

Review

Frequently Used Allopathic and Traditional Medicine for COVID-19 Treatment and Feasibility of Their Integration

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ABSTRACT To date, no satisfactory treatment for COVID-19 is available. This review reported few recent updates regarding the drugs (allopathy/traditional medicines) used for the treatment of COVID-19 concerning clinical studies. Content of the article spotlight the contribution of allopathic and Ayurvedic drugs to the scientific basis for utilization as a potential therapy against COVID-19 infection and provide new insights on the integration of allopathy and traditional medicine. It advocated the combination of these two systems of treatment will ascertain their integrations, and there would be a good possibility and scope for developing a model of integration in the management of COVID-19. Provided discussion may help researchers, physicians, and healthcare policymakers to encourage for effective and integrated use of allopathic and Ayurvedic medicines to control the COVID-19 pandemic more effectively.

KEYWORDS COVID-19, allopathy, traditional medicine, integration, promising therapy

At present, novel coronavirus (COVID-19) has become a pandemic problem.⁽¹⁻³⁾ Coronavirus was originally transmitted from animal/bird to human, and was rapidly transmitted from an infected to healthy human through air droplets released during coughing/sneezing and get entry into lung of a healthy person. Thus, coronavirus has been termed as an airborne infectious problem.^(4,5) As per World Health Organization report (20th December, 2021), 275,063,925 COVID-19 cases had been recorded in world.^(6,7)

Gammacoronavirus/deltacoronavirus infect birds/mammals but seldom infect human.⁽⁸⁻¹⁰⁾ Phylogenetic/genomic analyses showed that COVID-19 genome has more similarity with BAT-SARS-coronavirus.^(11,12) Coronavirus genome (29,903 nucleotides) contains two untranslated regions at 5'-end and 3'-end and 11 open reading frames. The 4 structural proteins are spike (S), matrix (M), envelope (E), and nucleocapsid (N)-protein.⁽¹¹⁻¹⁴⁾ Spike protein of SARS-CoV-2 binds with host ACE2 receptor to enter.^(15,16) Consequently, COVID-19 delivers RNA into host's cytoplasm. After translation, the ORF1a and ORF1ab encode polypeptide to the formation of replication transcriptions complex, which is responsible for replication of the viral genome thus producing (–)RNA genome by using viral (+)RNA as template. Sub-genomic RNA is produced by fragmented transcription which also leads to the formation of structural proteins.⁽¹⁷⁾

Finally, all components assembled in the host's cytoplasm and new virions release from infected host cell via exocytosis (Figure 1). COVID-19 produces 8 antagonist molecules or chemicals that can overcome/inhibit the host immune response.⁽¹⁸⁻²⁰⁾ At current, no curative drugs are available for COVID-19.⁽²¹⁻²³⁾ This article summarized the current use of allopathic/traditional medicine and their integration for COVID-19.

Allopathic Medicines Used for Treatment of COVID-19

Many allopathic antiviral drugs were used for controlling the COVID-19 infection. In the current scenario, chloroquine, hydroxychloroquine, remdesivir, lopinavir/ritonavir, and ribavirin are used for COVID-19 treatment.⁽²⁴⁾ But these drugs are not approved as antiviral drugs because a specific mechanism of action against COVID-19 infection is not deciphered yet. Various studies suggested the uses of different

