinavir/ritonavir, and ribavirin is more effective than lopinavir/ritonavir alone in relieving symptoms, reducing the duration of viral spread as well as hospitalization in patients with mild to moderate COVID-19 disease [37]. However, it is not recommended to use three or more antivirals at the same time [39]. Ribavirin in combination with vitamin C has been shown to improve therapeutic efficacy during viral upper respiratory infection [40]. These findings suggest that antiretroviral drugs, including lopinavir/ritonavir and ribavirin, may be useful in the treatment of COVID-19 disease.

The Ural Federal University, in collaboration with the Institute of Organic Synthesis, the Ural Branch of the Russian Academy of Sciences, and the Research Institute of Influenza, investigated azoloazins, a guanine nucleotide analog with an antiviral function that inhibits RNA synthesis. The first molecule used as a drug was Triazavirin. Although the study did not show statistical significance, maybe due to the limited size of the sample, it was expected to show benefits such as (i) controlling symptoms and (ii) reducing the frequent usage of concomitant therapies for vital organ supports [41].

Plitidepsin (Aplidin), a chemical compound extracted from ascidian *Aplidium albicans*, an exotic marine creature found on the coast of Ibiza, Spain, was found to exhibit antiviral activity against SARS-CoV-2. This is mediated through the inhibition of the target eEF1A, which is needed to make other cell proteins. Plitidepsin prevents the virus from making the proteins it needs, inhibiting its replication. Treatment with Plitidepsin demonstrated *in vivo* efficacy in two mouse models of SARS-CoV-2 infection with a reduction of viral replication in the lungs. It was reported to be 27.5 times more potent than remdesivir against COVID-19 [42].

In February 2020, China's National Health Commission and the National Administration of Traditional Chinese Medicine recommended the use of probiotics in patients with severe COVID-19, recognizing the potential role of the gut microbiome in influencing lung diseases [43]. It is worth noting that the intestinal epithelial cells, particularly the enterocytes of the small intestine, also express ACE2 receptors, which may explain the presence of SARS-CoV-2 in the stools of some infected patients. Several studies have demonstrated that probiotics can improve or alleviate lung disease conditions by modulating the immune system [18,43,44]. The use of prebiotics and probiotics to regulate the balance of the microbiome has been shown to be an effective tool to reduce the risk of bacterial and viral infections. Thus, a probiotic cocktail tailored to each patient may reduce the inflammatory

response resulting from SARS-CoV-2 infection and alleviate its severity [44,45]. In a study conducted by Zuo et al., alterations in the fecal microbiome were associated with the levels of SARS-CoV-2 in stools and COVID-19 disease severity in 15 antibiotics-naive patients, suggesting that gut dysbiosis may worsen the clinical manifestation of COVID-19 [46].

A few studies investigated ethanol therapy in COVID-19 infection intravenously and via inhalation/nebulization. The main proposal is that the therapy can reduce the inflammatory response related to the cytokine storm [47]. This therapy could inhibit virus replication due to the property of ethanol on RNA polymerase and, at the same time, its direct interaction with the bilayer lipid capsule of the coronavirus. Another effect of ethanol is to facilitate the breathing of the patient due to its bronchodilation properties, anti-cough effect, mucolytic properties, and sedative effect [48].

Concerning Western medicinal plants, *Thapsia garganica* is a very famous medicinal plant. Its roots are known for their therapeutic effects as diuretics, emetics, and purgatives. It is a common plant throughout the Mediterranean. Thapsigargin (CAS67526-95-8) is a sesquiterpene lactone isolated from the *Thapsia garganica* plant that functions as an inhibitor of the sarcoplasmic/endoplasmic reticulum Ca²⁺ ATPase (SERCA) pump. It seems to induce a potent host innate immune antiviral response that blocks some virus replication, such as the three main types of respiratory viruses in humans, including the coronavirus, when used before or during an active infection for at least 48 h after a single 30-min exposure. Thapsigargin is stable at acidic pH, so the administration is easier because it can be taken orally [49,50].

Further, concerning Western phytotherapy, a previous study from our group showed that *Moringa oleifera* has specific medical properties and immunological applications, so it is possible to speculate adequate and supportive therapy in SARS-CoV-2 infection when combined with WM [51].

Table 2. Conventional treatments for patients with COVID-19 infection.

Treatment	Agent or Device	Mechanism of Action	Reference
Oxygen therapy	Nasal cannula (HFNC)	The high-flow nasal cannula has been reported to be effective in improving oxygenation in hypoxaemic patients.	[24]
	Non-invasive mechanical ventilation (NIV and HFNO)	Non-invasive ventilation is meant to avoid intubation or to help after extubation. It refers to the administration of ventilatory support using an invasive artificial airway such as an endotracheal tube or a tracheostomy tube and high-flow nasal oxygen for the management of patients with acute hypoxemic respiratory failure.	[21]
	Invasive mechanical ventilation	If the case is severe, then mechanical ventilation should be administered; it is recommended to ventilate the patient in a prone position for more than 12 h/daily.	[21,24]
	ECMO (extracorporeal membrane oxygenation)	ECMO is an extracorporeal technique of providing prolonged cardiac and respiratory support to patients if the heart and lungs are no longer capable of providing an adequate amount of gas exchange or perfusion. It is strongly recommended in patients with refractory hypoxemia that is difficult to alleviate with protective lung ventilation.	[21,24]
	Hyperbaric oxygen chamber	During treatment, patients are exposed to 90 min of hyperbaric oxygen at 2.0 ATA, with or without air breaks. This involves breathing 100% oxygen at 1–1.5 times the atmospheric pressure, which results in a heightened concentration of dissolved oxygen in the plasma and tissues. This mechanism has been suggested to mitigate the hallmark features of severe COVID-19 disease, including progressive hypoxia and pulmonary inflammation.	[52]

Table 2. Cont.

