

REVIEW ARTICLE

A Possible Role of Medicinal Plants in finding a Cure for Covid-19

Asma Saleem Qazi, Nosheen Akhtar, Atif Ali Khan Khalil, Muhammad Saad Ahmed, Sara Mumtaz

ABSTRACT

Since the outbreak, COVID-19 (SARS-CoV-2) has affected more than 24 million people. COVID-19 pandemic appears to lack any effective antiviral drug or vaccine therapy. Previously, it has been reported that medicinal plants are effective against pneumonia caused by coronavirus (SARS-CoV). Secondary metabolites derived from medicinal plants also play pivotal role in strengthening the immune system as well as the killing of pathogens or viruses. The present review summarized the medicinal plants and their secondary metabolites that have antiviral potentials. Further studies are required to evaluate these medicinal plants and their secondary metabolites for possible treatment of COVID-19.

Key Words: Antiviral, Covid-19, Medicinal Plants, Traditional Herbal Medicine.

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Introduction

Corona viruses (SARS-CoV) are a large family of RNA viruses that can infect a wide range of mammalian and avian hosts with a broad spectrum of diseases. Corona viruses are diversified group due to higher mutation rate and recombination during replication.¹ Human corona viruses are pathogens which cause respiratory complications. In the past decades, Severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS) have placed human corona virus into the spotlight due to its higher pathogenicity.² The phylogenetic analysis of corona virus disease 2019 (COVID-19) showed that this novel corona virus is from the family of severe acute respiratory syndrome coronavirus, (SARS-CoV).^{3,4} hence, it is named as severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). The current pandemic has created a huge burden on the health care system of many countries.

The present therapeutic conditions and disease burden has made researchers to revisit potential efficacy of medicinal plants and herbs by identifying

potential phytochemicals and their derivatives in treating COVID-19. Plant-based medicines or herbal medicines are already in use for treating different viral infections.⁵ Traditionally, herbs were used as medicines to treat diseases however right dosage is important. Herbal derivatives are a variety of complex compounds, therefore it is a challenge to determine effective compounds in terms of therapeutic dose and reproducibility. Their diversified active molecular composition has the ability to identify, the specific receptors.^{6,7} This review aims to highlight the importance of plant-based natural products, herbs and their derivatives that shows potential antiviral activity for corona virus inhibition. It is hoped that the consolidated information presented in this review may be a guide for future research prospect.

1. Medicinal Plants and their chemical constituents with antiviral potential

Various plant-based natural products have been studied for their antiviral potential and it was reported that their main mechanism of action is inhibiting the viral replication.⁸ Although there are many but only a few have been discussed here to highlight their importance in viral therapeutics.

1.1. *Nigella sativa* L.

Nigella sativa L. (black cumin) has been globally acknowledged as an herbal medicine, It is effective against wide range of health problems.⁹ It belonged to the Ranunculaceae family and is a proven

Department of Biological Sciences

National University of Medical Sciences, Rawalpindi

Correspondence:

Dr. Asma Saleem Qazi

Assistant Professor, Biological Sciences

National University of Medical Sciences, Rawalpindi

E-mail: asma.qazi@numspak.edu.pk

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historical and religious remedy both in Islam and Christianity.^{10,11} Not only its seeds but the oil extracts have medicinal importance. It is reported that oil extracts can inhibit virus growth even with reduced titer of viral load in infected individual. Volatile oil from *Nigella sativa* also has significant anti-inflammatory properties at various doses.¹² The boiled extract of its seeds has bronchial relaxant properties and tracheal responsiveness. Some of its chemical constituents with medicinal importance are Nigellidine, quinone, α -hederin, thymoquinone, p -cymene, α -thujene, thymol, t -anethole, β -pinene, α -pinene, and γ -terpinene with anti-diabetic, anti-cancerous, antiviral, antibacterial, anti-inflammatory, anti-analgesic properties.^{13,14} Furthermore, some other studies reported use of black cumin with honey for COVID-19 treatment.¹⁵ Honey have flavonoids that have antibacterial, anti-inflammatory, antioxidant, antifungal and antiviral potential.¹⁶

1.2. *Curcuma longa* L.