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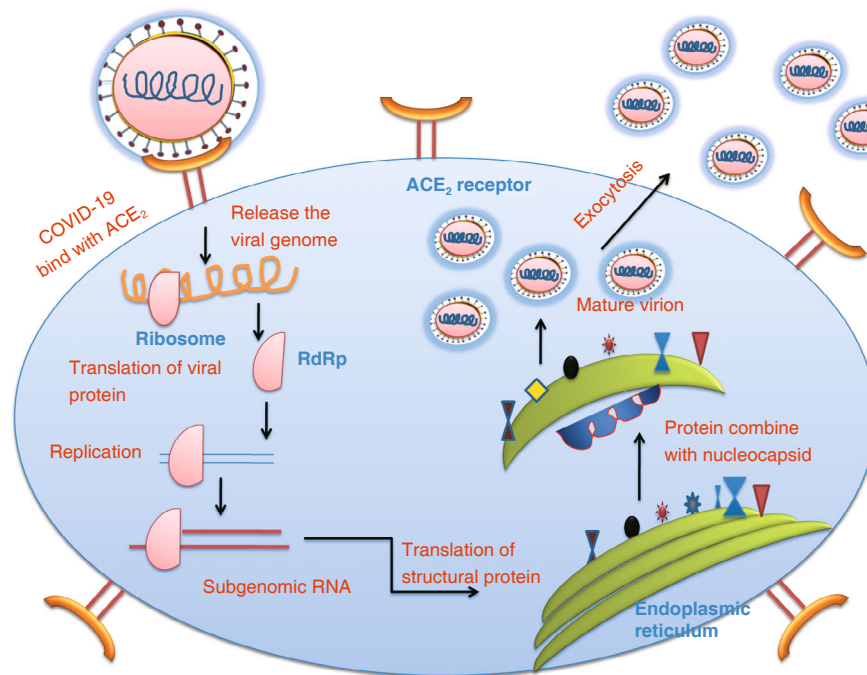


Figure 1. Mechanism of Invasion of Host Cell by COVID-19 and Spread of Infection

drugs for the treatment of COVID-19 infection but not a single proven antiviral drug is available against COVID-19 (Table 1). Therefore, we discussed some allopathic drugs that were given to COVID-19 patients during the course of treatment. Although their antiviral mechanism for COVID-19 is not known, COVID-19 patients got relief using the following drugs.

Chloroquine and Hydroxychloroquine

Chloroquine/hydroxychloroquine have satisfactory results in COVID-19 treatment. It works as a malarial drug since 1990. Their mode of action is based on pH mechanisms.⁽²⁵⁾ These drugs are weak base and accumulate in cell organelles like lysosomes and endosomes. After drug accumulation, an increase in pH within the cell organelles inhibits the endosomal process followed by the degradation of cellular enzymes. Altered pH is responsible for inhibition of the viral replication and also affects the endocytosis process. Chloroquine and hydroxychloroquine also play a critical role in the reduced glycosylation process of angiotensin converting enzyme 2 (ACE₂) receptors that results in inhibition of the COVID-19 binding with host cells.⁽²⁶⁾ A recent clinical study suggested that chloroquine is a better drug as compared than other drugs for the treatment of COVID-19. In this clinical study, chloroquine (500 mg) was given to the COVID-19 infected patients twice a daily for 10 days. Consequently, patients had relief after the chloroquine

treatment but other non-chloroquine treated patients have not felt relieved.⁽²⁷⁾ Another study reported that drug's outcome was more effective for controlling pneumonia, lung infection and improving other symptoms in COVID-19 infected patients.⁽²⁸⁾

Remdesivir, Ritonavir/Lopinavir, Umifenovir, Favipiravir, and Oseltamivir

Remdesivir (GS-5734: adenosine nucleoside analog) was originally made for the treatment of the Ebola and Marburg viruses.⁽²⁹⁾ However, it is also being used for treatment of COVID-19 infection because of its specific action against the RNA virus.⁽³⁰⁾ After metabolism inside the cell, the prodrug is transformed into the active "nucleotide triphosphate" metabolite form, which is responsible for inhibiting the viral RNA-dependent RNA polymerase.^(31,32) Thus, it prevents the synthesis of viral RNA and virus replication inside the cells.^(33,34)

Ritonavir/Lopinavir used in HIV, are responsible for the inhibition of protease enzymes to prevent viral infection.⁽³⁵⁾ Protease enzyme also plays an important role in the generation of viral cells and genome maturation. A recent study suggests that these drugs may be useful for controlling the COVID-19 infections.⁽³⁶⁾ In contrast, another clinical study shows the result that no benefit was observed by the Ritonavir/Lopinavir