Treatment	Agent or Device	Mechanism of Action	Reference
Monoclonal antibodies	Tocilizumab (Actemra)	Sarilumab and Siltuximab are both recombinant humanized monoclonal antibodies that act as IL-6 receptor inhibitors. They can be administered either intravenously at a dose of 8 mg/kg body weight (up to a maximum of 800 mg) in two infusions, 12 h apart, or subcutaneously at a dose of 162 mg, given in two simultaneous doses, one in each thigh (i.e., a total of 324 mg).	[6,25,34,53,54]
	Sarilumab (Kevzara)	A monoclonal antibody IL-6 receptor inhibitor with ongoing clinical trials for COVID-19. Sarilumab can be given either intravenously at 8 mg/kg body weight (up to a maximum of 800 mg) in two infusions, 12 h apart, or subcutaneously at 162 mg administered in two simultaneous doses, one in each thigh (i.e., 324 mg in total).	[6,25,34]
	Siltuximab (Sylvant)	A monoclonal antibody IL-6 receptor inhibitor. Siltuximab can be given either intravenously at 8 mg/kg body weight (up to a maximum of 800 mg) in two infusions, 12 h apart, or subcutaneously at 162 mg administered in two simultaneous doses, one in each thigh (i.e., 324 mg in total).	[6,25,34]
	Meplazumad (Nucala)	A humanized IgG1 kappa monoclonal antibody specific for IL-5. Meplazumad is proven to bind the host-cell-expressed CD147 to the spike protein of SARS-CoV-2, so it is involved in host cell invasion. Recent evidence revealed higher levels of blood vascular endothelial growth factor (VEGF) in COVID-19 patients compared with healthy controls.	[30]
	Bevacizumab (Avastin)	A humanized anti-vascular endothelial growth factor (VEGF) monoclonal IgG ₁ antibody and a VEGF-specific angiogenesis inhibitor. Biologics are targeted therapies that adhere to a certain marker on a cancer cell or, in the case of a drug such as bevacizumab, target the growth factor that supports tumor vasculature.	[25,30]
	Ecuzumab (Soliris)	Ecuzumab is a humanized monoclonal antibody that has a long-acting effect and targets complement C5, which inhibits hemolysis. The complement system has been found to be involved in the pathogenesis of other coronaviruses. In the ongoing SOLID-C19 clinical trial for COVID-19, Ecuzumab was utilized to modulate the activity of the distal complement, thereby preventing the formation of the membrane attack complex (MAC). By regulating this part of the immune response, mortality can be reduced while patients have the opportunity to recover from the virus with supportive medical care. Results from the SOLID-C19 trial study showed that the mean C-reactive protein levels dropped from 14.6 mg/dL to 3.5 mg/dL, and the mean duration of the disease was reduced to 12.8 days.	[5,30]
	Camrelizumab (SHR-1210)	An IgG4κ humanized monoclonal antibody that targets programmed cell death protein 1 (PD-1), a protein on the surface of cells, also known as CD279. It may limit the cytokine dysregulation that causes fatal respiratory disease.	[30]
Convalescent plasma	Also called immune plasma or hyperimmune plasma	Convalescent plasma is a unique plasma product that differs from other types of plasma products in that it is derived from individuals who have recovered from a specific infection. The plasma contains high levels of antibodies with sufficient biological activity to provide passive immunity to the recipient. Studies have shown that treatment with convalescent plasma can lead to a significant reduction in respiratory viral load, serum cytokine levels (IL-6, IL-10, TNFα), and mortality. Convalescent plasma works by inducing the production of antibodies, type I interferons, and proinflammatory cytokines.	[30,34]
Intravenous injection of gammaglobulin	Polyclonal antibody (pAb) therapy	The polyclonal antibody (pAb) is a mixture of IgG1 and other antibodies derived from healthy human plasma. Gamma globulin has no obvious effect. Can be used for severe and critically ill children.	[55,56]
Antimalarial	Chloroquine	Research has demonstrated that at a half-maximal concentration of 1.13 μM, SARS-CoV-2 viral infection can be blocked by raising the pH of the endosome, which is essential for viral fusion. Additionally, chloroquine and hydroxychloroquine have been shown to potentially inhibit specific enzymes by interacting with DNA, which could lead to an antiviral effect on SARS-CoV through altering the glycosylation of the ACE2 receptor and spike protein.	[31,55]
	Hydroxychloroquine	Significantly associated with viral load reduction/disappearance in COVID-19 patients, and its effect is reinforced by azithromycin.	[31,33,35]
	Artemisinin and its derivatives *	Has anti-inflammatory activity, NF-κB-coronavirus effect, and chloroquine-like endocytosis inhibition mechanism.	[31,55]

Table 2. Cont.

Treatment	Agent or Device	Mechanism of Action	Reference
Anti-fibrotic agents	Pirfenidone (Esbriet)	Pirfenidone (5-methyl-1-phenyl-2-[1H]-pyridone) is a promising novel anti-fibrotic agent with minimal adverse effects. It is currently approved for the treatment of mild to moderate idiopathic pulmonary fibrosis. Pirfenidone has been found to (1) inhibit apoptosis, (2) downregulate the expression of ACE receptors (the major cellular receptor for COVID-19), (3) decrease inflammation through several mechanisms, (4) ameliorate oxidative stress, (5) protect pneumocytes and other cells from COVID-19 invasion, and (6) potentially modulate cytokine storms. These characteristics suggest that pirfenidone may have potential for the treatment of COVID-19 patients. Ongoing clinical trials are exploring the safety and efficacy of pirfenidone in treating COVID-19.	[55,57]
Nucleoside analog	Remdesivir (GS-5734)	Remdesivir, an adenosine nucleoside analog, inhibits RNA polymerase activity and has shown in vitro inhibitory effects against SARS-CoV-1, MERS-CoV, Ebola virus, and Marburg virus. It has been identified as a promising candidate for COVID-19 treatment due to its ability to inhibit SARS-CoV-2 in vitro. At a half-maximal concentration of 0.77 μ M, remdesivir blocks viral infection and has demonstrated a shorter time to recovery in hospitalized adults compared to placebo. In clinical trials, it has also shown superior effectiveness compared to the combination of lopinavir/ritonavir + IFN beta. Remdesivir is currently approved for the treatment of COVID-19 in hospitalized adults and adolescents aged 12 and over with pneumonia who require supplemental oxygen.	[5,55]
	Azoloazins	A guanine nucleotide analog that inhibits RNA synthesis.	[41]
	GD31	A novel nucleoside analog and important class of antiviral agents that is in ongoing clinical trials for the treatment and prevention of COVID-19 (current as of 20 March 2020). Clinical trial ID is ChiCTR200002989 (ICTPR).	[25,30]
Anti-HIV	Lopinavir/ritonavir (Kaletra)	Combination therapy of lopinavir and ritonavir has shown to be relatively safe. Clinical trials for COVID-19 treatment with this therapy are currently ongoing. The combination inhibits the HIV protease enzyme, thus preventing the cleavage of polyproteins. The recommended dosage is 2 capsules twice daily, taken orally. Combination therapy has demonstrated complete recovery in patients with COVID-19-related pneumonia, as reported in a study with oseltamivir.	[2,30,33,34,37]
	Indinavir (Crixivan)	Potently inhibits the target's protease inhibitors (PIs). Results of this analysis also support its ability to effectively bind SARS-CoV-2-targeted proteins to inhibit COVID-19 infection.	[2,5,55]
	Darunavir (Prezista)	Proteinase inhibitor of 3-chymotrypsin-like protease (3CLPRO). Showed low activity but represents a promising drug target for the development of therapeutics agents for SARS-CoV, as well as for other human coronaviruses including SARS-CoV-2.	[2,5,25,30,55]
	Saquinavir (Invirase and Fortovase)	Not only binds well to the main protein indispensable for the virus replication, the M protein, but also combines with the S protein of SARS-CoV-2.	[2,5,55]
Anti-hepatitis C	Ribavirin	In ongoing clinical trials for COVID-19. Usually used in combination with interferon α (IFN). Competes for the active site of RNA-dependent RNA polymerase (RdRp). Ribavirin scored 109.5 μ M of half-maximal concentration against SARS-CoV-2.	[7,23,31]
	Sofosbuvir	Acts as a nucleotide polymerase inhibitor used for the treatment of hepatitis C. It is used in combination with interferon or Ribavirin (RBV).	[30,32]
	Velpatasvir	An inhibitor of the nonstructural protein 5A (NS5A) protein of HCV that may inhibit the SARS-CoV-2 RdRp enzyme. Represents a safe and effective antiviral option. Studies encourage the use of the dual-component HCV drugs (velpatasvir/sofosbuvir) as a re-purposed treatment against SARS-CoV-2.	[2]
	Paritaprevir	An anti-hepatitis C virus that binds with high affinity to the spike protein and other target proteins, namely, 2'-o-ribose methyltransferase and dihydroergotamine.	[2]
	Azvodine	An azidocytidine analog that inhibits viral reverse transcriptase and has been effective against HIV and hepatitis B and C viruses.	[5,30]
	IDX-184	A new anti-hepatitis C virus that binds with high affinity to the spike protein and more target proteins.	[2]

Table 2. Cont.

