

## Uses of the antiviral potential of medicinal plants and their derivatives or products in prevention and treatment of COVID-19

Sunil Chhimpa<sup>1</sup>, Kumud Kant Awasthi<sup>2</sup>, Chandra Shekhar Yadav<sup>2</sup>, Garima Awasthi<sup>2</sup>, Sameer Sharma<sup>3</sup> and Hemant Pareek<sup>4,5\*</sup>

<sup>1</sup>Centre for Converging Technologies, University of Rajasthan, Jaipur Rajasthan India

<sup>2</sup>Department of Life Sciences, Vivekananda Global University, Jaipur Rajasthan India

<sup>3</sup>Department of Zoology, Government P. G. College, Sawai Madhopur Rajasthan India

<sup>4</sup>Department of Zoology, S.K. Govt. College Sikar Rajasthan India

<sup>5</sup>Commissionerate College Education, Jaipur Rajasthan India

### Abstract

"COVID-19," which is the acronym of "coronavirus disease 2019" is a pandemic caused by novel virus of Coronaviridae family, genus Betacoronavirus, having single stranded RNA (ssRNA) as a genetic material. This virus is transmitted from bats to human and its mutated strain causes SARS-Cov2 (severe acute respiratory syndrome) by binding on ACE2 receptor in lungs of humans. The cov2 disease becomes outbreak from china to whole world due to global traveling. There is no precise therapeutics are available till date, only management includes isolation of patient, restrictions in traveling and supportive medical care for cov2 can prevent spreading of this virus. Therefore, only herbal treatment can play an important role to reduce and cure the pandemic disease due to their fewer side effects. Some known natural plant products, their extracts and their derivatives are good alternative to enhance body immunity against viral infections to overcome this pandemic cov2 disease.

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**Keywords:** COVID-19, ACE2 Receptors, Herbal treatment, Immunity, Vaccine, SARS cov2

### Introduction

Coronavirus is an enveloped virus having positive sense, single stranded RNA (ss RNA) virus, belonging to the *Coronaviridae* family and genus Betacoronavirus (Huang *et. al.*, 2020). The viruses of CoV family consist of several species and causes major upper respiratory tract diseases in mammals and birds. Onset of COVID-19 infection first time from Wuhan city, China and virus transmitted to humans by bat due to non vegetarian habit of human being (Zhou *et. al.*, 2020). In humans, this virus primarily causes common cold but complications including pneumonia and SARS can occur (Van der Hoek L. 2007). The novel human corona virus is responsible for severe acute respiratory syndrome (SARS COV2) caused a global threat including India in 2020 declared by World Health Organization (WHO). Due to increased global journey and urbanization, epidemic outbreaks caused by corona viruses represent a critical threat to public health, predominantly when therapies and preventive vaccines against viruses are not available. The World Health Organization (WHO) declared COVID 19 pandemic on January 30, 2020 originated from Wuhan city China.

Health organizations across globe are performing exhaustive teamwork and research to control its spread and illness. Human corona virus, SARS COV and COV2 bind to ACE2 (angiotensin converting enzyme 2) receptor expressed in target tissue lungs, intestine, kidney and blood

vessels (Wan Y *et. al.* 2020). Diabetic patients with type 1 and 2 have more ACE2 receptor on their corona virus target sites because they are treated with ACE inhibitors and angiotensin II type-1 receptor blockers (ARBs). Due to treatment of these patients with ACE inhibitors and ARBs, ACE2 receptor expression up-regulated the same therapies are used for patients of hypertension so diabetic and hypertension patients are more prone to corona virus COVID-2 infection (Wan Y *et. al.* 2020 and Li XC *et. al.* 2017). Therefore, current time demands to develop an effective antiviral treatment for CoV2 infection. Consequently, there is a burning need to discover novel antiviral drugs that shows high efficacy and low cost for the control of viral infections when vaccines and standard therapies are lacking.

Although there is no direct evidence of herbal medicine for COVID-19, some of the classical and herbal medications with proven immunomodulatory potential can be used as preventive medicines to counteract its symptoms. Herbal medicines and purified natural products can play a major role in treatment of novel corona virus and antiviral drug development. Herbal medicine is a class of medicine obtained from natural products so causing fewer side effects, less additives and preservatives.

Therefore, we choose writing a review over the use of herbs for the treatment of Corona virus against its global outbreak. Since, there is no scientific proof for availability of any allopathic treatment to cure and mitigate SARS COV-2 infection in till date. In China TCM (traditional Chinese medicine) and herbal drinks are being used to treat and increase the immunity against SARS COV-2 infection. The effect of herbal drug changed against the disease can be changed by given dose concentration to patients. Some herbal plants and their natural products are being used from a long time to increase immunity against viral particles some of them are enlisted below.