Table 1. List of Allopathic and Ayurvedic Drugs Used for Management of COVID-19 Infected Patients

Type of medicine	Name of drug	Molecular formula/ compounds/ingredients	Molecular weight (g/mol)	Possible mechanism	Reference
Allopathic	<i>Hydroxychloroquine</i>	C ₁₈ H ₂₆ ClN ₃ O	335.9	pH alteration, inhibiting replication	26
	<i>Remdesivir</i>	C ₂₇ H ₃₅ N ₆ O ₈ P	602.6	Inhibiting replication	29
	<i>Ritonavir/Lopinavir</i>	C ₃₇ H ₄₈ N ₆ O ₅ S ₂	720.9	Inhibition of protease enzyme to prevent the viral infection	36
	<i>Umifenovir</i>	C ₂₂ H ₂₅ BrN ₂ O ₃ S	477.4	Blocking agent for virus and cell membrane fusion process	32
	<i>Favipiravir</i>	C ₅ H ₄ FN ₃ O ₂	157.1	Reducing viral production	33
	<i>Corticosteroids</i>	–	–	Reducing inflammation in lungs	38
	<i>Oseltamivir</i>	C ₁₆ H ₂₈ N ₂ O ₄	312.4	Preventing proliferation of viruses in human body	34
Ayurvedic	<i>Ayush-64</i>	Chirayata, kuberaksha seeds, katuki root, saptaparna stem	–	Working as an immune booster	41
	<i>Withania somnifera</i>	Anaferine, anahygrine, beta-sisterol, chlorogenic acid, cysteine, scopoletin, cuscohygrine, pseudotropine	–	Working as an immune booster	45
	<i>Licorice (Glycyrrhiza glabra)</i>	–	–	Working as an immune booster	46
	<i>Alium sativum</i>	–	–	Working as an immune booster	49
	<i>Phyllanthus emblica</i>	–	–	Working as an immune booster	49
	<i>Coronil</i>	<i>Withania somnifera</i> , <i>Tinospora cordifolia</i> , <i>Ocimum sanctum</i> , <i>Cassia fistula</i> , <i>Piper nigrum</i> , <i>Eclipta alba</i>	–	Working as an immune booster	45
	<i>Ayush kwath</i>	<i>Ocimum sanctum</i> , <i>Cinnamomum zeylanicum</i> , <i>Piper nigrum</i> , <i>Zingiber officinale</i>	–	Working as an immune booster	53
	<i>Samshamani vati</i>	<i>Tinospora cardifolia</i>	–	Working as anti-inflammatory	54
Chinese medicine	<i>Qingfei Paidu Decoction (清肺排毒汤)</i> , <i>Yupingfeng Powder (玉屏风散)</i> , <i>Huoxiang Zhengqi Powder (藿香正气散)</i> , and <i>Lianhua Qingwen Capsule (连花清瘟胶囊)</i>	–	–	Working as an immune booster and also anti-inflammatory	40

drug of COVID-19 infection.⁽³⁷⁾

Umifenovir/Arbidol drug was developed for the treatment of the influenza virus. It acts as a blocking agent for the virus and cell membrane fusion process and also inhibits the virus-endosome fusion process.⁽³²⁾ This drug may be useful for the treatment of COVID-19 infection.

Favipiravir/6-fluoro-3-hydroxy-2-pyrazine-carboxamide was used for the treatment of RNA virus-like avian influenza virus. It entered into the infected cell by endocytosis process and converted into active form as a favipiravir-ribofuranosyl phosphate by the phosphorylation process.⁽³³⁾ This drug expresses the inhibitory effect on RNA-dependent RNA polymerase (RdRP). Consequently, RNA replication gets blocked. Recent study suggests that favipiravir may be another

approach for the treatment of COVID-19 infection.⁽³³⁾

Oseltamivir drug was originally made for the treatment of influenza A and B and acts by preventing the proliferation of viruses in the human.⁽³⁴⁾ Various clinical trials are ongoing for controlling the COVID-19 infection by oseltamivir drug alone and with other drug combinations.

