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**Review Article** 



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### Indian Medicinal Herbs: A Promising Elixir against COVID-19

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#### Abstract

The current situation shows that the world is in the strong grip of COVID-19 pandemic. Ineluctably, the safety measures could be undertaken in order to diminish the threat of infection. Moreover, to eradicate this spread of infection in a global level and saving the world from an expiring stage, there is an urgent need for social distancing and quarantines. At the end of January 2020, World Health Organization (WHO) formally proclaimed the COVID-19 as a public health emergency. Several research teams have confirmed that SARS-Coronavirus 2 belongs to coronavirus, whose genome is a dead ringer for the genome of bat coronavirus, clearly demonstrate that bat is the natural host of this virus. Novel coronavirus infects human respiratory system by binding with the angiotensinconverting enzyme 2 receptor (ACE2) of human lungs. Most significantly, increasing evidences showed human-tohuman transmission when a normal healthy person comes in close proximity with an infected person. The symptoms of COVID-19 patients include cough, fever, Sneeze, loss of taste, loss of smell, sore throat, fatigue and sometimes a low population of patients suffer with gastrointestinal infection symptoms. The unstoppable transmission of this viral outbreak is due to lack of drugs, vaccines and other therapeutics. Currently, there aren't any authorised vaccines for the hindrance of COVID-19, but the efforts still continue to develop effective vaccines. Hence, it is relevant to look at the potential role of natural and chemical agents in protecting and aiding the health care employees who are taking care of the patients, mainly the general population who are at a major risk of being exposed to the virus. Therefore, this review is an attempt to explore the therapeutic potential of various medicinal herbs, which can be used to treat a broad range of viral pathogens, COVID-19 in particular.

Keywords: Antiviral, herbal medicine, coronavirus, COVID-19, pandemic.

### **1. Introduction**

COVID-19, a global pandemic, is a highly transmissible severe acute respiratory disease, caused by a pathogenic virus called SARS-CoV-2 (Severe Acute Respiratory Syndrome-Corona virus 2) which spreads among humans mainly via physical contact. Corona virus RNA genomes, are considerably larger than any other known plus stranded RNA virus genome as they made up of 27,000 to 30,000 nucleotides (Cascella, Rajnik, Cuomo, Dulebohn, & Napoli.), where plus-strand RNA bacteriophages, picorna viruses, togaviruses, and flavi-viruses genomes are made up of 3,500 to 4,700, 7,200 to 8,400, 12,000 to 13,000, and 10,000 to 11,000nucleotides, respectively. Beside this feature of largest RNA, corona virus have some other unique characteristics among other plus-strand RNA viruses. These viruses have helical nucleo-capsids and generate a nested set of mRNAs that have a common 3 end. Though all nested mRNAs contain multiple open reading frames (ORFs), except the smallest one. However, only one ORF from the 5 end of each mRNA molecule is translated. According to the Baltimore classification scheme, corona viruses are class IV viruses because they are plus-strand RNA viruses (Chan JF T. K.).

### 2. Pathogenesis of COVID-19

COVID-19 has an incubation period of about three days. The most common symptoms are very much similar to viral pneumonia that includes fatigue, fever, sneeze, cough, shortness of breath (Bauch CT), commonly manifested in adults with chronic diseases such as heart disease. neurodegenerative diseases, diabetes, or high blood pressure. Human to human transmissions are taking place when there is an influx of infected aerosols or droplets pass into the lungs of healthy human through nasal or oral inhalation, from respiratory droplets, coughs, or sneezing of infected persons. It is reported, this disease has very high transmissibility rate but moderate to low mortality rate (3.7%)(Els Keyaerts, 2007). Other scientific evidence suggests that some of the more serious cases of COVID-19 may have

respiratory failure and Cytokine Storm Syndrome due to Acute Respiratory Distress Syndrome (ARDS), which is a major cause of death (The Ministry of Education Key Laboratory of Protein Science, Beijing Advanced Innovation Center for Structural Biology, Collaborative Innovation Center for Biotherapy, School of Life Sciences, Tsinghua University, Beijing, China).

