

## PROBABLE TREATMENT OPTIONS FOR COVID-19: A BRIEF REVIEW

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### ABSTRACT

Over the last few decades, we have observed several global outbreaks of severe respiratory infections. The current outbreak is novel severe acute respiratory syndrome corona virus 2 (SARS-CoV-2). It is a rapidly spreading disease affecting millions of people worldwide as well as birds and animals. It predominantly caused respiratory tract and gastrointestinal tract symptoms and other mild to very severe clinical signs. The countries most affected countries among all by the disease are the United States of America (USA), India, Brazil, Russia and France with recording the highest infection, morbidity, and mortality rates. Since early January 2021, many articles have been published on COVID-19. Most of these articles were consistent with the reports on the mode of transmission, spread, duration, and severity of the sickness. This worldwide pandemic has put a challenge to identify the therapeutics for its prevention and treatment. Currently, there's no specific treatment against the SARS-CoV-2 infection. Based on the different clinical phases and pathological features various drugs are used for its treatment. The volume and the pace of the clinical trials launched to evaluate the safety and efficacy of numerous agents reflect the need for high-quality evidence for various therapies to be practiced by clinicians. Thus, this review comprehensively discusses the most critical aspects and overall treatments used for COVID 19, including ayurvedic treatments and vaccines.

**Keywords:** A comprehensive review, COVID-19, global outbreak, pandemic infection, Recent advancements.

## INTRODUCTION

Recently World Health Organization (WHO) announced the current outbreak of pneumonia that began at the beginning of December 2019 somewhere in Wuhan City, Hubei Province, China<sup>[1]</sup> and named it '2019-nCoV' or Corona virus disease (COVID-19). The COVID-19 is a pathogenic virus. When phylogenetic analysis carried out with obtainable full genome sequences it was found that bats are the reservoir of COVID-19, but the intermediate host(s) has not been detected till now.<sup>[2-4]</sup> Corona viruses mostly cause gastrointestinal and respiratory tract infections and are inherently categorized into four major types: Gamma coronavirus, Delta coronavirus, Beta coronavirus and Alpha corona virus. The first two types mainly infect birds, while the last two mostly infect mammals. Six types of human CoVs have been formally recognized. These comprise HCoV HKU1, HCoV-OC43, Middle East Respiratory Syndrome corona virus (MERS-CoV), Severe Acute Respiratory Syndrome corona virus (SARS-CoV) which is the type of the Beta corona virus and HCoV229E and HCoV-NL63- member of the Alpha corona virus.<sup>[5-9]</sup> Corona viruses did not draw global concern until the 2003 SARS pandemic preceded by the 2012 MERS and most recently by the COVID-19 outbreaks. SARS-CoV and MERS-CoV are known to be extremely pathogenic and spread from bats to palm civets or dromedary camels and eventually to humans.<sup>[10-12]</sup>

COVID-19 is spread by dust particles and fomites while close unsafe touch between the infector and the infected individual. Airborne distribution has not been recorded for COVID-19 and is not known to be a significant transmission engine based on empirical evidence; although it can be imagined if such aerosol-generating practices are carried out in medical facilities. Faecal spreading has been seen in certain patients, and the active virus has been reported in a small number of clinical studies. Furthermore, the faecal-oral route does not seem to be a COVID-19 transmission engine; its function and relevance for COVID-19 need to be identified.<sup>[13-15]</sup>

However, there are already many concerns regarding the latest corona virus. Although it seems to be transferred to humans by animals, it is important to recognize individual animals and other sources, the path of transmission, the incubation cycle, and the features of the susceptible community and the survival rate. Nonetheless, very little clinical knowledge on COVID-19 disease is currently accessible and details on age span, the animal origin of the virus, incubation time, outbreak curve, viral spectroscopy, dissemination pathogenesis, autopsy observations, and any clinical responses to antivirals are lacking among the serious cases.<sup>[16-19]</sup>

**Symptoms:**

Coronavirus or covid-19 show symptoms related to respiratory tracks.