Treatment	Agent or Device	Mechanism of Action	Reference
Anti-influenza	Oseltamivir (Tamiflu)	A neuraminidase inhibitor target viral release that prevents the already replicated virus from leaving the host cell. Acts against influenza A and B viruses and is being trialed in patients with COVID-19.	[7,30,58]
	Baloxavir marboxil (Xofluza)	M2 ion channel blocker/adamantanes target viral uncoating. Neuraminidase inhibitors, such as oseltamivir, target viral release, which prevents the already replicated virus from leaving the host cell. Has weak in vitro activity against SARS-CoV-2. Further studies are needed.	[25,34,37]
	Favipiravir (Avigan)	A nucleoside analog that can inhibit the activity of RNA polymerase of the influenza virus. It was found in a recent in vitro study to have anti-SARS-CoV-2 activity. Has a broad-spectrum activity. Approved by Shenzhen Health Commission for treating COVID-19 patients in China, and it is also currently used in Japan.	[55]
	Umifenovir (Arbirol)	Claimed to inhibit viral entry into target cells and stimulate the immune response. According to Chinese guidelines, it can inhibit the replication of SARS-CoV-2 in low concentrations of 10–30 µM.	[25,30,34,55]
	Triazavirin (Riamilovir)	A new synthetic antiviral drug that inhibits the synthesis of viral RNA and prevents the replication of genomic fragments.	[13,30]
	Zanamivir (Relenza)	3-CLPRO is vital for the replication of the virus, and Zanamivir shows potential as the main 3-chymotrypsin-like protease proteinase.	[2,55]
Anti-hepatitis B	Novaferon	Novaferon inhibited viral replication and protected cells from SARS-CoV-2 attack. It exhibited anti-SARS-CoV-2 effects in vitro and in vivo. Inhalation of Novaferon for COVID-19 treatment is safe.	[25,39]
Chemotherapy	Venetoclax (ABT-199)	Binds in vitro with high affinity to nucleocapsid protein and 2'-o-ribose methyltransferase.	[2]
Immunostimulant	Polyinosinic: polycytidylic acid, poly(I:C)	A synthetic analog of dsRNA that can strongly induce type I interferon.	[25,30]
Cell-permeable, tumor-promoting	Tapsigargine	Tapsigargine has been shown to have inhibitory activity against SARS-CoV-2. In a study, pre-treatment of Calu-3 and NHBE cells with Tapsigargine inhibited SARS-CoV-2 replication, with similar results in the inhibition observed against the OC43 virus in A549 and MRC5 cells. Additionally, Tapsigargine was found to prevent virus reproduction in cells for at least 48 h following a single 30-min exposure.	[49,50]
Anticancer drug	Plitidepsin	Prevents SARS-CoV-2 from replicating in the lungs of mice.	[42]
Anti-tumor activity	Teniposide (VM-25)	Teniposide is a semisynthetic derivative of podophyllotoxin with antitumor properties. Its mechanism of action primarily involves the G2 and S phases of the cell cycle. Teniposide has high affinity binding to target proteins, including spike protein, 2'-o-ribose methyltransferase, and dihydroergotamine.	[2]
Anti-inflammatory drugs	Baricitinib	Inhibits the JAK-STAT signaling pathway and may impair the interferon-mediated antiviral response, which could potentially facilitate the progression of SARS-CoV-2 infection. When administered in combination with antiviral drugs such as Remdesivir, it may enhance the efficacy of the drug in reducing viral infection.	[5,30]
	Glucocorticoids	The use of glucocorticoids for the treatment of COVID-19 should be avoided due to their potential to impair innate immunity and cause immune suppression. However, based on chest imaging results, in cases of severe dyspnea, methylprednisolone may be used for a short period (3–5 days) with a recommended dosage of no more than the equivalent of 1–2 mg/kg methylprednisone per day.	[6,7,55]
	Ruxolitinib (trade names Jakafi/Jakavi)	Encompasses Janus kinase inhibitor, JAK inhibitors, jakinibs. Ruxolitinib acts against JAK1/JAK2 with potent anti-inflammatory properties consistent with the CRS, which increases activation of the JAK/STAT pathway. Many patients have severe respiratory disease due to COVID-19.	[5,25,30]
	Atomization inhalation of alfa-interferon	Studies showed a significant reduction in viral titer in the culture of SARS-CoV-2 pretreated with IFN-I. Therapy with α-interferon atomization inhalation reduces the time of duration of high blood levels of inflammatory markers including IL-6. Can be considered in 5 million U per dose for adults in sterile injection water, twice a day.	[25]

Table 2. Cont.

Treatment	Agent or Device	Mechanism of Action	Reference
GI microbiome modulators *	Probiotics/prebiotics	Personalized nutrition and supplementation can have a positive impact on the gut microbiome profile, leading to improvements in immunity. This approach may be used as a prophylactic measure to minimize the impact of COVID-19, not only in elderly and immunocompromised patients but also in the general population. In China, up to 71% of COVID-19 patients were administered antibiotics, and the use of probiotics resulted in a reduction in diarrhea and decreased susceptibility to subsequent infections.	[6,7,17,43]
Anti-migraine drug	Dihydroergotamine (ZINC000003978005)	An anti-migraine drug and a derivative of ergotamine. A potent molecule that inhibits coronavirus's main protease enzyme 3CLPRO and binds with high affinity to nucleocapsid protein and 2'-o-ribose methyltransferase of SARS-CoV-2.	[2]
Alcohol vaporization or nebulization or inhalation therapy	Ethanol therapy (70%)	The inhibitory property of ethanol on RNA polymerase responds to virus replication and could directly involve the bilayer lipid capsule of the virus. It is suggested to administer 50 mL of ethanol 70% per half a liter of dextrose 5% at 12 hrs. If the patient is under mechanical ventilation, 50 mL of ethanol 70% should be poured into a humidifier. The cumulative administered ethanol in two of these dosages is less than the FDA permission dosage.	[47]

* Also used in CM treatment of COVID-19 infection.

3.2. COVID-19 Prevention and Treatment with CM

Based on the theoretical system of Chinese medicine (CM), plague refers to virulent infectious diseases caused by epidemic factors such as special epidemic toxins. Given the highly infectious nature of COVID-19 and the similarity of symptoms during its onset, it can be classified as a plague [58] within the framework of CM.

In 2020, several recommendations were made based on CM principles to prevent COVID-19 [24]. Some of these recommendations cited in the literature include:

- Wear Chinese herb bags or sachets containing herbs and spices such as *Syzygium aromaticum* (cloves), *Fineleaf schizonepeta*, *Perilla frutescens*, *Atractylodes lancea*, *Cinnamomum cassiae*, *biond magnolia flower*, *Asarum sieboldii*, and *Elettaria cardamomum*, 2 g each. Crush these into powder and put them into bags for external use, changing them every 10 days [24,38];
- Perform indoor herbal medicine fumigation with moxa in the room, using 1–5 g/m² for 30 min per day [24,38];
- Take a foot bath using Chinese herbs, including *Artemisia vulgaris* 10 g, *flos Carthamus* 10 g, and dried *Zingiber officinale* (ginger) 6 g. Soak the herbs in boiling water and bathe the feet in the medical liquid when the temperature is suitable, as hot as possible, for about 20 min [24];
- Take a preventive formula prescription of Chinese herbs, including *Astragalus mongholicus* 12 g, roasted rhizoma *Atractylodis macrocephalae* 10 g, *Saposhnikovia divaricata* 10 g, *Cyrtomium fortunei* 10 g, *Lonicera caprifolium* (honeysuckle) 10 g, dried citrus *reticulata* peel or orange peel 6 g, *eupatorium* 10 g, and *Glycyrrhiza glabra* (licorice) 10 g. Take the decoction once a day for adults for 5 days [24,38];
- Drink medical tea made of *Perilla frutescens* leaf 6 g, *Schizonepeta* leaf (agastache) 6 g, dried *Citrus reticulata* peel or orange peel 9 g, stewed *Amomum subulatum* (amomum tsao-ko) 6 g, and three slices of *Zingiber officinale* (ginger). Soak the herbs in hot water and drink the water just like enjoying tea [24].

Regarding treatment, CM, along with other complementary medical systems, focuses on preventing the disease by strengthening the immune system and nourishing the lungs, as well as removing toxins from the body, to improve the elimination of the virus [59]. Several treatment proposals were published from the beginning of the pandemic situation, mainly based on Chinese phytopharmacology. For example, CM doctors used a heavy dose of bitter and cold herbs to clear heat and detoxify, purging the viral infection in the early stage, as well as to cool blood and remove blood stasis promptly in the middle and late stages [51].

Lori Hsu [20] compiled and translated the Chinese guidelines used for preventing and treating COVID-19 disease in China. These guidelines incorporate the foundational principles of Chinese medicine (CM) known as the Six Stages of Cold Invasion, as described in Zhang Zhong-Jing's "Treatment of Febrile and Miscellaneous Diseases from the Shang Han Za Bin Lin" diagnosis. According to this theory, the virus can rapidly progress through all three Yang stages, followed by all three Yin stages, and even engage in "stage hopping," meaning the infection can rapidly and deeply penetrate the body.