Corticosteroids

Various corticosteroids are used for the treatment of COVID-19 infections like dexamethasone, prednisone, methylprednisolone, hydrocortisone, etc. Corticosteroids are mainly useful for lower respiratory infections and other allergies. The various studies suggests that corticosteroids are helpful to remove the inflammation from lungs during COVID-19 infection. Dexamethasone can control COVID-19 infection from

ventilated patients and on oxygen support system patients. Dexamethasone showed a 35% decline in the death rate from COVID-19 patients on ventilated patients and also reduce a 20% death rate on oxygen support system patients.⁽³⁸⁾ Thus, dexamethasone showed the effective result against COVID-19 infection. Methylprednisolone is another effective corticosteroid against COVID-19 infection. A study demonstrated that methylprednisolone high dose was effective on COVID-19 patients as compared to dexamethasone. It also reduces the recovery time of COVID-19 patients.⁽³⁹⁾ It is capable to control chronic pneumonia infection during the COVID-19 infection. All the above studies provide strong evidence that corticosteroids are very effective against COVID-19 infection throughout the world.

All above discussed allopathic drugs were used against COVID-19 but these drugs also have shown limitation like require more recovery time and not effective to every stage of COVID-19 infection. These drugs were adopted into routine care for hospitalized COVID-19 patients at many hospitals. However, lack of evidence on their safety and efficacy further recommends extensive clinical trials for evaluating these drugs as an impending treatment for COVID-19 patients. Some clinical trials of these antiviral drugs were carried out but they were limited to the hospitalized patients. Hence more research is needed to develop some more efficacious antiviral molecules along with their specific mode of action and other evidence.

Traditional Medicines Used for COVID-19 Treatment

India has the old traditional medicine system known as the ayurvedic drug system. Indians have been using ayurvedic drugs as traditional medicines for treatment of various antiviral and other diseases but research and development on dosage, processing, and techniques are still lacking in the field of traditional medicine as compared to allopathic medicine. It is well-known that traditional medicine mainly improves the human immune system and provides the immunity against various viral and bacterial infections, therefore, this system is gaining faith and public are shifting from allopathic drug to traditional drugs due to side effect of the synthetic product of allopathy. In present situation, human beings are facing COVID-19 infections for which Indian ayurvedic drugs can prove helpful for improving

immunity of the human body (Table 1). Chinese medicine (CM) is well known traditional medicine and it showed a highly therapeutic role to control the SARS infection.⁽⁴⁰⁾ Following are the traditional medicine that was used for the treatment of infection during COVID-19 pandemic.

Ayurvedic Medicine

Ayush-64

Ayush-64 is an anti-malarial ayurvedic drug. It is formulated by a combination of the chirayata, kuberaksha seeds, katuki root, and saptaparna stem.⁽⁴¹⁾ A study suggests that it also worked as an anti-viral drug and removed the influenza-like illness.⁽⁴²⁾ In this study, a total of 38 patients were enrolled with suffered from influenza infection. After hospitalization, patients were treated with Ayush-64 for 1 week. Patients showed the improvement of influenza-like illness symptoms. Ayush-64 may be used as a supportive drug in COVID-19 infection because Ayush-64 had shown good results in malarial and viral infection. But an experimental study is not done yet with COVID-19. Ayush-64 components have capable to reduce the viral and bacterial count from the human body. Hence, this drug is helpful to fight COVID-19.