***Most common symptoms:***

- fever
- cough
- tiredness
- Loss of taste or smell.

***Less common symptoms:***

- sore throat
- headache
- aches and pains
- diarrhea
- a rash on skin, or discoloration of fingers or toes
- red or irritated eyes.

**Serious symptoms:**

- difficulty breathing or shortness of breath
- loss of speech or mobility, or confusion
- chest pain.

Patients may suffer from nasal congestion, difficulty in breathing and pneumonia followed by lowering of lung efficiency. In chest X-ray bilateral infiltrates are seen to some extent.

The incubation period predictions are from between 2 to 14 days. Older people and those with underlying medical conditions like cardiovascular disease, diabetes, chronic respiratory disease, and cancer are more likely to develop serious illness<sup>[20-24]</sup>

The best way to prevent and slow down transmission is to be well informed about the disease and how the virus spreads. Protect yourself and others from infection by staying at least 1 meter apart from others, wearing a properly fitted mask, and washing your hands or using an alcohol-based rub frequently. Get vaccinated when it's your turn and follow local guidance.

**Preventative Measures and Policies Enforced by the World Health Organization (WHO)**

- Get vaccinated when a vaccine is available to you.
- Stay at least 1 meter apart from others, even if they don't appear to be sick.
- Wear a properly fitted mask when physical distancing is not possible or when in poorly ventilated settings.
- Choose open, well-ventilated spaces over closed ones. Open a window if indoors.

- Wash your hands regularly with soap and water or clean them with alcohol-based hand rub.
- Cover your mouth and nose when coughing or sneezing.
- If person feel unwell, they must stay at home and self-isolate until recovery.

There is presently no specific vaccine or specific drug regime used to treat critically ill patients. The management of patients mainly focuses on the provision of supportive care, e.g., oxygenation, ventilation, and fluid management. Combination treatment of low-dose systematic corticosteroids and antiviral and atomization inhalation of interferon have been encouraged as part of critical COVID-19 management <sup>[24-29]</sup>.

## MODE OF TRANSMISSION

### Animal-to-Human Transmission

Although the infection is zoonotic, the mode of transmission of COVID-19 in humans is not clear, but the bats are suggested to be the reservoir for the human SARS-CoV-2. Based on codon similarities between the human SARS-CoV-2 and the *Bungarus multicinctus* snake coronavirus, it appears the snakes are also potential reservoirs for the infection. The Malayan pangolin (*Manis javanica*) is a natural reservoir of the SARS-CoV-2, and they are suggested to play a significant role in the transmission of COVID-19 to humans. <sup>[30-31]</sup>

### Human-to-Human Transmission

COVID-19 is known to exhibit human-to-human transmission, the primary mode of transmission in the current pandemic. COVID-19 patients spread the disease to those in close contact. <sup>[32-34]</sup> However, since many COVID-19 patients are asymptomatic and can serve as carriers, they may have unknowingly transmitted the virus to others. This mode of transmission includes:

### Horizontal Transmission

There are 3 main modes of horizontal transmission of COVID-19 in humans: <sup>[35]</sup>

### Direct Contact

This mode of transmission may occur through direct interaction with virus-contaminated objects or surfaces and infecting people through the mouth, nose, or eyes. In addition, a direct correlation between air pollution and COVID-19 was observed. Thus, exposure to indoor polluted air is likely to be directly associated with the disease, especially among refugees and migrant workers who live in feeble conditions. However, home isolation for an infected population may be a potential factor to other health problems if the place where they are socially isolated is not adequately ventilated. Therefore, an understanding of the consequences of the relationship between indoor air quality and the COVID-19 pandemic should be considered. <sup>[36]</sup>

