#### CLINICAL PHARMACOLOGY (L BRUNETTI, SECTION EDITOR)



# Ayurveda and Allopathic Therapeutic Strategies in Coronavirus Pandemic Treatment 2020

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#### Abstract

**Purpose of Review** In the last month of 2019, i.e., December, COVID-19 hit Wuhan city in China. Since then, it has infected more than 210 countries and nearly about 33.4 million people with one million deaths globally. It is a viral disease with flu-like symptoms; hence, prevention and management is the best option to be adopted for its cure.

**Recent Findings** Many healthcare systems, scientists, and researchers are fighting for the cure of this pandemic. Ayurvedic and allopathic treatments have been studied extensively and approached for the cure of COVID-19. In addition to ayurvedic treatments, the Ministry of Ayush, India, has also recommended many remedies to boost up immunity. Allopathic studies involved several antiviral drugs which were used in different combinations for the treatment of COVID-19.

**Summary** Comparative analysis of Ayurveda and allopathic treatment strategies were carried out in the present study. Depending upon the patient's conditions and symptoms, Ayurveda is useful for the treatment of COVID-19. Allopathic treatments inhibit viral infection by targeting majorly endocytosis, and angiotensin-converting enzyme (Ace) receptor signaling. In this article, we summarize different ayurvedic and allopathic medicines and treatment strategies which have been used for the treatment of COVID-19, a global pandemic.

Keywords COVID-19 · Symptoms · Ayurveda · Allopathic · Homeopathy

# Introduction

In the last decade, different strains of coronaviruses had presented with challenging health issues to human society. The most popular viruses in this category are severe acute respiratory syndrome coronavirus (SARS-CoV) and Middle East respiratory syndrome coronavirus (MERS-CoV). With an increase in the population, migration, and social life, these viruses showed an increased rate in the recombination of intra- and inter-species

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which made them adapt to every recent host [1]. In 2003, SARS-CoV was one of the most dangerous emergencies in the world for human infection. In its initial stage of infection, it infected nearly 1755 humans with 298 major cases. The severe acute respiratory syndrome coronavirus (SARS-CoV-2019) emerged in 2019 in the month of December in Wuhan city of China, which again made the life of humans miserable with numerous fatal health issues and slowly and gradually this virus entrapped the whole world [2, 3]. The crown-shaped coronavirus leads to serious infections which was a brief part of the human SARS virus and affected the whole world which leads to a loss in business, tourism, and human life [1].

By the end of February 2020 and the start of March 2020, SARS-CoV-19 was declared as an international pandemic by the World Health Organization (WHO). The symptoms of this infection were similar to that of normal flu but included different categories like patients with mild symptoms, asymptomatic patients with no symptoms, and high symptomatic patients. Before the doctors, scientists, and researchers could study and come up with a cure for treatment, this virus had already infected more than lakhs of people across the world with the human coronavirus pathogens, i.e., HCoV-22E and HCoV-OC43,

which affects the upper respiratory tract. In 2005, the other novel pathogen of humans which were diagnosed during the SARS-CoV pandemic in the Netherlands included CoV-NL63 and HCoV-HKU1. This CoV-NL63 (group I) infected children suffering from bronchiolitis and the HCoV-HKU1 (group II) virus infected the adults in Hong Kong with chronic pulmonary infection. In September 2012, the WHO diagnosed another coronavirus which was MERS-CoV, which speeded up in a deadly manner in the Middle East, South Asia, and Africa and more than 75% of cases were diagnosed in Saudi Arab. It was identified that the family line of this virus is group 2 betacoronavirus, i.e., Tylonycteris bat coronavirus HKU4 (Bat-CoV HKU4) whose primary host is bats and HKU5-CoVs pathogen whose primary host is *Pipistrellus* bats which are single-stranded positive RNA bat viruses which are widely distributed during the coronavirus pandemic and very close to humans for infection [4-7]. Bats were the primary host and act as a repository for causing infections not only in SARS-CoV, but were also a causative agent in the MERS CoV. Additionally, camels were also suspected as a source of infection within the crossed species hindrance to contaminate people [8]. So it was remarked as bats are the significant supplies of various alpha coronaviruses and its ancestry of different beta coronaviruses [9]. In China, the common repository of the SARS viruses was the horseshoe bats, but bats being the definitive cause of the MERS virus species were yet to be discovered [10].