Infection is the primary component of secondary Hemophagocytic Lymphohistiocytosis (sHLH), also known as Macrophage Activation Syndrome (MAS). It is a life-threatening health issue formed by a complex group of hyper-inflammatory syndrome that occurs when there is a deviation from interaction the of genetic predisposition(Yin-tan). It is characterized by sudden and severe hyper-cytokinaemia due to improper survival of histiocytes and cytotoxic Tlymphocytes which eventually leads to haemophagocytosis, multiple organ failure, and high mortality. The elementary components of sHLH are cytopenias, continuous fever, and hyperferritinaemia. The immune response showing how SARS-CoV-2 infects and affects the immune system is not fully expatiated (Kogan A). However, it is reported MERS and SARS avoid antibodies and weaken immune responses. At the time of a viral infection, the immune system produces the body's immune response. CD4+ and CD8+ T cells play a significant role in weakening the virus and reducing the risk of self-injury (Els Keyaerts, 2007). CD4+ T cells promote the synthesis of antibodies by making T celldependent B cells (Sanchez-Pinto). While CD8+ T cells are cytotoxic and destroy the infected cells. About 80% of tumour cells between the lungs of SARS-CoV affected patients are CD8+ T cells (Xiaolu Tang, 2020). They possess a vital functions in the extinction of coronaviruses in the infected cells. In addition, helper T cells produce pro-inflammatory cytokines by the NF-kB signaling pathway (Yushun Wan, 2020).

### **3. Transmission of COVID-19**

COVID-19 disease were first spread into human from Huanan Seafood Wholesale Market of Wuhan (Chen Y). At early stage it was thought that transmission was only happened by animal to human. But after few days' researchers understood, it was culminated that the virus could also be transmitted from human-to-human (Shuai Xia, 2020 There are also recommendations that individuals who remain asymptomatic could transmit the virus (World Health Organization, 2020). Along with sneezing and coughing, aerosol transmission is also possible in case of long exposure to high aerosol level in a closed spaces.

# 4. Indian medicinal herbs and their effects on COVID-19

Since the historic period, Indian herbs have always been useful in treating several dangerous diseases, including viral infections (Yan Li, 2015). The importance and beneficial effects of using these herbs lies in the fact that these medicinal herbs help to build a strong immunity in human body (Savarino A, 2003). Integrated approach of Ayurvedic, Yoga and Naturopathy, Unani, Siddha and Homeopathy (AYUSH) systems of medicine concentrates on prevention through dietary management, modification of prophylactic lifestyle, involvements for strengthening immunity and simple remedies lying on the symptoms (Ravishankar, 2008). Indian medicinal plants that are recommended by AYUSH for COVID-19 (Els Keyaerts, 2007).

Other studies on coronavirus using medicinal plants are rather least in India. A study has shown anti-mouse coronaviral activity by the following plants: -

- Clitoria ternatea
- Evolvulus alsinoides
- ➢ Gymnema sylvestre
- Abutilon indicum
- ➢ Leucas aspera
- ➤ Cassia alata
- ➢ Vitex trifolia
- Indigofera tinctorial
- Sphaeranthus indicuss
- Clerodendruminerme Gaertn
- Pergularia daemi

Among the above plants, *Vitex trifolia* and *Sphaeranthus indicus* possess the ability to decrease inflammatory cytokines using the NF-kB pathway, which has been involved in respiratory distress in SARS-CoV.

Clitoria ternatea, firmly known as blue \* bellvine, Asian pigeon wings, butterfly pea,blue pea, cordofan pea and Darwin pea, is a plant species of the Fabaceae family (Niladri Maity, 2012). It has been identified as а metalloproteinase inhibitor. A metalloproteinase, for example ADAM17, is involved in ACE shredding which is connected with an amplified formation of viruses. This metalloproteinase can be targeted using this plant.

• Report says, the plants *Glycyrrhiza glabra* and *Allium sativum* can target the viral replication of SARS-CoV (Els Keyaerts, 2007).

✤ Clerodendrum inerme Gaertn, also known as Volkameria inermis, the glory bower, is a flowering plant species from the genus Volkameria of the family Lamiaceae. It can deactivate the viral ribosome.

♦ Strobilanthes cusia belongs to the genus Strobilanthes, in the family Acanthaceae. It is an herbaceous, perennial plant producing a cluster of erect, branched stems that can become more or less woody. It can grow 50 - 150 cm tall. It has the ability to block the viral RNA genome synthesis and induce papain like protease activity targeting the HCoV.

✤ Hyoscyamus niger (commonly known as black henbane, henbane or stinking nightshade) is a poisonous plant of Solanaceae family.