### **Aerosol**

COVID-19 virus is primarily not airborne. Instead, the virus is present in the aerosols of expired air, coughs, and sneezes, which are the main media for virus spread from COVID-19-positive people. The virus remains viable for at least 3 hours in aerosols and as long as 48 to 72 hours on stainless-steel and plastic surfaces.<sup>[37]</sup>

### **Droplet**

Respiratory air typically contains an abundance of droplets of sizes  $<5 \mu\text{m}$  in diameter. Coughing and sneezing cause increased expulsion of these droplets from the oral cavity and respiratory tract. In COVID-19 patients, these droplets contain a virus that, if inhaled or ingested, will cause disease.<sup>[38]</sup>

### **Faeces and Body Fluids**

COVID-19 transmission may also occur via faeces, urine, tears, sweats, and conjunctival secretions. The role of faeces in the transmission of COVID-19 is unclear. There are suggestions that the gastrointestinal system is an essential route for the spread of SARS-CoV-2.<sup>[39-40]</sup> Incidentally, there are high expressions of ACE2 in the gastric glandular, colon, ileal, duodenal, and rectal cells, suggesting the virus may spread via the faecal-oral route. Unlike in the respiratory tract, where the clearance of the occurs within 2 weeks, the feces can remain positive for corona virus RNA for longer than 4 weeks, even after the patient no longer show symptoms of the disease.<sup>[41-43]</sup>

### **Vertical Transmission**

It is believed that COVID-19 can potentially be transmitted vertically due to the high expression of ACE2 receptors in the human maternal–fetal interphase. This indicates that the COVID-19 pandemic puts pregnant women and foetuses at risk of being infected.<sup>[44-45]</sup> At the beginning of the disease, cases of vertical COVID-19 transmission were very few and mostly incidental. However, the potential for vertical transmission of COVID-19 has not been ruled out.<sup>[46]</sup>

## **TREATMENT**

### **Antiviral Therapy**

Although there are several compounds under development, there is no drug that is proven effective for treating COVID-19. Currently, the treatment for COVID-19 is mainly supportive.<sup>[47-50]</sup> There are, however, some encouraging results from the use of certain broad-spectrum antiviral drugs like nucleoside analogues and HIV-protease inhibitors that could attenuate viral infections

**Lopinavir/Ritonavir (LPV/r)**

Lopinavir/Ritonavir LPV/r, treatment with LPV/r produced minimal clinical improvement or decreased the frequency of respiratory distress in COVID-19 patients.<sup>[51-53]</sup> However, this treatment might help shorten the duration of viral shedding. Patients treated with LPV/r showed unwanted side effects such as gastrointestinal symptoms. Thus, further clinical trials are needed to evaluate LPV/r's efficacy in treatment.<sup>[54]</sup>

**Interferon Alpha (IFN- $\alpha$ )**

IFN- $\alpha$  nebulization's and sprays are used in COVID-19 treatment.<sup>[55]</sup> IFN- $\alpha$  2b, when used in combination with other antiviral drugs, has been shown to contribute to complete recovery for COVID-19. Subcutaneous injection of IFN- $\alpha$  2b combined with LPV/r shortened the length of hospitalization and accelerated viral clearance in COVID-19 patients. However, the IFN- $\alpha$  2b treatment must be applied with precautions because overdoses can cause myelo suppression and affect the liver and renal functions.<sup>[56-58]</sup>

**Remdesivir**

Remdesivir is a nucleotide analogue broad-spectrum antiviral agent. An early study showed that remdesivir was effective in shortening the recovery time in adults hospitalized with COVID-19.<sup>[59-60]</sup> However, human clinical trials have shown that the drug is ineffective, fails to prevent death in severe COVID-19 patients, and has side effects. Subsequently, the WHO issued a recommendation against the use of remdesivir in hospitalized COVID-19 patients, citing that there is no clear evidence on the effectiveness of the drug in improving the outcome of these patients.<sup>[61]</sup> However, a very recent study showed that remdesivir is more effective and safer than standard care of treatment for the COVID-19 because it is associated with faster time to clinical improvement, reduction in mortality rate, and fewer incidence of serious adverse events.<sup>[62-63]</sup>