#### Pandemic Virus COVID-19

SARS-CoV virus is a ribonucleic acid-containing infectious agent, which is transferable from vertebrates to animals. SARS-CoV infection is mainly developed in people through social contact and migration [11]. The viral genome has a basic protein named replicase which helps in the replication of the genetic genome in the host cell and is methylated at the 5' end and the polyadenylated tail at 3' end because of which the genetic material gets connected to the ribosome's and then replication starts [12]. On the other hand, there is a non-basic protein known as protease, used for the isolation of the proteins present in the chain [13, 14] which helps in the formation of different types of cytokines that leads to the production of lymphocytes. These lymphocytes act as a barrier and prevent viral genome from replicating which results in an increase in the inflammatory reactions [15]. This coronavirus is an enormous group with severe infections causing the symptoms like regular cold, fever, and respiratory disorders (shortness of breath), which helps the virus to propagate and leads to the replication and transmission. The basic symptom is common cold, which led to the discovery of six wellknown different species of coronaviruses which were first distinguished from the patients in the 1960s [16-19]. The incubation period of this virus is around about 5.8 days including the range of almost 2.1 to 11.1 days [20]. It is recommended by doctors and health organizations that coronavirus lasts for about 14 days which is the maximum time period and special precautions should be taken like social distancing, sanitization, self-quarantine, and wearing of masks and gloves [21]. The main target site for this crucial pathogenesis of the SARS-CoV includes the respiratory system and the main diseases which are related to heart injuries and anemia. The data records received from different hospitals across the world observed that by the end of 2019 and at the start of June 2020, it was reported that the COVID-19 crisis leads to patients with the higher plasma level of proinflammatory cytokines like interleukin 1(IL-2), IL-6, IL-7, IL-10, IL-12, interferons gamma (IFN $\gamma$ ), interferons alpha (IFN $\alpha$ ), tumor necrosis factor alpha (TNF $\alpha$ ), and transforming growth factor beta  $(TGF\beta)$  [22]. There are a large number of treatments and therapies available for this antiviral infection. But until now, there is no suitable vaccination for this pandemic but various pharmaceutical companies and researchers are working on it and human trials are going on. This short review summarizes the role of allopathic and Ayurveda in coronavirus infections. Each field plays an important role in their respective areas and will definitely prove fruitful in the early management of COVID-19 patients. Until now, there is no treatment for coronavirus but our government has issued management and precaution guidelines along with a supporting healthcare system which could provide great relief in the outbreak of COVID-19. Many approaches like social distancing, wearing a mask, and medical grounds are used to control the pandemic disease. The main approach to regulate this disease was allopathic and Ayurveda.

# Role of Homeopathy and Ayurveda in COVID-19

From the last 200 years in the late 1700s, a German physician named Dr. Samuel Hahnemann founded the homeopathy as a therapeutic medicine which helped to treat many epidemics, fearful, and severe diseases like cholera, fever, chikungunya, hepatitis, and malaria. The preventive measures of homeopathy are eminent and undeniable; as homeopathic medicines act remarkably on a health condition and cure the diseases. The scientific literature related to homeopathy is highly witnessed [23–26]. There are numerous confirmations that in the year 1918-1919, when Spanish flu emerged, homeopathy had shown amazing results, during which around about 21 million patients died around the world and about 5,00,000 in the USA alone. A study revealed that there was a difference in the mortality rate among the patients which were treated by homeopathy and physicians, i.e., 1-2% appeared differently as they were treated by homeopathy as compare to 50-60% of patients who were treated by allopathic [27, 28]. In homeopathic treatment, every patient after being fully diagnosed and analyzed received medicines. The medical grounds of homeopathy have a clear protocol of sanitation, antibiotics, and vaccinations to control the infections [29-31].

In diseases like dengue which causes hemorrhagic fever, homeopathy has helped in improving the platelet count and therefore there is a slowdown in the clinical center for about 2-3 days [32]. Likewise, there are many diseases in which homeopathy has acted as a buffer or control to decrease the mortality rate by about 15-16% conversely with the people who got simply institutional management. So, by looking at the past history, it can be observed that there are many instances in which homeopathy had shown extraordinary results and it can be equivalently used for the COVID patients but no study has shown its effects on Covid-19. The homeopathic medicines like Belladonna 3c, Eupatorium perfoliatum Q, Grindelia, Calcarea carb, Chinimum sulph, Bryonia, Gelsemium, Phosphorus, Thymulin, Camphora, Influenzinum, Antim tart, and a combination of few tinctures and homeopathic drugs prove to have a high rate of frequency to reduce severe pain, ache, and many more ailments in viral diseases [33].