Another medically important plant which is native to Asia is Justicia adhatoda, commonly known as Malabar nut, adulsa or adhatoda. The leaves of this plant contain phytochemicals, the most important and useful being vasicine, a quinazoline alkaloid. thapsus Verbascum (commonly the great known as mullein or common mullein) is a species

of mullein. Phytochemicals within the flowers and leaves of this plant include saponins, polysaccharides, mucilage, flavonoids, tannins,lig nin glycosides, and essential oils. The leaves of this plant also contain rotenone (Mingxiang Ye, 2020).

All the above three plants can reduce infections caused by influenza viruses. We can study the molecular mechanism by which these plants target influenza virus to test if these plants target any molecules that is similar in SARS-CoV-2 and the Influenza viruses (Anwarul Hassan Gilani, 2008).

✤ Some more medicinal plants that have the inhibitory characteristics against ACE are Coriandrum sativum, Cynara scolymus, Boerhaavia diffusa, Punica granatum Cassia occidentalis, Coscinium fenestratum, and Embelia ribes.

Plant Source	Mechanism of Action
Allium sativum	Proteolytic and hemagglutinating activity and inhibition of viral replication
Clerodendrum inerme Gaertn	Inactivation of viral ribosome
Glycyrrhiza glabra	Inhibition of viral replication and modulation of membrane fluidity
Sphaeranthus indicus	Inhibition
Vitex trifolia	Reduction
Sambucus ebulus	Inhibition
Strobilanthes cusia	Blocking of viral RNA genome synthesis
Clitoria ternatea	Metalloproteinase inhibitor
Strobilanthes callosa	Blocking
Andrographis paniculata	Suppression

#### Table-1: Indian medicinal herbs that might inhibit the HcoVs.

## **5.** Role of Aromatic Herbs and Essential oils in treating COVID-19

Most of the commercially available antiviral mechanisms often lead to the development of resistance, comes with the problem of side effects, recurrence of infections, and many more (Bavari, 2019). The medicine industry is constantly monitoring phytochemical emissions, medicinal plants, and aromatic herbs for the purpose of identifying lead compounds, with a particular focus on alternative anti-retroviral drugs (Yan Li, 2015). Spices, herbal medicines, essential oils (EOs), and natural products make available a rich versatile source for the discovery and production of new antiviral drugs (Jincun Zhao, 2012). Currently, there are no suitable or approved drugs against COVID-19, however, alternative therapies and natural remedies are suggestible (Timothy P. Sheahan, 2017).

Aromatic herbs, spices, herbal teas, and medicinal plants used in ethnobotanical medicine can represent some very useful sources. At the time of the SARS outbreak in 2003, the effectiveness of herbal therapy and phytomedicine for the prevention of viral infections were demonstrated.

As such, various countries, including Algeria, are promoting the use of medicinal plants and herbs to combat SARS-CoV-2 infections (Maria L. Agostini, 2018). In fact, after the epidemic of SARS, many groups began searching for natural agents and phytochemical compounds over traditional medicines which can treat coronavirus (Mingxiang Ye, 2020). Among few medicinal plants or isolated compounds that have inhibitory impacts on different strains of human coronavirus, four medicinal plants show the effects of moderate inhibition on SARS-CoV: Lycoris radiata (red spider lily), Artemisia annua (sweet worm), Pyrrosia lingua (fern), and Lindera aggregata, which is an evergreen shrub, a member of the laurel family (Abbott Laboratories North Chicago, U.S.A., 2000). The antiviral effects of these releases were dose-dependent and ranged from low to high concentration of releases, depending on the estimated herbal remedies. In particular, L. radiata has shown a very strong anti-bacterial activity against bacterial stress (Yan Li, 2015).

• It has been found that an active ingredient in licorice root, i.e., Glycyrrhizin, has an anti-SARS-CoV effect by stopping the replication of the virus. In another study, glycyrrhizin (*Glycyrrhiza glabra*, family Fabaceae) also showed antiviral properties when tested for its in vitro antiviral activity in ten different SARS-CoV strains.

• **Baicalin**, a part of the Baikal skullcap (*Scuttelaria baicalensis*) plant, was tested in this study under similar conditions. It was revealed that Baicalin also has the anti-SARS-CoV potential. It prevent the recurrence of HIV-1 virus in vitro as well. However, it should be kept in mind that in vitro findings may be inconsistent with in vivo clinical practice, as the oral concentration of these molecules in humans may not receive a blood serum volume similar to that tested in vitro dose.