**Ribavirin**

Ribavirin is a guanosine analogue antiviral compound that has been used to treat infections caused by respiratory syncytial and hepatitis C viruses and viral haemorrhagic fever. However, there is no clear evidence that Ribavirin is beneficial in the treatment of COVID-19.<sup>[64-65]</sup>

**Chloroquine and Hydroxychloroquine**

There are conflicting reports regarding the efficacy of chloroquine and hydroxychloroquine in the treatment of COVID-19. In vitro studies have shown that chloroquine is effective in inhibiting COVID-19 viral replication. Chloroquine or hydroxychloroquine block viral infections by interfering with the glycosylation of cellular receptors for the virus.<sup>[66-68]</sup> The mechanism of action of chloroquine and

hydroxychloroquine on SARS-CoV-19 are the same; however, hydroxyl-chloroquine may be more effective than chloroquine in reducing viral load. The antiviral effect of hydroxychloroquine is reinforced by the use of azithromycin.<sup>[69]</sup>

### **Arbidol**

Arbidol is a potent broad-spectrum antiviral agent with activity against enveloped and non-enveloped viruses. Arbidol exerts its antiviral effect by blocking viral fusion with cells and inhibiting viral entry. Arbidol is used in the treatment of COVID-19 with variable results. In fact, Arbidol is shown to be superior to LPV/r in the treatment of COVID-19.<sup>[70]</sup>

### **Favipiravir**

Favipiravir is an RNA-dependent RNA polymerase (RdRp) inhibitor. The favipiravir derivative, ribofuranosyl triphosphate, targets the influenza RdRP. In moderately severe, nonventilated COVID-19 patients, Favipiravir improved time to clinical recovery and decreased mortality rate.<sup>[71-72]</sup>

### **Glucocorticoids**

Early use of low-dose corticosteroids, especially dexamethasone, prednisone, and methylprednisolone, for a short duration was found to be useful in improving symptoms of COVID-19. However, there is no published evidence that corticosteroid treatment is effective against this disease. Corticosteroids have immunosuppressive properties and are thus not recommended for use to treat COVID-19 unless indicated.<sup>[73]</sup>

### **Immunoglobulin and Hyper-Immune Serum**

Serum antibodies are effective against MERS and SARS corona virus infections. Immunoglobulins have the advantage of providing protection against common infections, large donor pool, and commercial availability, while hyper-immune serums provide targeted immunity.<sup>[74]</sup>

### **Teicoplanin**

Teicoplanin, a glycopeptide antibiotic routinely used to treat bacterial infections, was found to produce in vitro anti-SARS-CoV-1 effect. The compound is among a list of alternative or complementary molecules used as therapeutic agents for COVID-19. Teicoplanin inhibits cleavage of viral spike protein by cathepsin L at the late stage of viral life cycles, thus, preventing the release of viral genomic RNA and curbing viral replication.<sup>[75-76]</sup> The drug appears to have similar effects on SAR-CoV-2, making it a potential compound in the treatment of COVID-19.



### **Heparin**

COVID-19 patients at high risk of thromboembolic disease.<sup>[208]</sup> The hypercoagulability state associated with the disease requires additional therapeutic interventions like the use of heparin. However, the use of prophylactic heparin in COVID-19 is still contentious. There are other anticoagulants and antiplatelet agents that can be used as alternatives to address the hypercoagulability state in COVID-19.<sup>[77]</sup>

### **Aspirin**

Aspirin, an anti-inflammatory and antiplatelet agent, can prevent the development of a hypercoagulability state and reduce the risk of thromboembolic incidence in COVID-19 patients. The drug also reduces the risk of death in patients with severe COVID-19.<sup>[78]</sup>