There were numerous people who were infected by the virus and showed progressive circulation in their history in China's Wuhan village in December 2019 [34]. The name of

the homeopathic therapies was previously reported to prevent viral infections that are presented henceforth [35-38]. Arsenicum album is formed when for continuously 2-3 days arsenic is heated with distilled water. On the basis of the fact sheet released by the CCRH (Central Council for Research in Homeopathy), Arsenicum album 30 can be considered as "prophylactic medicine" COVID-19 [39]. The inflammatory symptoms shown by COVID-19, Arsenic toxicity, and HIV infection are the same and there is a definite synergy between them and may have the suitable potential to aggravate each other. Therefore, Arsenicum album may be considered as a suitable remedy for COVID-19 treatment. Arsenic is one of the constituents in it which showed its enumerating impact on the different macrophage cells as well on tumor cells. Also, it showed decreased NF-κβ hyperactivity (nuclear factor kappalight-chain-enhancer of activated B cells; diminished verbalization of reporter quality of green fluorescent protein (GFP) in transfect HT29 cells) and decreased TNF- $\alpha$  (tumor *necrosis* factor-alpha) release in macrophages. Arsenic album-30 was advised to be taken once in a day for 3 days. The tincture of album-20 is arsenic trioxide which is highly diluted and it works to prevent disease [37]. The proposed mechanism of action of Arsenicum is shown in Fig. 1. Until now, there is no



Fig. 1 Schematic representation of mechanistic insight of Arsenicum via downregulation of NF- $\kappa\beta$  and TNF- $\alpha$  in macrophages

clinical proof for homeopathy medicine as a drug for COVID-19 treatment [40, 41].

Furthermore, for more than 3000 years, Ayurveda, a Sanskrit word, originated in India. Nowadays, it is considered as a traditional system of medicine which helps in the management of infection and maintains the homeostasis of disease. It also helps in building the strength of the mind and soul, and teaches the body to fight against stress. During COVID-19, Ayurveda is also playing an important role as it has enough possibilities and potential for the prevention of infection and treatment for corona victims. The asymptomatic cases in India help in implementing the role of Avurveda, through the regular use of Avurveda medicines and home remedies. But still, the confirmation imagined by Traditional Chinese Medicine (TCM) cannot be disregarded in China [42, 43]. This is directly understood that at the time of the pandemic, approximately 3100 TCM-related workers had been passed on to the Hubei district. TCM was officially accepted by the Chinese guideline on end and used as a cure for COVID-19 [44,45]. This is especially important to observe that specific TCM wards were set up, and quarantine centers were developed which had used Chinese drugs for treatment using western medication [42].

With the accomplishment of TCM in controlling an infectious pandemic, it was reasonable and major to examine how Ayurveda can help in treating COVID-19 [46, 47]. By this time, it was the Ministry of AYUSH which created a standard to change Indian social protection [48] and to show the power of AYUSH to build up prosperity [49]. With this ultimate objective of AYUSH, Ayurveda during the COVID-19 pandemic, people were divided into four specific classifications [50] along with characters and natural herbs for treatment which is tabulated in Table 1.

This classification has huge necessary information which was complete and well managed. Subsequently, it is advised that genuine information of factors that are important should be done on each case. These variables should incorporate age, sex, manifestations, topography, and contact history which results in a clear prescription and should be recorded. On the other hand, TCM did not control COVID-19 cases. Equivalent philosophy was also adopted and has been used in Ayurveda and it should pursue its own skill for finding and coming about remedies optional on roga and rogi bala.