The Zhongnan Hospital of Wuhan University Novel Coronavirus Management and Research Team, the Evidence-Based Medicine Chapter of China International Exchange and Promotive Association for Medical and Health Care [CPAM], developed a rapid advice guideline to diagnose and prevent COVID-19 (Table 3) [24]. The Office of the State Administration of Chinese medicine recommends the use of Qingfei Paidu decoction, a general prescription for patients with mild or severe symptoms, as well as those in convalescence. This decoction is based on Mahuang decoction, Xiaochaihu Tang, Wuling Powder, Shegan Mahuang decoction, and Ju-Zhi-Jiang decoction. Additionally, a Huoxiang Zhengqi capsule, a classic prescription used for dispelling dampness, regulating spleen and stomach function, and inducing diaphoresis, is recommended as Chinese patent medicine [19,24,59].

Table 3. CM treatments for patients with COVID-19 infection.

Treatment Modality	Treatment Strategies:	Formulas	Reference
Phytotherapy	If the body temperature is above 37.8 °C	Da Qing Long Tang (Major Bluegreen Dragon decoction) should be given immediately to keep the patient from developing a high fever. Depending on the fever, another dose may be necessary 4–8 h later.	[20]
	If the temperature is below 37.8 °C	Ge Gen Tang (Kudzu decoction) with Fu Ling (Poria) and Bai Zhu (Rhizoma Atractylodis macrocephalae).	[19,20]
	If there is no change in chest imaging	In WM, She Gan Ma Huang Tang (Belamcanda and Ephedra decoction) is recommended for pulmonary effusion, pulmonary edema, and/or inflammation in the lungs.	[20]
	If there is a change in chest imaging at the time of admission	Ze Qi Tang (Euphorbia decoction) and Fu Ling Si Ni Tang (Frigid Extremities decoction with Poria) should be given immediately. If She Gan Ma Huang Tang (Belamcanda and Ephedra decoction) is insufficient, give Ze Qi Tang to remove the water and phlegm retention in the lungs. At the same time, if it is necessary to strengthen the heart by stimulating Yang Qi, give Fu Ling Si Ni Tang.	[20]
	If the patient's cough sounds turbid	In this case, this may indicate phlegm retention in the trachea, so add Qian Jin Wei Jing Tang (Reed Decoction Worth a Thousand Gold Pieces).	[20]
	If the patient has an irritating dry cough, and water is retained in the diaphragm	Ling Gan Wu Wei Jiang Xin Ban Xia Xing Ren Tang (Poria, prepared licorice, Schisandra, ginger, Asarum, Pinellia and apricot kernel decoction).	[20]
	If the patient is suffering from "heat above and cold below"	Pao Fu Zi to warm the lower jiao appropriately. When the Kidney Yang is sufficient, the breath is incorporated.	[11,20]
	If the patient has nausea	This may mean the disease has entered the Shao Yang level. Modified Xiao Chai Hu Tang (Minor Bupleurum decoction) is prescribed in this case.	[11]

Table 3. Cont.

Treatment Modality	Treatment Strategies:	Formulas	Reference
	Preventive formula (children)	Astragalus mongholicus 6 g, roasted rhizoma Atractylodis macrocephalae 5 g, Saposhnikovia divaricata 5 g, Cyrtomium fortunei 5 g, Lonicera caprifolium (honeysuckle) 5 g, dried citrus reticulata peel or orange peel 5 g, eupatorium 5 g, and <i>Glycyrrhiza glabra</i> (licorice) 5 g. Take the decoction once a day for 5 days.	[6,24,38]
	If heat-clearing (children)	Has antivirus activity and is indicated for inflammation and throat disorder: use Radix Scutellaria and herb Artemisia annuae Rhizoma Balamcandae.	[60]
	For the treatment of upper respiratory infections (children)	Semen Armenicae and Semen Coicis are indicated to nourish the lungs. Semen Armenicae is one of the most prescribed formulas for the treatment of COVID-19 in children.	[60]
	For common cold (children)	Ma Xin Shi Gan Tang (herb Ephedrae and herb Gypsum Fibrosum) have antiviral properties against influenza.	[60]
Diet therapy	Food immunomodulatory properties by stimulating phagocytosis	Rice bran, wheat bran, Lawsonia alba (hina), Echinacea purpurea (eastern purple coneflower), Plumbago zeylanica (Ceylon leadwort), and Cissampelos pareira Linn (velvetleaf).	[7,11]
	Food for lack of fluids	Drink a glass of juice (pear and pineapple) every day. Clear soup with bones not only in the evening. Avoid hot food. Drink tea, especially Scrophularia. Avoid excessive alcohol and coffee.	[7]
	Food for phlegm	Avoid over spicing, cold food, and cold beverages. Avoid everything that makes patient feel tired after the meal. Drink hot water. Taste the mixture of 5 sapsors to make the wheel run.	[7]
Acupuncture	Medical observation phase	To promote the flow of vital Qi and enhance the functions of the lung and spleen, as well as to eliminate pathogens and improve organ defenses against them, the following acupoints are recommended: (1) Fengmen (BL12), Feishu (BL13), Pishu (BL20); (2) Hegu (LI4), Quchi (LI11), Chize (LU5), Yuji (LU10), (3) Qihai (CV6), Zusanli (ST36), Sanyinjiao (SP6). Choose one or two acupoints from each group for each treatment session. Specific matches for symptoms include (1) fever, dry cough, and throat, treated with Dazhui (GV14), Tiantu (CV22), Kongzui (LU6); (2) nausea, vomiting, loose stool, greasy tongue coating, and soft pulse, treated with Zhongwan (CV12), Tianshu (ST25), Fenglong (ST40); (3) fatigue, weakness, and lack of appetite, treated with Zhongwan (CV12), four points around the umbilicus (1 cun each side from umbilicus), Pishu (BL20); (4) clear runny nose, shoulder and back soreness, pale tongue coating, and slow pulse, treated with Tianzhu (BL10), Fengmen (BL12), and Dazhui (GV14).	[6,61]

Table 3. Cont.

Treatment Modality	Treatment Strategies:	Formulas	Reference
Clinical treatment phase (confirmed cases)		<p>To stimulate the vital Qi of the lung and spleen, protect the viscera, dispel the spread of pathogens, “reinforce the earth to generate metal/gold”, stop the tendency of the disease, lighten the mood, and enhance the confidence to overcome the disease. The main acupoints are divided into two groups. Group 1 includes Hegu (LI4), Taichong (LR3), Tiantu (CV22), Chize (LU5), Kongzui (LU6), Zusanli (ST36), and Sanyinjiao (SP6), and group 2 includes Dazhu (BL11), Fengmen (BL12), Feishu (BL13), Xinshu (BL15), and Geshu (BL17). To treat light and general cases, 2–3 main points should be selected from groups 1 and 2 each time. To treat severe cases, 2–3 main points from both groups should be chosen. Matching points are as follows: For symptoms combined with prolonged fever, Dazhui (GV14) and Quchi (LI11) or ear tip and fingertip bloodletting are recommended. For symptoms combined with chest tightness and shortness of breath, Neiguan (PC6) and Lieque (LU7) or Juque (CV14), Qimen (LR14), and Zhaohai (KI6) are recommended. For symptoms combined with coughing up phlegm, Lieque (LU7), Fenglong (ST40), and Dingchuan (EXB1) are recommended. For symptoms combined with diarrhea and loose stools, Tianshu (ST25) and Shangjuxu (ST37) are recommended. For symptoms combined with coughing up sticky and/or yellow phlegm and constipation, Tiantu (CV22), Zhigou (TE6), Tianshu (ST25), and Fenglong (ST40) are recommended. Finally, for symptoms combined with low fever, hidden fever, or even no fever, vomiting, loose stools, and pale tongue or pale rose tongue with white greasy coating, Feishu (BL13), Tianshu (ST25), Fujie (SP14), and Neiguan (PC6) are recommended.</p>	[6,61]

Table 3. Cont.