Withania somnifera

Withania somnifera is also known as ashwagandha. A study suggests that *Withania somnifera* inhibits viral replication during the bursal disease.⁽⁴³⁾ Bursal disease is a highly infectious disease of chickens. Another *in-silico* study suggests that *Withania somnifera* also acts as a replication inhibitor in COVID-19 infection and prevents COVID-19 entry in the host cell.⁽⁴⁴⁾ *Withania somnifera* may be used as an alternative approach to prevent the COVID-19 infection but needs detailed experimental work. *Withania somnifera* was used as anti-diabetic herb in India. Coronil kit contains *Withania somnifera* and was used for COVID-19 infections because human blood sugar level was increased during COVID-19 infection.⁽⁴⁵⁾

Glycyrrhiza glabra

Glycyrrhiza glabra is a well-known medicinal herb. It is also used to control respiratory illness and viral infection. *Glycyrrhiza glabra* contains the glycyrrhizin compound as the pharmacologically active agent. Glycyrrhizin plays a major role for controlling the cellular damage of hepatitis B and C infection.⁽⁴⁶⁾ A study

suggests that glycyrrhizin is also used as an antiviral drug in SARS infection. Its mechanism of action is based on inhibiting the viral replication in the host cell.⁽⁴⁷⁾ Another *in-silico* study suggests that glycyrrhiza may be used as a possible replication inhibitor in COVID-19 infection.⁽⁴⁸⁾ *Glycyrrhiza glabra* may be an alternative approach for preventing the COVID-19 infection.

Alium sativum

A. sativum, a popular herb in India, is mainly used for the treatment of fungal and viral infections. Its extract is known as ajoene. A study suggests that ajoene worked as a protective agent against HIV infection. It protected the CD⁺ cell during HIV infection at an early stage.⁽⁴⁹⁻⁵²⁾ *A. sativum* may be used in COVID-19 as a supportive agent due to the antiviral properties but an experimental study against COVID-19 infection has not been reported yet.

Phyllanthus emblica

P. emblica is known as Amla and belongs to the *Euphorbiaceae* family. *P. emblica* fruit is mainly used to prevent the infection from HIV-1 and also showed protective action against the hepatitis B virus and influenza virus.⁽⁴⁹⁾ It has been thought to provide support against COVID-19 infection by acting as an immunity booster. However, in the literature, there is no data regarding the *in vivo* and *in vitro* studies against COVID-19.

Coronil

Coronil is an Ayurvedic drug formed by Patanjali Research Institute, India. It is available as a kit form. It contains multiple components like *Withania somnifera*, *Tinospora cordifolia*, *Ocimum sanctum*, *Cassia fistula*, *Piper nigrum*, and *Eclipta alba*. *W. somnifera* provides help to control the blood sugar and *Tinospora cordifolia* works against chronic fever and also helps to improve immunity and remaining components provide help to reduce inflammation and improve the lungs conditions. Thus, this Ayurvedic medicine is helpful to improve the human health system during COVID-19 infection. This kit was used against 367 patients suffering from COVID-19 infection in India then approx 67% of patients were recovered from COVID-19.⁽⁴⁵⁾

Ayush Kwath

Ayush kwath, a mixture of ayurvedic herbs, is another effective medicine against COVID-19 in

India. It contains *Ocimum sanctum*, *Cinnamomum zeylanicum*, *Piper nigrum*, and *Zingiber officinale*. These components help to reduce chronic fever and inflammation from the lungs and also work as immune boosters.⁽⁵³⁾ Hence, this product is used against the COVID-19 in India as an immune booster. Ayush Kwath provides protection not only for COVID-19 but also for other diseases like malaria, common cold, etc.

Samshamani vati

Samshamani vati is a well-known ayurvedic drug in India. It contains *T. cardifolia* extract and is highly used against fever conditions. It has anti-inflammatory and anti-asthmatic properties which are highly useful against COVID-19. It is also helpful to against the various type of viral infection.⁽⁵⁴⁾

CM

CM is recommended for COVID-19 patients by the National Health Commission of the People's Republic of China. Thousands of people are recovered from COVID-19 infection by CM treatment in China.⁽⁵⁵⁾ Various CM could be available for COVID-19 infection like Qingfei Paidu Decoction, Yupingfeng Powder, Huoxiang Zhengqi, and Lianhua Qingwen Capsule, etc. Qingfei Paidu Decoction and Yupingfeng are effective for COVID-19 and have more than 90% effective rates.⁽⁴⁰⁾ These drugs help to control the inflammation and improve human immunity during COVID-19 infection. CM mainly works for enhancing human immunity and controlling the inflammation in the lungs. Hence CM is a very useful medicine during COVID-19 throughout the world (Table 1).