• **Lycorine**, a poisonous alkaloid found in several Amaryllidaceae species, such as the bush lily (*Clivia miniata*), the amazing lily (Lycoris), and the daffodils (Narcissus). It has an extremely

strong anti-viral action against SARS-CoV. Many previous studies suggest that lycorine appears to have a broad inhibitory properties against Herpes Simplex Virus (HSV, type I) and Poliomyelitis virus.

# 6. Mode of antiviral action of Medicinal Herbs

Numerous research and studies on plant extraction have been performed on different Proteins involved coronavirus strains. in replication of coronavirus and the formation of ion channels were key targets (Anurodh Shankar Agrawal, 2016). Researchers have found a genetic component that inhibits the reproduction of in vivo and in vitro strains. Numerous phytochemical compounds and therapeutic plant properties show antiviral characteristics against coronaviruses, and their primary mechanism of action is via prevention of viral replication (World Health Organization (WHO), 2020). Resistance to antiviral compounds may be due to changes in the type of HIV virus as they multiply. It has been studied by experiments that saikosaponin, a naturally occurring triterpene glycosides derived from herbal remedies such as Chinese thoroughwax, parsley, and Figwort, has antiviral efficacy against HCoV-22E9, a type of CoV that causes infection in humans and animals along with human coronavirus OC43 is one of the most common cold viruses (Peterson., 2020). Such natural molecules downregulate and inhibit the initial process of HCoV-229E infection, including viral penetration and attachment (Yan Li, 2015).

# 7. Clincal trials with Chinese herbal medicines

Nearly 23 regions in China have developed various strategies to prevent COVID-19, using the appropriate herbal medicines that are used in Chinese traditional medicine.

> *Radix astragali*, Bunge and *Astragalus mongholicus* is a popular Chinese medicine. Its active compounds can help strengthen the immune system and reduce inflammation.

Astragalus is sometimes also administered as an injection in hospitals (Scragg JN, 1966).

Radix glycyrrhizae or liquorice root is one of the 50 most important plants used for phytomedicine. Among the genus Saposhnikovia,Radix saposhnikoviae, Saposhnikovia divaricate, is the only species (Anurodh Shankar Agrawal, 2016).

> Atractylodis macrocephalae rhizome is hailed as the most important Qi drug. It tonifies and enhances the spleen. It is the dry rhizome of *Atractylodes lancea*, *Atractylodes chinensis* Koidz, or another nearby plant such as Japonica atractylodes(Yan Li, 2015).

> Lonicera japonica Flos, a member of the family Caprifoliaceae, is among the most widely used traditional medicine (Niladri Maity, 2012). It has bioactive substances such as caffeic acid derivatives, essential oils (EOs), flavonoids, and terpenoids (Reed F. Johnson, 2016). It has antiinflammatory, antimicrobial, anticancer, antioxidant, and immune-converting properties (Anurodh Shankar Agrawal, 2016).

Solution Golden Bell (*Fructus forsythia*) has long been known as a remedy for all patients at risk of skin infections. This plant has shown extensive inhibitory activity against bacteria. It has the potential of suppressing the influenza and leptospira virus and other viruses. This plant also shows anti-inflammatory properties (Cheema, 2019).

### 8. Use of Traditional Ayurvedic "Kadha" for prevention and management of the novel Coronavirus (SARS-CoV-2)

Since the advent of the novel Coronavirus, a growing number of patients have shown a high rate of worldwide transmission (Ravishankar, 2008). The use of molecular dynamics simulation evaluate the helpful properties to of phytochemicals and active pharmaceutical agents present in Indian herbs and spices are extensively used in Ayurvedic medicines in the form of "Kadha" to control the respiratory disorders such as coughs, colds and flu (Anurodh Shankar Agrawal, 2016). A wide range of phytochemicals existing in these herbs with significant levels of suspension and ability can prevent various stages of SARS-CoV-2 infection. The phytochemicals contained in these herbs have important antiinflammatory properties. The binding of active components present in the various plants used in the preparation of Kadha with viral proteins and target proteins can prevent and treat COVID-19 (Yan Li, 2015).