### **Role of Allopathic in COVID-19**

In the allopathic approach, treatment in coronavirus included intravenous infusion of fluid, oxygen therapy, and life support

 Table 1
 Four specific classifications of Ayurveda medication during the pandemic period of COVID-19

Groups	Characters	Herbs	Reference
No symptoms and also unexposed	Do not assimilate those people who do not have related side effects neither they have hazard issues. They doubtless they are most likely invulnerable from disease because of parthenogenesis [48]	For purification of the body herbs like Allium sativum strip, Curcuma longa powder, Trachyspermum ammi seeds, and Loban were used whereas for respiratory tract Swarna Prashana, and mass prophylaxis of rasayana, Brahma Rasayana, Chyavanprasha or Amrit Bhallataka, Rasayana + Samhita were used	[51-60]
Mild symptoms	Have very less symptoms like fever, tiredness, cough, etc. and no need to be hospitalized. Home quarantine and to maintain social distance with family members too.	Nardiya, Ginger Root, Gojihvaadi Kashaya, Pippali rasayana, Sanjeevani vati, C. vati, Solanum surattense, Dashamul kwath, Talishadi Sitopaladi, and Yashtimadhu	[61], [68–70]
Medium symptoms	Moderate to maximum symptoms. Took place with high hazard gathering. Severe symptoms like difficulty in breathing, pain in chest, and deafness; also, they can lose movement too. The patient took into consideration from initial stage and co-recommended with Ayurveda drugs	P. rasayana, Laghu Vasant Glycyrrhiza glabra, Semecarpus anacardium, Tribhuvan keerti rasa Brihata Vata Chintamni rasa, Mrityunjaya rasa, and Siddha makardhvaja rasa	[69], [71–74]
Quarantined	People who did not have any clear signs but still they are in danger because of contact history with patients. Tested on the basis of their contact history.	<ul> <li>Sanjeevani vati, Chitrakadi vati, Guduchi (<i>Tinospora cordifolia</i>), Shunthi (<i>Zingiber</i> officinale),</li> <li>Haridra (<i>C. longa</i>), Sanjivani vati, <i>T. cordifolia</i>,</li> <li><i>Z. officinale</i>, <i>C. longa</i>, Ocimum sanctum,</li> <li><i>Glycyrrhiza glabra</i>, Adhatoda vasica,</li> <li>Andrographis paniculata, Swertia chirata,</li> <li>Moringa oleifera, Triphala</li> </ul>	[61–67]

system in critical cases. It was advisable if anyone prevails symptoms of the virus like flu, fever, and breathlessness, they should contact the doctor immediately. This virus is similar to the human immunodeficiency virus (HIV) in terms of virus replication and proteins. Different administrating drugs were found to clear and handle in vitro action against SARS-CoV and MERS-CoV [75, 76].

## Chloroquine and Hydroxychloroquine

Chloroquine and hydroxychloroquine have a possibility of curing an intestinal disorder, systemic lupus erythematosus (SLE), and rheumatoid joint torment (RA) [77]. Chloroquine and hydroxychloroquine obstruct glycosylation of host receptors, proteolytic, and maturation of endosomes. These mechanisms have immunomodulatory shocks to host cells by bringing down the cytokine level and control of autophagy and lysosomal [78, 79••]. In vitro studies revealed that in the low micromolar concentration, chloroquine crushes SARS-CoV-2 with a halfmaximal credible center (EC50) and hydroxychloroquine with a lower EC50 for SARS-CoV-2 differentiated, i.e., EC50 = 6.14  $\mu$ M and chloroquine: EC50 = 23.90  $\mu$ M [80••].

The treatment of COVID-19 included the oral dosage of chloroquine (500 mg) and hydroxychloroquine (400 mg) on daily basis [81–83]. But still, there is a lack of data which proves the mechanism of chloroquine and hydroxychloroquine. Pharmacokinetic studies reviewed that the ideal dose of hydroxychloroquine for treating COVID-19 patients should be replaced by 200 mg twice instead of 400 mg on daily basis [80••]. Unusually, elective outlines are made for 600 mg of total dose step by step by dividing reliant on freedom and clinical experience for Whipple's disease [81].

#### Lopinavir/Ritonavir and Other Antiretrovirals

The Food and Drug Administration (FDA), USA, recommended and certified lopinavir/ritonavir, an oral drug for HIV, with in vitro activity against other novel coronaviruses through the control of 3-chymotrypsin-like protease [84, 85]. There is no in vitro study data for lopinavir/ritonavir against SARS-CoV-2 [86] but a review on lopinavir/ritonavir was assessed for the treatment of SARS and MERS which showed clinical observations and analysis of SARS with less mortality rate and incubation rates, along with experimental research. The studies revealed that drugs should be used during the early stages of viral replication, i.e., beginning 7–10 days; otherwise, late initiation with lopinavir/ritonavir had no effect on clinical outcomes [87, 88].