### **Ivermectin**

Ivermectin is an oral anthelmintic that is used to paralyze and kill gastrointestinal parasites. Recently, ivermectin was shown to inhibit SARS-CoV-2 replication *in vitro*.<sup>[79]</sup> The drug inhibits viral replication by inhibiting viral protein movement within the cell. Based on the *in vitro* data, the equivalent dose required to produce antiviral effects in the human body exceeds the recommended therapeutic dose, thus, not practical for human use. However, very recently, a meta-analysis of randomized clinical trial studies suggests that ivermectin may offer beneficial effects towards COVID-19 outcomes.<sup>[80-82]</sup>

### **Famotidine**

Famotidine is a histamine-2 receptor antagonist (H2RA) that is used to prevent gastrointestinal ulceration. H2RA was found to inhibit HIV replication. Thus, the drug was suggested as an optional prophylactic medication in COVID-19. In a recent retrospective study, among hospitalized COVID-19 patients, the use of famotidine was linked to the reduction in disease deterioration. This may suggest that the effect of H2RA is beyond anti-acid activity but also has a potential complementary drug in COVID-19 since it improves clinical outcomes in non-hospitalized patients.<sup>[83]</sup>

### **Nitazoxanide**

It is an FDA approved broad-spectrum thiazolide antiparasitic agent for the treatment of *Giardia duodenalis* and *Cryptosporidium parvum* infections in adults and children  $\geq 1$  year. It is rapidly metabolized to its active metabolite, tizoxanide, and has *in vitro* antiviral activity against a variety of viruses, including hepatitis B and C viruses, influenza viruses, rotavirus, Ebola virus, norovirus, Middle East respiratory syndrome coronavirus (MERS-CoV), and SARS-CoV-2.<sup>[84]</sup> The mechanism of antiviral activity is not fully characterized. It impairs the post-translational processing of viral proteins by inhibiting the host enzymes and it also has inhibitory effects on pro-inflammatory cytokines. Nitazoxanide is generally well tolerated having common side effects such as



abdominal pain, diarrhoea, headache, nausea, vomiting, urine discoloration, and, rarely, ocular discoloration.<sup>[85]</sup>

### **Melatonin**

Melatonin is a well-known anti-inflammatory and anti-oxidative molecule. The safety of the melatonin is of utmost importance if we have to use it in treating COVID-19. Melatonin is safe to use in short-term even in higher doses. The various minor adverse effects like occasional headache, dizziness, nausea and sleepiness; in overall melatonin's safety in humans is very high. In clinical trials it has been showed that the oral intake of 3 mg, 6 mg and 10 mg of melatonin is satisfactorily safe compared to placebo by patients in ICU.<sup>[86]</sup>

### **Inflammatory Cytokine Inhibitors**

Inflammatory cytokine storm is a common manifestation in COVID-19. In severely ill patients, the concentration of pro-inflammatory cytokines, such as IL-6, tended to be high. High cytokine levels indicate a poor prognosis in COVID-19.<sup>[87]</sup> Thus, among the complementary therapeutic approaches in COVID-19 is the management of the inflammatory responses. Among the anti-inflammatory drugs shown to reduce the risk of hospitalization in COVID-19 patients are colchicine,<sup>[88]</sup> prostaglandins non-steroidal and anti-inflammatory drugs, except ibuprofen. Carprofen, a human and celecoxib, a veterinary anti-inflammatory drug, also inhibited a crucial enzyme in the replication and transcription of SARS-CoV-2.<sup>[89]</sup>