Integrating Allopathic and Other Traditional Medicines for Effective Therapy

In the COVID-19 pandemic, allopathic and traditional medicine should be integrated. Doctors utilized both medicines simultaneously to treat COVID-19 patients. Many countries integrated traditional medicine during this pandemic into their health systems. Traditional medicines were used in combination or as alternatives to allopathic medicines to manage COVID-19 infection more effectively because traditional medicine is a major healthcare provider entity around the globe particularly in remote and rural areas. A large group of people is dependent on traditional medicines for their primary healthcare mainly in developing and underdeveloped countries and areas. Indian traditional medicinal

systems (Ayurveda, Siddha, and Unani) and Chinese traditional medical systems have a very rich history, and from time to time research findings acknowledged the importance of such systems because herbs are a vital source of novel potent therapeutic molecules.

A study was performed to know the interaction of herbs and chemical drugs.⁽⁵⁶⁾ Herb *Hypericum perforatum* lowers concentrations of amitriptyline, cyclosporin, digoxin, indinavir, theophylline, and warfarin in blood. *Panax ginseng* (ginseng) lowers blood concentrations of alcohol and warfarin. *Allium sativum* (garlic) changes pharmacokinetic variables of paracetamol.⁽⁵⁷⁾ Some herbal medicines are given to COVID-19 patients along with allopathic drugs for better recovery. In this way, the treatment pattern during this pandemic situation give a learning and further indication towards integration of allopathic and traditional medicine that is highly affordable and provides an opportunity to address some of the challenges in the treatment of disease. Many herbs interact with the chemical moiety of the drug and they enhance their bio-availability, but sometimes herbs' interaction is negative where they produce toxic effects after interacting with chemical substances. It causes such actions which are sometimes beneficial and sometimes detrimental to health. Pros and cons are always associated with any issue and this needs to be taken care of. It warrants more research on these issues so that the adverse events of combination of herbal and chemical drugs can be monitored and integrations are promoted to refrain from such practices. Several steps have been taken to promote such traditional medicines into clinical practice. Hopefully, incorporation and integration of traditional medicines with allopathy in clinical practice will help to provide quality healthcare to all.

Conclusions

In the current scenario, mankind is going through a serious problem due to COVID-19 and despite incredible advances in modern science and technology, allopathic medicine is unable to provide satisfactory treatment for COVID-19. Therefore, we should think to adopt such a holistic approach of integration of allopathy and traditional medicine for the diagnosis and treatment of the disease more effectively. To date, there is no precise single drug or combinatorial therapy for the prevention of COVID-19 infection. Hopefully, the other potential therapy will be available soon against COVID-19 infection, but it would be always better and could be the best practice to use

allopathy and traditional medicine for mankind. At the current time, any effective chemical drug is not available to cure COVID-19, and available chemical drugs show very high side effects and limitations on the human body known post-COVID-19 effects. The available chemical drug can reduce the specific symptoms like inflammation and fever, but not perform multiple actions in the human body during the COVID-19 infection. Thus, the lack of drugs is responsible for the high mortality rate throughout the world. Hence, there is an urgent need of effective therapy to control COVID-19 infection. Thoughtful integration of these two treatment systems could expand the treatment workforce. Successful integration of traditional/allopathic medicine will help patients and the health care system to walk together to address the current global problem effectively. Integration of two therapies (traditional/allopathic) may be an effective key to control COVID-19 infection but it requires more experimental works to find the appropriate drugs and integration of drugs therapies.

Conflict of Interest

All authors declare that they have no conflict of interest.

Author Contributions

Aditya U: information collection, design, writing manuscript draft; Gopal P: design, draft writing; Dharm P: design, draft writing; Awanish K: conceptualization, design, and finalize manuscript.

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