A number of herbs are used in the preparation of the ayurvedic Kadha, such as, Tulsi (*Ocimum tenuiflorum*), Ginger (*Zingiber officinale*), Haldi (*Curcuma longa*), Cardamom (*Elettaria cardamomum*), Giloy (*Tinospora cordifolia*), Black pepper (*Piper nigrum*), Lemon (*Citrus limon*), Clove (*Syzygium aromaticum*), and Ashwagandha (*Withania somnifera*) (Wu C. L., 2020).

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Herbs	Phytochemicals present
Tulsi ( <i>Ocimum tenuiflorum</i> )	Linalool
	Oleanolic acid
	Cirsilineol
	Isothymusin
	Isothymonin
	Eugenic acid
	Estragole
	Orientin
	Vicenin
	Rosmarinic acid
	Beta-caryophyllene
	Ursolic acid
	Eugenol
	Cirsimaritin
	Apigenin
	Carvacrol
	Curcumin
	Vanillic acid
	Ar-turmerone
	Trans-Ferulic acid
	Vanillin
Haldi ( <i>Curcuma longa</i> )	Calebin A
	Demethoxycurcumin
	Bisdemethoxycurcumin
	Alpha-turmerone
	Beta-turmerone
	Cyclocurcumin
	Atlantone
Giloy (Tinospora cordifolia)	Berberine
	Tinocordifolin
	Tinosporide
	Tinocordioside

### Table-2: Following are the list of Phytochemicals found in those herbs that are used in the preparation of Kadha.

	Cordioside
	Tinocordifolioside
	Magnoflorine
	Choline
	Jatrorrhizine
Ginger (Zingiber officinale)	1-dehydrogingerdione
	Bisabolene
	Zingiberene
	6-gingerol
	4-gingerdiol
	Citral
	Eucalyptol
	6-gingerdione
	10-gingerdione
	6-shogaol
	Piperamine
	Piperine
	Piperamide
	Nerolidol
	Beta-caryophyllene
	Sarmentosine
	Piperic acid
Black pepper ( <i>Piper nigrum</i> )	Chavicine
	Formylpiperidine
	Trichostachine
	Guineensine
	Isochavicine
	Pipericide
	N-Formylpiperidine
	Piperolein B
	Pentadienoylpiperidine
	Brachyamide B
	Retrofractamide A
	Sarmentine
	Dihydropipericide

Ashwagandha (Withania somnifera)	Withanolide
	Anaferine
	Withanolide B
	Choline
	Withaferin A
	Withanolide A
	Withanone
	Somniferine
	Limonene
	Protocatechualdehyde
	Geraniol
Cardamom ( <i>Elettaria</i> cardamomum)	Protocatechuic acid
caraamomum)	Linalool
	Alpha-terpinyl acetate
	Linalyl acetate
	Vanillin
	Rhamnetin
	Campesterol
	Beta-caryophyllene
	Kaempferol
	Eugenin
	Acetyl eugenol
Clove (Syzygium aromaticum)	Eugenol
	Methyl salicylate
	Eugenitin
	Stigmasterol
	Oleanolic acid
	Flavonol glucosides
	Gallic acid
	Acetyl eugenol
Lemon (Citrus limon)	Vitamin C
	Quercetin
	Phloroglucinol
	Eriodictyol
	Umbelliferone

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### 9. Conclusion

Most viruses are still very deadly, fatal and incurable, although some can be regulated or prevented by life-enhancing substances, which, however, are expensive and unavailable to maximum people. Therefore, the discovery of effective and inexpensive antiviral safe. molecules is one of the most universal emergencies of drug research. Therefore. researchers from various medical fields are conducting research on various aromatic herbs and ethnomedicinal plants depending on their effect as an antivirus. World-wide research on ethnomedicine and phytomedicine over the past 50 years has led to the discovery of antiretroviral drugs from natural products and now we can say various aromatic herbs and medicinal plants have powerful and potent antiviral properties. Several oils, extracts and organic materials are usually shown to contain the same successful features.

COVID-19 has appeared as the most enormous and terrifying viral infection. Major concern among public health have taken precautions against the virus throughout the world. The Government of every country is continuously making efforts to minimize physical contact by promoting countrywide lockdowns in public places, including various steps to confirm the safety of the people, like physical distancing and self-quarantine which helps in limiting our social interactions. This will help to reduce the risk of spreading the COVID-19 among people by breaking the transmission chain.

### **Conflict of Interest**

The authors of this paper have no conflict of interest.

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