### **Respiratory Support**

The most critical support for patients with respiratory distress and/or hypoxemia is oxygenation. Conventional oxygen therapy may not be sufficient in adults COVID-19 patients with acute hypoxemic respiratory failure. In these patients, depending on severity, oxygenation may be supplied either by high-flow nasal cannula, endotracheal intubation, or invasive mechanical ventilation. The target for optimal oxygen saturation in adults with COVID-19 is 92% to 96%. In cases of severe lung failure, extracorporeal membrane oxygenation (ECMO) is used to re-establish pulmonary gas exchange. The estimated mortality in patients with severe COVID-19 who received ECMO is <40%.<sup>[90]</sup>

### **Circulatory Support**

Severe COVID-19 is associated with circulatory and cardiac involvement, which can be fatal.<sup>[91]</sup> venous extracorporeal membrane oxygenation (VV-ECMO) support is often instituted in patients with COVID-19-related acute hypoxaemic respiratory failure. This treatment is only appropriate in patients with cardiac disease. In COVID-19 patients with heart failure and decreased cardiac output, it is necessary to institute extracorporeal life support (ECLS).

### **Blood Purification Treatment**

Blood purification treatment comprising plasma exchange, perfusion, absorption, and blood/plasma filtration<sup>[92]</sup> can be applied during the cytokine storm at the early and middle stages of COVID-19. The treatment removes inflammatory factors that could potentially cause damage and death to severely ill COVID-19 patients.

### **Biologicals**

Tocilizumab is a humanized monoclonal antibody against the IL-6 receptor. IL-6, a pro-inflammatory cytokine implicated in the pathogenesis of many diseases. Although recommended for use in COVID-19 patients to reduce lung tissue inflammation,<sup>[93]</sup> tocilizumab did not appear to be effective in preventing death in moderately ill hospitalization patients. However, a very recent meta-analysis study showed that tocilizumab treatment is associated with a reduction of mortality rate from COVID-19.<sup>[94]</sup>

### **Convalescent Plasma**

The COVID-19 convalescent plasma (CP) is a source of anti-SARS-CoV-2 antibodies. It can potentially induce passive immunization in the COVID-19 patients to improve viral clearance and destroy virus-infected cells through cell-mediated cytotoxicity. CP treatment may be used in hospitalized patients with rapid disease progression.<sup>[95-96]</sup> The treatment was shown to increase lymphocyte counts, inflammation markers, and enzymes of inflammation like C-reactive protein (CRP), alanine aminotransferase (ALT) and aspartate aminotransferase (AST).

### **VACCINE**

Vaccination is highly effective in preventing SARS-CoV-2 infection. Anti-SARS-CoV-2 monoclonal antibodies (mAbs) may also be effective as post-exposure prophylaxis (PEP) for certain groups of people who are at risk of progression to serious COVID-19 and who have not been fully vaccinated or who are not expected to mount an adequate immune response to vaccines.

Six efficacious vaccines for COVID-19, by Pfizer Inc. and BioNTech SE, Moderna, Oxford-AstraZeneca, Gamaleya Research Institute, Sinopharm, and Sinovac are now available.<sup>[97]</sup>

### **BNT162b2**

The Pfizer-BioNTech BNT162b2 (generic name tozinameran, brand name Comirnaty) mRNA vaccine encapsulated in lipid nanoparticles with an efficacy rate of 95% requires refrigeration at  $-70^{\circ}\text{C}$  for transportation.<sup>[98]</sup>

**mRNA-1273**

The Moderna vaccine, mRNA-1273, is also an mRNA vaccine encapsulated in lipid nanoparticles. The mRNA-1273 has an efficacy rate of 94.1% and is stable for 6 months while requiring less stringent transportation conditions at  $-20^{\circ}\text{C}$  than BNT162b2.<sup>[99]</sup>

**AZD1222 (ChAdOx1 nCoV-19)**

The Oxford-AstraZeneca AZD1222 vaccine, also known as ChAdOx1 nCoV-19 vaccine, uses a vector, the modified chimpanzee adenovirus ChAdOx1. The AZD1222 is stable below the average refrigerator temperature.<sup>[100]</sup>