Treatment Modality	Treatment Strategies:	Formulas	Reference
	Convalescence phase	To eliminate any remaining viruses, restore vitality, and repair the functions of the visceral organs such as the lungs and spleen. The main acupoints used are Neiguan (PC6), Zusanli (ST36), Zhongwan (CV12), Tianshu (ST25), and Qihai (CV6). For patients with a deficiency of Qi in the lungs and spleen, symptoms may include shortness of breath, fatigue, poor appetite, vomiting, stomach distension, lack of energy for defecation, loose stools, and a tongue with a slightly fatty and white greasy coating. Those with chest tightness and shortness of breath should be treated with Danzhong (CV17), Feishu (BL13), and Zhongfu (LU1). For those with obvious spleen and stomach symptoms such as indigestion and diarrhea, treat with Shangwan (CV13) and Yinlingquan (SP9). For patients with deficiency of both Qi and Yin, symptoms may include weakness, dry mouth, thirst, palpitations, excessive sweating, poor appetite, low or no fever, dry cough with phlegm, dry tongue with less saliva, and fine or weak pulse. Those with obvious weakness and shortness of breath should be treated with Danzhong (CV17) and Shenque (CV8). For those with obvious dry mouth and thirst, treat with Taixi (KI3) and Yangchi (TE4). Those with palpitations should be treated with Xinshu (BL15) and Jueyinshu (BL14). Those with excessive sweating should be treated with Hegu (LI4), Fuliu (KI7), and Zusanli (ST36). For insomnia, treat with Shenmen (HT7), Yintang (GV29), Anmian (EX), and Yongquan (KI1). For patients with deficiency of both lung and spleen and stasis of phlegm blocking the meridians, symptoms may include chest tightness, shortness of breath, disinclination to speak, fatigue, sweating when moving, cough with phlegm, blocked phlegm, scaly dry skin, mental fatigue, and poor appetite. These patients should be treated with Feishu (BL13), Pishu (BL20), Xinshu (BL15), Geshu (BL17), Shenshu (BL23), Zhongfu (LU1), and Danzhong (CV17). For those with phlegm blocked, treat with Fenglong (ST40) and Dingchuan (EXB1).	[6,61]
Moxibustion	Self-therapy	Moxibustion therapy is indicated for the stimulation of specific acupuncture points including Zusanli (ST36), Neiguan (PC6), Hegu (LI4), Qihai (CV6), Guanyuan (CV4), and Sanyinjiao (SP6). The recommended duration for each acupuncture point is approximately 10 min to achieve optimal therapeutic effects.	[61]
	Application therapy	The application of either moxibustion hot paste or warming moxibustion cream is recommended for points such as Zusanli (ST36), Neiguan (PC6), Qihai (CV6), Guanyuan (CV4), Feishu (BL13), Fengmen (BL12), Pishu (BL20), and Dazhui (GV14).	[6,61]

Table 3. Cont.

Treatment Modality	Treatment Strategies:	Formulas	Reference
Tuina/ acupressure	Intermittent pressure over acupressure points	Hegu (LI4), QuChi (LI11), Sanyinjiao (SP6), Waiguan (TW 5), Danzhong (CV17), Zusanli (ST36).	[6,62]
	Tuina	Chest-soothing and Qi-regulating manipulation.	[6,62]
	Meridian massage	The application of various massage techniques, including kneading, pressing, rubbing, tapping, and patting, on the lung and heart meridians of the upper limb, as well as the spleen and stomach meridians below the knee, is recommended. The duration of each operation should be around 15–20 min.	[6,18]
Qigong	Traditional exercises	Therapeutic exercises such as Yi Jin Jing (Muscle/Tendon Change Classic), Tai Chi, Ba Duan Jin (Eight Pieces Brocade), Wu Qin Xi (Five Animal Exercise), should be performed according to the individual's condition. It is recommended to practice once a day, with each session lasting 15–30 min.	[6,12,62]
	Breathing	Breathing of six healing sounds, turtle breathing Qigong (to benefit the lungs), healthy Qigong, daoyin, eight-step lung-benefiting exercise, Ba Duan Jin (Eight Pieces Brocade), meditation.	[6,59]
Foot bath	Chinese herbs to treat wind-heat and eliminate pathogens.	Prepare a medicinal decoction by combining <i>Nepeta cataria</i> L., <i>Artemisia absinthium</i> , <i>Mentha</i> , <i>Houttuynia cordata</i> , <i>Folium Da Qing Ye</i> , <i>Eupatorium fortune</i> , <i>Acorus tatarinowii</i> , <i>Polygonum flaccidum</i> , <i>radix Curcumae</i> , and <i>Syzygium aromaticum</i> in equal quantities of 15 g, along with 3 g of borneol. Afterward, pour the decoction into a footbath, add warm water, and wait until the temperature reaches around 38 to 45 °C before soaking the feet for approximately 30 min. This therapeutic approach aims to help dispel wind and heat, as well as eliminate pathogens from the body.	[61]

It is worth noting the existence of published medical staff recommendations based on CM, such as:

- To counter direct and daily contact, medical staff are recommended to use additional herbs to strengthen and protect themselves. Some examples are Gan Cao Gan Jiang Tang (licorice and ginger decoction), Gui Zhi Tang (cinnamon twig decoction), Fu Ling (Poria), and Bai Zhu (Rhizoma *Attractylodes macrocephalae*). The balance between Yin and Yang and the draining of dampness excess from the body can be accomplished by successfully applying the abovementioned formulas to improve the Zong Qi (Chest Qi) [19,24,59];
- In the case of extensive contact with patients for longer periods, clinic practitioners need additional and stronger herbs to decrease water retention and clear the lungs, such as She Gan Ma Huang Tang (Belamcanda and Ephedra decoction). At the same time, the room's air temperature and humidity need to be controlled to avoid the retention of fluids in the lungs [20];
- When staff statistics indicate the risk of overworking and exhaustion, it is necessary to enhance their Yang energy using Fu Ling Si Ni Tang (Frigid Extremities decoction with Poria) [20];

- In the case of a dry throat, it is immediately recommended to use Ge Gen Tang (Kudzu decoction) with Fu Ling (Poria) and Bai Zhu (Rhizoma *Attractylodis macrocephalae*) [19,20,24];
- Most patients with mild COVID-19 perform Qigong exercises under the guidance of medical practitioners to improve the pain and fatigue associated with COVID-19 disease [6];
- For pediatric patients, the Chinese Center for Disease Control and Prevention has approved three traditional guidelines (see Table 3) [60].

Current clinical and experimental research has demonstrated the potential of acupuncture-moxibustion to modulate the immune system, while also exhibiting anti-inflammatory and anti-infective properties, thereby playing an active role in the prevention and management of infectious diseases. In fact, acupuncture-moxibustion has been utilized as a complementary therapy with promising outcomes in the treatment of COVID-19 [6,61]. Acupuncture intervention for COVID-19 infection is recommended in three phases (Table 3), i.e., (1) the medical observation phase, (2) the clinical treatment phase, and (3) the convalescence phase, depending on the pathogenic stage [61]. The acupuncture technique is applied with a gentle reinforcing and reducing method, and needles are retained at each acupoint for 20–30 min, followed by moxibustion for 10–15 min. Treatment frequency should be once daily. Although the risk of infection associated with needle acupuncture treatment is minimal, this may pose a potential limitation to its use.

As we have noted, in the specific context of the COVID-19 pandemic, it has been possible to use certain traditional Chinese medicine (TCM) protocols, because the viral infection is considered an external pathogenic agent with corresponding homogenized characteristics. However, it is important to emphasize that TCM is a customized and highly individualized therapeutic approach, and prescriptions and therapeutic techniques should only be considered after an individualized diagnosis of each patient. Even though an external agent is invading, different constitutions and diverse functional homeostatic states will likely react in different ways to the same viral infection. Therefore, after the initial prescription, close patient follow-up is necessary. Whenever necessary, prescriptions should be adjusted to address new functional states and correlated symptoms. These adjustments may need to be made every 48 h or every week, depending on the individual patient's condition.

3.3. Other Complementary Approaches for COVID-19 Prevention and Treatment

3.3.1. AYUSH

Other ancient systems of medicine, such as AYUSH, the three Indian Systems of Medicine, are still widely used among the Indian population and are based on established knowledge and practices related to disease prevention and promoting health and well-being [63], using natural substances [64]. These traditional systems of medicine employ processes such as sweating, Turkish bath, massage, purging, vomiting, exercise, leeching, etc. to eliminate toxic agents.