#### Ribavirin

A guanine basic drug named ribavirin handles viral ribonucleic-subordinate and polymerase whose activity against various coronavirus makes it a challenger for the treatment of the COVID-19 outbreak. In vitro studies of this drug proved to show advancement against SARS-CoV by blocking the replication of the virus. This mechanism required a high dose of this drug, i.e., 1.2 to 2.4 g orally as expected along with blend treatment. Past studies told that the patients got either endogenous or enteral cooperation [89] and no data exists in its role with the respiratory syncytial disease in COVID-19 [90]. The trial on 30 patients confessed questionable results in which out of 30 examinations, 26 were re-evaluated, with 4 assessments exhibiting hematologic and liver toxicity [38]. On the other hand, in the treatment of MERS, ribavirin was mixed with interferons and its clinical studies resulted in no observable and remarkable effect on viral clearance [77, 91]. Due to a lack of clinical data with ribavirin for SARS-CoV-2 strategies, its supportive occupation must be extrapolated from other nCoV data.

#### Remdesivir

Remdesivir (other name GS-5734) is a prodrug monophosphate which helps in the absorption of Cadenosine nucleoside triphosphate. It was studied that the antimicrobial activity of this drug against RNA proved to be contagions especially in the family of Coronaviridae and Flaviviridae. Due to its low EC50 value, it proved to be therapeutic against the emergence of Ebola virus disease based on its selectivity against host polymerase of Ebola [92•]. Because of broad reach, presently, remdesivir and its in vitro studies against coronavirus help in treating SARS-CoV-2 with EC50 and EC90 estimations of 0.77 µM and 1.76 µM, respectively, and are proved to be a fruitful expected treatment for COVID-19 [93••, 94••]. On the other hand, in murine lung defilement models accompanied by MERS-CoV, remdesivir drug prohibited the lung channel and lessened viral lung titers more than comparator agents [94...].

#### Dexamethasone

Dexamethasone is a type of chemically derived corticosteroid which acts as an immunosuppressor. It abridged deaths by 1/3 in patients getting invasive mechanical ventilation and by 1/5 in patients being delivered oxygen without invasive mechanical ventilation. However, therapy did not decrease the death in patients not getting breathing support at randomization. Therefore,



Fig. 2 This illustration depicts the mechanisms of action of allopathic drugs via various routes including inhibition of endocytosis process, viral proteolysis, replication complex, and ACE2 during COVID-19 infection

dexamethasone abridged 28-day mortality among those getting invasive mechanical ventilation [95..]. Mechanistically, it inhibits the growth of the cytokines which cause infection and is therefore useful in this COVID-19-related hyperinflammation or cytokine storm. It has a high rate of activity and also lasts for a longer duration as compared to other cortisone [96-101]. Studies have shown that it is only useful in those cases where the condition of the patient is critical and cannot be used for the generalized treatment of all patients [102]. The mode of action of various allopathic drugs is summarized in Fig. 2. These above-discussed drugs mainly inhibit angiotensin-converting enzyme 2 (ACE2), endocytosis, non-structural protein 3C-like protease, and nonstructural proteins RNA-dependent RNA polymerase (RdRp) to stop viral infection and growth.

#### Conclusion

COVID-19 is considered as pandemic worldwide and spreading at an alarming rate. Therefore, it has been essential to explore various strategies to overcome the effect of this dreadful viral disease. This review summarizes the utility of currently opted therapies for COVID-19. No suitable medicine is found to exist currently for this virus infection. The rapidly increasing patient's data of COVID-19 is triggering scientific communities to come forward to develop some possible therapy. The most reassuring treatment is considered to be remdesivir. This drug is known to possess strong antiviral activity as proven by several in vitro studies. Oseltamivir has not presented with suitability, and corticosteroids are at present not recommended. On the other hand, homeopathy and Ayurveda may be promising, but not applicable towards all types of patients. Therefore, the present study concludes that COVID-19 infection can be prevented by following government guidelines and opting immune-boosting Ayurveda routes.

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#### **Compliance with Ethical Standards**

#### Conflict of Interest None

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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