Curcumin (diferuloylmethane) is a natural compound, a polyphenol extracted from turmeric (*Curcuma longa* L.). It is used as a food additive and also has medicinal importance. Its mode of action against viruses is that it cut off virus adhesion to the host cell.¹⁷ It plays vital role against treating influenza, hepatitis C and HIV virus. It has the potential to integrate catalytic core of enzymes and forbid it from binding from different substrates against human respiratory syncytial virus, thus preventing the infection.^{18,19}

1.3. *Trigonella foenum-graecum* L.

Trigonella foenum-graecum L. (Fenugreek) has pharmacological potential against inflammations, cancer, viruses and bacteria.²⁰ They help in controlling various enzymatic activities, fever, body pain.²¹ So it is considered as one of the remedies to relieve some symptoms of SARS-CoV viruses.

1.4. *Olea europaea* L.

Olive oil extracted from *Olea europaea* L. contains various polyphenolic compounds that possess antiviral, antioxidant, anti-bacterial, anti-inflammatory and anti-allergic activities.²² Olive oil derivatives like oleuropein, tyrosol, hydroxytyrosol, verboscoside, ligustroide, demethyleuropein are considered a potent antimicrobial and antiviral agents against herpes, hepatitis, rota, influenza type

3, bovine rhino, canine parvo, and feline leukemia virus. The olive leaf extract is also found effective in control of viral infection.²³

1.5. *Zingiber officinale* Roscoe

Zingiber officinale Roscoe (Ginger) is a commonly used as a folk medicine or spice. Its chemical constituents are terpenes, phenolic compounds lipids, polysaccharides, raw fibers and organic acids. Its phenolic compounds are well known for the health benefits. Ginger has been proved to have antifungal, antibacterial, antiviral, anti-inflammatory and anticancer activities.²⁴ It has also been noted that ginger is beneficial against human respiratory viruses like human respiratory syncytial virus. It is reported that ginger block viral attachment.²⁵ There is potential in investigating role of ginger against coronavirus as many studies have shown its effect against other viruses.

1.6. *Aloe vera* (L) Burm.f

It is one of the extensively studied medicinal plants worldwide. Many reports show the pharmacological potential of this plant including antiviral activities.^{26,27} Mainly, anthraquinones in *Aleo vera* imparts antiviral activity, however, many other bioactive molecules were also identified including catechin, emodin, quercetin, azidothymidine, kaempferol, acyclovir, acemannan, aloin. Recently, Jang-Gi et al, reported that ethanol extracts of *Aleo vera* have significant anti-influenza virus activity.²⁸ Its potential antiviral activity is also reported against COVID-19, both separately or in combination with other plant species.²⁹ Extracts of *Aloe vera* can inhibit the expression of pro-inflammatory markers and receptors involved in the induction of acute respiratory distress.³⁰

1.7. *Glycyrrhizae uralensis* fisch

Glycyrrhizae Radix et Rhizoma is the herbaceous plant, approved as antiviral by the China food and drug administration (CFDA). Many studies documented that *Glycyrrhizae* inhibits attachment of virus, entry in the cell and replication. Li and Peng reported that *Glycyrrhizae* is effective plant against combating SARS.³¹ *Glycyrrhizae Radix* has an anti-inflammatory potential and reported for the treatment of inflammatory lung condition.³² During the current pandemic this herb is used in different traditional formulas to treat the disease, regardless of disease stage.³³

1.8. *Azadirachta indica* A. Juss

Azadirachta indica A. Juss which is also called Neem, is an important medicinal plant and its clinical significance is mentioned in age-old medical systems like Ayurveda and Siddha. The insecticidal, antimicrobial, larvicidal, antimalarial, antibacterial, antiviral, and spermicidal effect of different parts of the plant, has been reported.³⁴ Roy and Bhattacharyya reviewed different studies which documented promising antiviral potential of neem.³⁵ No experimental data is available to correlate the medicinal potential of neem for the treatment of COVID-19 patients but as neem crude extract is a widely used Ayurvedic medicine to treat normal fever and malarial fever³⁶ which are the common systems of Covid-19, this medicinal plant is highly recommended for treatment of patients suffering from Covid-19.³⁵

1.9. *Camellia sinensis* L

Different refined forms of tea especially black tea and green tea are rich sources of multi-functional bioactive molecules exhibiting antioxidative, anti-inflammatory, antitumorigenic and antiviral properties.³⁷ Epigallocatechin gallate (EGCG) is a polyphenolic catechin present in *Camellia sinensis* (L.), especially in green tea and reported to inhibit Covid-19.³⁸ Similarly, Theaflavins (TFs) are polyphenols, found abundantly in black tea, documented to have inhibition potential for Covid-19.³⁸

2. Different herbal treatment in practice

Extensive research has been done to understand the mode of action and pathogenesis of viral infection. Apart from modern medicine different traditional medicines are also in practice like Unani, Ayush, Chinese herbal, African herbal treatment.³⁹ In this section, the highlighted portion will be from different herbal treatment practices around the globe. However, comprehensive studies on proper understanding of these treatments modalities are still scarce.