Ayurveda and Yoga may support COVID-19 patients by improving the quality of standard care, since these are recommended measures for a healthy lifestyle rather than merely prescribed medicine. Ayurveda's greatest treasure is the concept of building the strength of mind and body to face stressors, including infection. A robust immune response to maintain homeostasis is critical for a good recovery, which requires a favorable cytokine balance. AYUSH uses ingredients of animal and marine origin, and Rasayana botanicals, such as Ashwagandha, may be effective in improving immunity in COVID-19, as they demonstrate immunomodulatory and antioxidant effects [65]. Ashwagandha also has potential mechanisms of action in vascular integrity and the management of pyrexia-related targets of COVID-19.

Similar to CM, from the Ayurvedic point of view, COVID-19 is a janapadodhwamsa vikara, meaning an epidemic disease [66]. Unani medicine takes special care of the elderly as a population that may be more susceptible to acquiring different diseases once they have weaker bodies, i.e., Abdan-i Zaifa. Some preventive measures are provided to maintain health: i) the diet should follow the Mizaj (temperament); ii) a nutritive and easily digestible diet should be eaten; iii) frequent meals should be eaten in small quantities; iv) drinking cold water should be avoided; v) good bowel habits should be maintained; vi) adequate sleep should be maintained; vii) moderate exercises should be performed. Stress-relieving measures are equally important to follow. Certain Unani drugs such as *Cyperus rotundus* (Sa'd Koofi), *Paeonia emodi* (Ood Saleeb), and *Delphinium denudatum* (Jadwar) may also be beneficial. Table 4 shows some of the recommendations published in 2020 following AYUSH principles.

Table 4. Complementary treatments for patients with COVID-19 infection.

Type of Treatment and Description		Reference
Nutritional care	Curcumin	Found in tumeric; recommended daily intake range should be 3 mg/kg body weight. Binds to three protein receptors: (1) receptor-binding domain-S (RBD-S); (2) peptidase domain of Angiotensin-converting enzyme 2 (PD-ACE2), and (3) SARS-CoV-2 main protease. [5,17]
	Sugar avoidance	Avoid simple sugars due to their immunosuppressant effects. [67]
	Use of spices	Many warming spices have anti-viral properties (they act in different stages such as targeting the viral replication of SARS-CoV or have the potential to inactivate the viral ribosome, etc.). These include <i>Allium sativum</i> (garlic), <i>Zingiber officinale</i> (ginger), <i>Thymus vulgaris</i> (thyme), <i>Origanum vulgare</i> (oregano), and <i>Salvia officinalis</i> (sage). They are easily added to teas and food dishes. [5,8,18,67]
	Fruits and vegetables	Colored fruits (e.g., elderberry) and vegetables can reduce proinflammatory mediators by enhancing immune cell profiles. Flavonoids have been shown to inhibit the viral 3CL protease. [17,18,63]
	Several species of mushrooms	Can be obtained from the diet or by supplementation. Have multiple powerful antiviral actions against several influenza viruses and other infections. [17]
	Good diet	The suggested daily dietary regimen entails the consumption of freshly prepared, piping hot vegetable soups containing ingredients such as radish, trigonella leaves, and drumstick vegetable pods, as well as protein-rich legumes such as lentils, green gram/mung beans, and chickpeas, seasoned with beneficial spices such as ginger (<i>Zingiber officinale</i>), garlic (<i>Allium sativum</i>), and cumin seeds (<i>Cuminum cyminum</i>). [5,8]
	Probiotics and diets rich in fiber	Improves gut dysbiosis and stimulates the immune system to fight viruses by increasing the T-cells' regulation to help fight inflammation. [17,23]
	Vitamin C	Powerful antiviral action by increasing the production of NK cells. [7,22–24]
	Vitamin A	Enhances NK cells and T-cell proliferation by enhancing the secretion of IL-2 and signaling in T-cells. [7,22–24]
	Vitamin D3	Vitamin D3 is essential for immune function by increasing cytokine responses, antimicrobial peptides, and surface defensins as part of the first line of defense against viral particles that can attach to the respiratory tract. [7,67]

Table 4. Cont.

Type of Treatment and Description		Reference	
Sunshine	Sunshine not only increases vitamin D3 production but also supports the immune system independent of vitamin D3.	[27,67]	
Astragalus	Has immunostimulatory and anti-inflammatory properties. Inhibits the overproduction of nitric oxide and inflammatory cytokines.	[21,24]	
Echinacea	Echinacea purpurea helps with the resolution of inflammation post-infection. Echinacea purpurea strengthens the pathogenic infection through the activation of the neutrophils, macrophages, polymorphonuclear leukocytes (PMN), and NK cells.	[18]	
Zinc	Studies have demonstrated that compounds capable of inhibiting RNA polymerase activity have exhibited inhibitory effects against previous coronaviruses. Chloroquine, a zinc ionophore, has been found to impede the replication of SARS-CoV and other viruses. Adequate intake of zinc, vitamin C, and vitamin D may represent a promising pharmacological approach to combat COVID-19 infection, as these nutrients are in high demand during contact with the virus and the inflammatory response.	[7,18,23]	
“Earthing,” or grounding	“Earthing” or grounding refers to the practice of physically connecting the body, particularly the feet, to the surface of the earth. This connection allows for an influx of electrons into the body, which can lead to a variety of health benefits such as anti-inflammatory effects, enhanced immunity, anticoagulation, increased blood oxygenation, and potential antipyretic effects. Given these effects, earthing may play a significant role in managing patients with COVID-19 infection. Some plants, including the roots of Moringa, are known to have grounding properties and have been used as traditional medicines to enhance feelings of serenity, balance, and centeredness, particularly during times of change or uncertainty.	[8]	
AYUSH–Ayurvedic	Medicated water	Consuming hot or warm water is a common home remedy that is believed to provide various health benefits. In traditional medicine, several spices commonly used in the kitchen are added as single or multiple agents to boiling water and consumed throughout the day. These spices include dried ginger (<i>Zingiber officinale</i>), licorice root (<i>Glycyrrhiza glabra</i>), rhizomes of <i>Cyperus rotundus</i> , roots of <i>Vetiveria zizanioides</i> , Indian sarsaparilla (<i>Hemidesmus indicus</i>), coriander (<i>Coriandrum sativum</i>), fennel seeds (<i>Cuminum cyminum</i>), cinnamon bark (<i>Cinnamomum verum</i>), and catechu bark (<i>Acacia catechu</i>). These spices are believed to have various medicinal properties that may be beneficial for overall health and well-being.	[8,17,63]
	Daily diet	Fresh, hot soups made from a combination of vegetables such as radish, trigonella leaves, and drumstick vegetable pods, along with pulses such as lentils, green gram/mung beans, and chickpeas, can be seasoned with a variety of spices including ginger (<i>Zingiber officinale</i>), garlic (<i>Allium sativum</i>), cumin seeds (<i>Cuminum cyminum</i>), and mustard seeds (<i>Brassica nigra</i>) to enhance flavor and provide potential health benefits.	[5,24,63]
	Diet from day 1–13	Rice porridge.	[8]
	Diet from day 14–30	Include milk and butter oil (Ghee).	[8]

Table 4. Cont.