**Gam-COVID-Vac**

The Gamaleya Research Institute of Epidemiology and Microbiology, Russia, developed the Gam-COVID-Vac, trade-name Sputnik V, primarily approved for use in Russia.<sup>[236]</sup> Sputnik V is a viral two-vector vaccine based on two human common cold adenoviruses formulated as frozen (storage temperature  $-18^{\circ}\text{C}$ ) and freeze-dried (storage temperature  $2-8^{\circ}\text{C}$ ) dosage forms.<sup>[101]</sup>

**BBIP-Cor-V and BBIBP-Cor-V**

The Chinese Sinopharm BBIBP-Cor-V and Sinovac Corona Vac vaccines are conventional inactivated vaccines. The efficacy of BBIBP-Cor-V is 79.34%. Based on the Turkish clinical trial, the efficacy rate of the Corona Vac vaccine is 91.25%. Both the BBIBP-Cor-V and Corona Vac vaccine can be transported and refrigerated at  $2-8^{\circ}\text{C}$ .<sup>[102]</sup>

**Table No.1:** Vaccines used for Covid 19

Vaccine	Use	Vaccine efficacy (95% CI)
mRNA-1273 Other names: Spikevax, Elasomeran, COVID-19 Vaccine Moderna; TAK-919 COVAX U Severe illness: 100% (non-estimable) [45] Children 12–17 years: efficacy 100% (press Release) [17] Developer: Moderna	WHO         COVAX	Symptomatic illness: 94.1% (89.3– 96.8)         Severe illness: 100% (non- Estimable)
VIRAL VECTOR VACCINES	WHO	Symptomatic illness: 70.4%

<p>AZD1222</p> <p>Recombinant replication deficient ChAdOx1 adenoviral vector Vaccine encoding full length Spike protein</p> <p>Other names: ChAdOx1_nCoV-19, COVID-19 Vaccine AstraZeneca, Vaxzevria, Covishield</p> <p>Developers: University of Oxford, AstraZeneca</p> <p>Serum Institute of India</p>	<p>EU Approved in</p> <p>161 countries</p>	<p>(54.8–80.6)</p> <p>Symptomatic illness, with dose interval 12 weeks: 81.3% (60.3–91.2)</p> <p>Severe illness: 100% (press release)</p>
<p>Sputnik V</p>	<p>Approved in 69 countries</p>	<p>Symptomatic illness: 916% (856–95.2)</p>

## SUPPORTIVE CARE

### Vitamin D

Several dietary supplements and drugs have been recommended to enhance immunity and reduce the risk of acquiring COVID-19. Vitamin D is recommended for COVID-19 patients because the level of this vitamin is markedly low in severe COVID-19 patients, while vitamin D-deficient patients show high inflammatory responses. Vitamin D as an anti-inflammatory supplement offers beneficial effects that suppresses viral replication, reduces the development of pneumonia, and reduces mortality in COVID-19. <sup>[103-105]</sup>

### Vitamin C

Vitamin C (ascorbic acid) is a water-soluble vitamin that is believed to have beneficial effects in patients with severe and critical illnesses. <sup>[106]</sup> Vitamin C plays a role in the prevention and treatment of viral infections by scavenging free oxygen radicals, reducing the accumulation of pro-inflammatory cytokines, and enhancing antimicrobial ability. There is insufficient data to consider vitamin C as a complementary treatment for COVID-19. <sup>[107]</sup> However, vitamin C is suggested to be administered to severe cases of COVID-19 because of its safety profile, low cost, and potential for rapid upscaling of

production. In this regard, Hiedra et al in the USA found a significant decrease in inflammatory markers (ferritin and D-dimer) and a trend to decrease FiO2 requirements after intravenous vitamin C administration in seventeen COVID-19 patients.<sup>[108]</sup>

**Zinc**

The trace mineral zinc is hypothesized to prevent viral attachment to the nasopharyngeal mucosa and inhibit viral replication. One study showed that zinc inhibits RNA polymerase and plays a central role against coronavirus infections.<sup>[109]</sup> Zinc is essential in preserving tissue barriers, such as the respiratory epithelium that prevents entry of pathogens into cells, the immune and redox system and prevents progression of COVID-19.<sup>[110]</sup>

**AYURVEDIC TREATMENT**<sup>[111-115]</sup>

In India, AYUSH has approved following medicines for the treatment of Covid19. Below is the list of various medicines and their dose.