2.1. African herbal treatment

Herbal treatment has long history in different cultures. Patients have benefitted but for its application at global level, these traditional medicines have to go through in vitro and in vivo analysis to establish efficacy, toxicity and safety doses. Only then, effective COVID-19 treatment can be reported.^{40,41}

Table 1: African Herbal Practice

Herb	Mode of action	Country	Forms of use
<i>Artemisia annua</i> L	Antiviral	Madagascar	Leaf and root extract
<i>Euphorbia Hirta</i> L	Antiviral	Nigeria	Plant Aqueous extract
<i>Azadirachta indica</i> A. Juss (Neem)	Antiviral	Ghana	Leaf extract

2.2. Unani herbal medicine

Apart from being in practice since centuries, their efficacy and toxicity are not published. According to Unani medicines, the symptoms of COVID-19 matches with "Nazla-e-wabaiya" as mentioned in their books.⁴² Table 2 shows their active ingredient and mode of action.⁴³

Table 2: Unani Herbal Ingredients and Mode of Action

Unani name	Part used	Active ingredient	Mode of action	Method
Unnab	Fruit	Betulinic acid	Anti-proliferative	Oral
Sapistan	Fruit	Trepenoid s, flavinoids	Antioxidant, antiviral	Oral
Habb ul aas	Berry	Flavinoids	Antioxidant	Oral
Tukhm-e-Kahu	Seed paste	Folate, Leutin	Anti-inflammatory	Oral
Elwa	Leaf sap	Anthrones	Anti-inflammatory	Locally applied
Zafran	Stamen	Safranal, crocin	Antioxidant	Locally applied

2.3. Ayush Herbal treatment

The ministry of Ayush and Council of scientific and industrial research has started clinical trials in collaboration for testing the formulation used against COVID-19.⁴⁴ Some of the medicines currently under studies are ashwagandha, guduchi, yasthimadhu, peepli.⁴⁵

2.4. Chinese herbal treatment

At least 10 clinical trials are ongoing with traditional Chinese medicines (TCM) for finding effective treatment of COVID-19.⁴⁶ Past studies have shown that TCM can be effective by inhibiting the viral

Table 3: Ayush/Indian Traditional Practice

Indian Traditional practice	Herbs	Effectivity against	Recommended usage	Form of extract
Ayurveda	Tinospora cordifolia	Chronic fever	Two times a day for 15 days	Aqueous
Siddha	Andrographis paniculata	Fever and cold	Two times a day for 14 days	Aqueous
Homeopathy	Arsenicum album 30	Effective against SARS-CoV-2	Daily once in empty stomach for 3 days	Tablet
Ayurveda	Agastya Haritaki	Upper Respiratory infection	Two times a day	Powder
Homeopathy	Bryonia	Lung inflammation	As needed	Tablet
Siddha	Kaba sura kudineer	Fever, cough, sore throat, shortness of breath	Two times a day	Tablet

ribosomal protein replication and^{40,46} One of the TCM for COVID-19 treatment, Qingfei Paidu decoction (QPD, mixture of 20 herbs) consists of *Scutellaria baicalensis*, *Magnolia officinalis*, *Pogostemon cablin*, Glycyrrhizin, *Ephedra* spp., *Atractylodes macrocephala*, *Armeniaca* spp., Herbacetin, Scutellarin, Quercetin, Baicalin, Nicotianamine and Forsythia suspense. These compounds were found effective against viruses of upper respiratory tract infections.^{47,48}

Conclusion

In the treatment and prevention of COVID-19 medicinal plants and their standardized crude extracts or compounds can play vital role. The present review highlighted possible therapy, mechanism of action of medicinal plants, their standardized crude extracts and chemical constituent for the treatment of COVID-19. Further evaluation and testing, especially molecular mechanisms and simulation are required to identify the effect of medicinal plants and their chemical compounds on COVID-19.

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