Type of Treatment and Description		Reference	
Mouth rinse and gargle	Gargling or rinsing the mouth with warm liquids and oils can effectively cleanse the mouth and throat while providing systemic benefits. Oily decoctions and warm liquids can thoroughly clean the oral cavity, pharynx, and tonsillar area, forming a protective biofilm that may induce immunomodulatory, antioxidant, and antimicrobial effects on the mucosa.	[8,26]	
Nasal oil application	Applying medicated oils made from Ghee or vegetable oils such as sesame or coconut in the nostrils is believed to protect the respiratory tract against pathogen invasion. Two drops of sesame oil should be applied to each nostril every morning to prevent respiratory diseases and dry nasal mucosa.	[5,18,63]	
Steam inhalation	Hot fomentation with aromatic oils such as menthol provides satisfactory clinical relief in nasal and throat congestion, bronchoconstriction, headache, and sinusitis. Its role in improving nasal conditioning, improving nasal mucus velocity, and reducing congestion and inflammation has been reported in several clinical studies.	[8,18]	
Polyherbal formula	<i>Sudarsana Churna</i> : alleviates or cures all types of fevers, including <i>Agantuja jwara</i> , <i>Sannipata jwara</i> , etc.; <i>Dhanvantara Gutika</i> : cures <i>Svasa</i> , <i>Kasa</i> , <i>Vaata anulomana</i> (aiding the normal flow of <i>vayu</i>); <i>Talisadi Churna</i> : cures <i>Jwara</i> , <i>svasa</i> , <i>kasa</i> , <i>aruchi</i> (loss of taste); <i>Deepanam</i> (stimulates digestion).	[5,8,67]	
Non-pharmacological measures	Good sleep, mental relaxation, good lifestyle behavior, and Yoga are recommended.	[8]	
Yoga	Several studies guarantee the role of Yoga breathing techniques (pranayama), postures (asanas), and procedures (yogic kriya) in improving lung health and exercise tolerance. Pranayama is known to improve lung function.	[62]	
Meditation	Meditation is found to reduce inflammation markers and influence markers of the virus-specific immune response.	[7,63]	
	Siddha is a kind of medical treatment that emphasizes the treatment of respiratory and digestive issues related to chronic diseases.	[8]	
Rasayana botanicals	All act as potential immunomodulators: <i>Withania somnifera</i> (Ashwagandha), <i>Tinospora cordifolia</i> (heart-leaved moonseed), <i>Asparagus racemosus</i> (Shatavari), <i>Phyllanthus embelica</i> (Indian gooseberry), and <i>Glyceriza glabra</i> (licorice).	[8,17]	
AYUSH–Unani	Prophylactically	The herb <i>Cydonia Aqueua oblonga</i> (Quince), trade name Behidana 3 g, taken twice a day for 14 days shows antioxidant, immune-modulatory, anti-allergic, muscle relaxant, and anti-influenza activities. Take: <i>Zanjabeel</i> (<i>Zingiber officinale</i>), <i>Gilo</i> (<i>Tinospora cordifolia</i>), <i>Aslassus</i> (<i>Glycyrrhiza glabra</i>), <i>Khameera Marwareed</i> , and <i>Safoof Asgand</i> .	[5,63]
	High fever	Immunity enhancer: <i>Habb-e-Mubarak</i> (1–2 g) 1 g (pill) twice daily < 6 years old; 2 g (pill) twice daily > 12 years old. <i>Habb-e-Mubarak</i> is a solid preparation (pill) made with the ingredients: <i>Myrica esculenta</i> (Kaifal) 1 part and <i>Caesalpinia bonducella</i> (Maghz-e-Karanjwa) 2 parts. Immunity enhancer: <i>Habb-e-Bukhar</i> (250–500 mg) also has a beneficial action in all kinds of phlegm. Take 250 mg (pill) twice daily for patients 6–12 years of age and 500 mg (pill) twice daily for >12 years old. Made with <i>Tian Zhu Huang</i> , <i>Cinchona</i> bark, sedimented starch, <i>Acacia Arabica</i> (Lam.), <i>Willd.</i> (Tabasheer, <i>Kanakana</i> , <i>Satt-e-Gilo</i> , and <i>Samagh-e-Arabi</i>).	[28]

Table 4. Cont.

Type of Treatment and Description		Reference
	Sore throat	Immune system booster: Sharbet-e-Toot Siyah (<i>Morus nigra</i>) has shown significant beneficial effects on a sore throat, resolving pharynx and larynx inflammation, tonsillitis, tongue and throat soreness, and other relevant oral or respiratory disorders. <i>Morus nigra</i> prevents abnormal catarrhs from dropping into the pharynx and acts as a febrifuge due to its cold and moist nature, making it effective in reducing fever associated with upper respiratory tract infections. The recommended dosage is 10 mL twice daily for ages 6–12 and 20 mL twice daily for those over 12 years old. [28]
	Difficulty in breathing	Laoq-e-Katan ingredients: linseed (<i>Alsi</i>), flaxseed oil (<i>Roghan Alsi</i>), inulin (<i>Shakar Safaid</i>), citric acid (<i>Sat Leemun</i>), sodium benzoate (<i>Natroon Banjawi</i>). Take Laoq-e-Katan: (1) 6–12 years old (10–20 g): 5 g twice daily or 125 mg (pill) twice daily; (2) >2 years old: 10 g twice daily or 250 g (pill) twice daily. [28]
Homeopathy	In the early stages	<i>Aconitum napellus</i> , <i>Arcenicum Album</i> , <i>Eupatorium perfoliatum</i> , <i>Gelsemium</i> , or <i>Ipecacuana</i> . [54,68]
	In the later stages	<i>Bryonia</i> or <i>phosphorus</i> as the main drugs. [54,68]
	In the final stages	<i>Antimonium Tartaricum</i> , <i>Baptisia</i> , or <i>Camphor Officinalis</i> . [54,68]
Ozone (O ₃) therapy	Alternative therapy in the different phases of SARS-CoV-2 infection	There is strong evidence supporting the biological properties of ozone in the various stages of SARS-CoV-2 infection. Ozone has the potential to inactivate the virus directly via O ₃ oxidation or indirectly via ROS and LOPs oxidation. Moreover, it could enhance both cellular and humoral immune systems, making it a useful therapy in the early stages of COVID-19 infection. Furthermore, ozone has been shown to improve gas exchange, reduce inflammation, and modulate the antioxidant system, suggesting its potential use in the cytokine storm (hyperinflammation) and hypoxemia phases. [27,29]
Osteopathic manipulative treatment (OMT)	General benefits	Improves the function of the chest wall and the associated respiratory structures. Improves lymphatic drainage of the pulmonary parenchyma. [67]
	In pneumonia	Manual manipulation techniques manage lymphatic flow, respiratory function, and immunological defense by targeting anatomical structures involved in these systems. [67]
Halotherapy	Inhaled sodium chloride aerosol	Shows many of benefits such as: (1) thins the mucus in the airway to make it easier to expel, making coughs more productive and less stressful, especially in patients with thick sputum; (2) decreases edema of the bronchial mucosa; and (3) enhances the functioning of the cilia epithelium, leading to better functioning of the alveolar macrophages. There is an idea that salt reduces inflammation and kills microbes in the lungs, thus reducing the risk of infections (including anti-allergic mechanisms). [69]
Aromatherapy		Peppermint, eucalyptus, pine needle, and juniper berry oils are known to have respiratory benefits, including opening up the airways and improving breathing capacity. These oils also possess expectorant properties, which can help alleviate respiratory symptoms associated with mild cases of COVID-19. Though they are not a substitute for medical treatment, these oils can be a useful adjunct therapy for those with mild symptoms who have not been hospitalized. [18]

3.3.2. Functional Food

The role of food has evolved from mere sustenance to preventing and treating diseases while promoting overall physical and mental well-being. The concept of functional foods was first introduced in Japan in the early 1980s and has since gained popularity worldwide, catering to the demand for healthier products. According to Foods for Special Health Use (FOSHU), functional foods refer to natural or formulated foods that contain specific ingredients to aid bodily functions while providing nutrition [44].

With an increasing demand for healthier living, functional foods are gaining popularity in the Western world. Naturopathy suggests that good nutrition strengthens immunity, as exemplified by the adage “feed a cold and starve a fever.” Protein-rich foods, glucose, and vitamin C and D are recommended for better and faster recovery from viral infections. For instance, combining vitamin C and red ginseng may alleviate lung inflammation induced by viral infections by increasing T-cell and NK cell activity [70]. Table 4 presents some of the published nutritional care recommendations for COVID-19.

It is worth noting that further research is needed to explore the effectiveness of functional foods and their active components in preventing and treating diseases, including COVID-19. Nonetheless, the increasing interest and demand for these types of foods suggests their potential benefits in improving health and well-being.