**Table no.2:** Ayurvedic Medicines used for COVID-19.

Clinical severity	Clinical Presentation	Medicines*	Doses & Timing
Symptomatic COVID-19 Positive	For prevention of disease progression to symptomatic and severe form and to improve recovery rate	Guduchi Ghanavati (Samshamani vati or Giloy vati having Aqueous extract of Tinospora cordifolia IP) or the powder of Tinospora cordifolia	500 mg extract or 1-3 powder twice daily with warm water for 15 days or one month or as directed by Ayurvedic physician
		Guduchi + Pippali (Aqueous extracts Tinospora cordifolia IP and Piper longum IP)	375 mg twice daily with warm water for 15 days or as directed by Ayurveda physician
		AYUSH 64	500mg twice daily with warm water for 15 days or as directed by Ayurveda physician
Mild COVID-19 Positive**	Symptomatic management Fever, Headache, Tiredness Dry Cough, Sore throat Nasal congestion	Guduchi + Pippali (Aqueous extracts Tinospora cordifolia IP and Piper longum IP)	375 mg twice daily with warm water for 15 days or as directed by Ayurveda physician
		AYUSH 64	500 mg twice daily

			with warm water for 15 days or as directed by Ayurveda physician
Post COVID Management	Prevention of Post COVID Lung complications like Fibrosis, Fatigue, Mental Health	Ashwagandha (Aqueous extract of Withania somnifera IP) or its powder	500 mg extract or 1-3 g powder twice daily with warm water for 15 days or one month or as directed by Ayurveda physician
		Chyawanprasha	10 g with warm water / milk once a day
		Rasayana Churna (compound herbal powder made up of equal amounts of Tinospora cordifolia, Emblica officinalis and Tribulus terrestris)	3 g powder twice daily with honey for one month or as directed by Ayurveda physician

## CONCLUSION

Although some drugs are being investigated, there is currently no effective treatment for COVID-19. Fortunately, several newly developed vaccines have proven to be highly efficacious for the disease. However, until sufficient herd immunity is achieved in the population, precautions, such as wearing masks, avoiding crowds, social distancing, and regular washing of hands, are still imperative to prevent the further spread of the disease. There are many risk factors associated with COVID-19 infection and its severity, including age, sex, socio demographic behaviour, co morbidities, and the psychological condition of the patient. Older adults and healthcare workers are particularly susceptible to the COVID-19. For that reason, these people were among the first groups scheduled to receive the vaccine. Although COVID-19 is primarily a pulmonary disease, it is also associated with cardiac, dermatologic, haematological, hepatic, neurological, and renal complications. The critically COVID-19 patients are particularly at high risk for thrombo embolic events. Although the immediate clinical manifestations of the COVID-19 are generally clear, the long-term effect of the disease is still unknown. The role of vertical transmission in neonates and the incidence of COVID-19 in children is not clear. However, immune compromised children and those with underlying cardiovascular disorders are at risk of acquiring the severe disease.

The emergence of a new strain of SARS-CoV-2 is causing concern. The new strain appears to spread quickly but does not seem to cause any more severe COVID-19. The

current vaccines appeared to be efficacious in the prevention of infection by the new SARS-CoV-2 strain. However, the data are still preliminary, and the long-term effect of disease by the new SARS-CoV-2 strain is still unknown.

### CONFLICT OF INTEREST

The authors declare that they have no conflict of interest

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