3.3.3. Homeopathy

Homeopathy, developed by Hahnemann (1755–1843), is a personalized approach to therapy that aims to address the individual’s unique symptoms and underlying imbalances. Homeopathy can be used as a complementary therapy in the early stages of COVID-19 when respiratory symptoms are common in other viral upper respiratory diseases (Table 4) [71]. In response to the COVID-19 pandemic, India’s Ministry of ‘AYUSH’ has recommended the use of the homeopathic remedy ‘Arsenicum album 30’ as a prophylactic measure to prevent infection. This recommendation is supported by the Prime General Secretary of Liga Medicorum Homeopathica Internationalis (LMHI). Additionally, the UK Department of Health and Social Care has recommended the use of Gelsemium 30c and Bryonia 30c for COVID-19 treatment [68]. Homeopathy has been a subject of debate in the scientific community, with some studies showing promising results, whereas others question its effectiveness. Nonetheless, it remains a popular complementary therapy in many parts of the world.

3.3.4. Aromatherapy

Aromatherapy is an ancient healing practice that has been used for centuries in Egypt and India to treat various ailments. It involves using essential oils that contain the plant’s natural fragrance. Some of these oils have shown potential in opening up respiratory passages and improving breathing capacity, as well as acting as mucous expectorants. They may be used to alleviate mild COVID-19 symptoms in patients who do not require hospitalization.

Despite a study by Loizzo et al. in 2008 suggesting that a distilled oil extracted from *Laurus nobilis* berries was effective in combating SARS-CoV, there is still a lack of clinical research in this area [72]. However, there is one study that found the essential oil of *Eucalyptus* to be beneficial in improving the innate cell-mediated immune response and acting as an immunoregulatory agent against infectious diseases. This study is reported in Table 4 [18].

3.3.5. Halotherapy

Halotherapy, a centuries-old therapy, has gained popularity in recent times, particularly in Eastern Europe and Russia, where individuals flock to natural salt caves to alleviate symptoms of asthma, bronchitis, colds, and sinus infections. Modern-day halotherapy involves the use of artificial salt caves, which are climate-controlled rooms made of slabs or bricks of salt that have salt nano-particle diffusion. These facilities can be found in some spas and standalone centers in the US and Europe [69]. Though the literature on halotherapy is limited, a study reported in Table 4 suggests that it can be effective in reducing inflammation and the risk of infection. Halotherapy is a non-invasive, drug-free therapy that shows great promise in treating respiratory illnesses, and further research is needed to determine its efficacy and safety.

3.3.6. Ozone Therapy

As of 2020, there were around 80 clinical trials underway to find an effective treatment for COVID-19 infection. Interestingly, only three of these studies investigated ozone therapy as an alternative and cost-effective option [29]. Ozone possesses unique biological properties that allow for its potential use in various stages of SARS-CoV-2 infection. The virus is rich in cysteine residues, which must remain intact for viral activity. Since sulfhydryl groups are susceptible to oxidation, ozone could inactivate the virus through direct (O_3) or indirect oxidation (ROS and LOPs), making it useful in the early stages of COVID-19 infection. Additionally, ozone therapy appears to improve gas exchange, reduce inflammation, and modulate the antioxidant system, which could be beneficial in the cytokine storm phase and the hypoxemia and/or multi-organ failure phase. However, more experimental studies need to be conducted to confirm the biological properties of ozone as a safe complementary therapy for SARS-Cov-2 infection. Such research is crucial for understanding the full potential of ozone therapy and its potential use as a complementary therapy for COVID-19.

4. Discussion

The interactions discussed between different complementary medical systems and Western Medicine (WM) are important for implementing a more comprehensive approach to health, defined by the United Nations as “a state of complete physical, mental, and social well-being and not only the absence of affections and illnesses” [73]. To ensure the right to health for all people, four minimum conditions must be met by the state: financial availability, accessibility, acceptability, and quality of public health services in the country. In countries where access to pharmaceuticals is limited due to cost, herbal medicine may offer a potential solution when used individually or in combination with traditional medication. In this regard, the WHO Traditional Medicine Strategy: 2014–2023 [74] advocates for the formulation of proactive policies aimed at facilitating the integration, regulation, and supervision of traditional medicines. It also emphasizes the implementation of action plans to enhance the role of traditional medicines in maintaining the health of the population. This strategic approach will prove instrumental in fostering innovative solutions that align with a broader vision of improved healthcare and patient autonomy.

As diets become less natural, fresh, local, and nutrient-dense, a better understanding of functional foods and herbs to prevent immune senescence, promote healthy aging, and aid the healing process may become increasingly important.

The concept that a robust immune response is critical for maintaining immune homeostasis is a shared idea between WM and CM. Hippocrates famously said, “Let food be thy medicine and medicine be thy food,” and the Chinese ancient statement that “medicine and food are isogenic” is still recognized in traditional Chinese medicine (TCM). Food and herbs can also be used as dietary or complementary therapy in WM to prevent infection and strengthen immunity. Garlic and *Moringa oleifera* are two examples of commonly used herbs with therapeutic purposes in both Western and different complementary medicines.

Obesity has been found to increase the risk of developing severe pneumonia in COVID-19 patients, and according to TCM, obesity is linked to dampness, both external and internal, which is a predisposing factor for COVID-19. The humidity of the weather is also believed to be related to the proliferation of SARS-CoV-2, with the spread being lower in warm and wet climates. WM and CM both recommend regular physical activity, with Qigong and Yoga being traditional practices that promote lung health and exercise tolerance for COVID-19 patients. Oxygen therapy is also used in WM to improve symptoms in COVID-19 patients.

The integration of complementary medicine, which also takes into account the psychological aspects of patients, and WM may offer valuable experiences in the ongoing global fight against COVID-19. Although CM and WM have different approaches to the treatment and evaluation of COVID-19, they share the same preventive care measures. When used in combination, they exhibit complementary effects, as shown in the literature.

With distinct approaches yet overlapping characteristics, both therapies have a place in today's evolving healthcare landscape. Consequently, it is imperative to conduct in-depth analyses of the ways in which these therapies are accepted and integrated into healthcare systems across different regions. Furthermore, the establishment of effective regulatory and supervisory systems or institutions is essential to enhance the credibility of complementary practices and products, ensuring their quality, safety, and effectiveness. Emphasizing the importance of consumer choice, these measures will help to provide assurance while facilitating the integration of these therapies into mainstream healthcare.

Future advances and recognition of CM and other complementary medicines require a major upgrade in the role and quality of Chinese medical translation as well as research using modern scientific approaches to provide high-quality evidence for their integration into Western medical healthcare systems. In recent years, remarkable progress has been achieved in the processing and investigation of medicinal plants, encompassing modern extraction techniques and the identification of key constituents. These can provide a significant contribution to the quality control and standardization of herbal medicine and supplements to guarantee the quality and safe use of these products.

5. Conclusions

COVID-19 has caused a significant number of deaths worldwide, and as of yet, no approved treatment exists for this disease. However, in 2020, evidence emerged showing that it is possible to improve the symptoms and progression of the disease using an integrative medicine approach that combines Western medicine (WM) with other complementary systems of medicine. Integrating WM, complementary medicine, and other treatments may help prevent the disease from progressing to a critical condition. Therefore, it is crucial to avoid severe symptoms and prevent the spread of the disease by implementing all adequate interventions, medical observations, and diagnoses, which can enrich an integrative approach with success.

Regarding future perspectives, besides implementing national regulations, it is essential to establish relevant guidelines to standardize regulations to prevent the transmission of SARS-CoV-2 and, consequently, COVID-19 infection. It is imperative to invest in prevention and to gain more knowledge in understanding the pathogenesis associated with SARS-CoV-2 infection to develop alternative vaccines for new variants and effective treatments for severe disease.

Some pertinent outstanding questions can be proposed, such as:

- (i) How important is it to integrate both medical systems, WM and complementary medicine, for prevention?
- (ii) Are conventional drugs used to treat COVID-19 easily accessible in all countries, and what is the cost?
- (iii) How long will we have to wait for new, efficient drugs? In the meantime, could integrated strategies be useful from a global perspective?

These questions may lead to significant advancements in our understanding of COVID-19 and pave the way for better treatment options and prevention strategies.

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