Extracts of Dioscorea plant showed immunogenic activity due to the presence of an antigen agent and an adjuvant agent which is prepared from a tuber of a Dioscorea plant. This extract can be obtained from the tuber of any of these Dioscorea species namely *D. batatas*, *D. ecne*, *D. alata L.*, *D. pseudojaponica*, or *D. alata L. var. purpurea*). The antigen agent can be a polypeptide, such as a viral protein or a tumor antigen protein or a nucleic acid encoding the polypeptide. These can be used to treat viral diseases such as infection by a coronavirus (e.g., SARS), orthomyxovirus (e.g., influenzavirus), an adenovirus, a herpesvirus (e.g., HSV-I, HSV-II, CMV, or VZV), a poxvirus (e.g., an orthopoxvirus such as variola or vaccinia, or molluscum contagiosum), a picornavirus (e.g., rhinovirus or enterovirus), an a paramyxovirus [e.g., parainfluenzavirus, mumps virus, measles virus, and respiratory syncytial virus (RSV)], a papovavirus (e.g., papillomaviruses causing genital warts, common warts, or plantar warts), a hepadnavirus (e.g., hepatitis B virus), a flavivirus (e.g., hepatitis C virus or Dengue virus), or a retrovirus (e.g., a lentivirus such as HIV). The herbal preparation from these plants can directly used as a dietary supplement, health food and health drink to mitigate viral infection and to increase immune system strength for human being (Yang *et. al.*, 2009).

The combination of interferons and phytoconstituents also shows potential antiviral therapy such as interferon-beta (IFN- $\beta$ ) and glycyrrhizin have been shown eliciting significant antiviral activity in body against SARS coronavirus (Cinatl *et. al.*, 2003).

Some natural products are also found to be very effective against corona virus some of them are as saikosaponins (A, B2, C, and D) are naturally occurring triterpene glycosides obtained from medicinal plants *Bupleurum* spp., *Heteromorpha* spp., and *Scrophularia scorodonia*. These products exert antiviral activity against HCoV-22E9 by preventing the early stage of HCoV-22E9 infection and viral attachment and penetration at target site (Cheng *et. al.*, 2006). Extracts

of *Lycoris radiata*, *Artemisia annua*, *Pyrrhosia lingua* and *Lindera aggregata* also showed anti-SARS-CoV effect from a screening analysis using hundreds of Chinese medicinal herbs (Li *et. al.*, 2005). Water extract from *Houttuynia cordata* have evidence of several antiviral mechanisms against SARS-CoV by inhibiting the viral 3CL protease and blocking the viral RNA-dependent RNA polymerase activity (Lau *et. al.*, 2008). nsP13 helicase enzyme and 3CL protease can reduce SARS-CoV enzymes activity as well as Myricetin, scutellarein, and phenolic compounds from *Isatis indigotica* and *Torreya nucifera* respectively (Lin *et. al.*, 2005; Ryu *et. al.*, 2010; Yu *et. al.*, 2012).

South India is the rich source of plant biodiversity where numbers of medicinal plant and their products are being used from ancient time. Out of them some are reported in Karnataka state of India. The extracts obtained from various medicinal plants from this state showed broad spectrum antiviral activity, are members of different plant families such as *Gymnema sylvestre* R. Br. (Asclepiadaceae), *Pergularia daemia* (Forsskal) Chiov. (Asclepiadaceae), *Sphaeranthus indicus* L. (Asteraceae), *Cassia alata* L. (Caesalpiniaceae), *Evolvulus alsinoides* L. (Convolvulaceae), *Clitoria ternatea* L. (Fabaceae), *Indigofera tinctoria* L. (Euphorbiaceae), *Abutilon indicum* G. Don. (Malvaceae), *Vitex trifolia* L. (Verbenaceae), *Clerodendrum inerme* (L.) Gaertn (Verbenaceae), and *Leucas aspera* Spr. (Lamiaceae). Above medicinal plants directly shows virucidal activity in vitro assay against MCV (Mouse corona virus) and also anti-HSV activities at a concentration as low as 0.4 µg/mL (S. Vimalanathan *et. al.*, 2009).

After the outbreak of COVID-19, the rate of mortality had reported low at Guangdong (0.1%) compared with Wuhan city mortality rate (2.6%) in infected people. This was because of herbal drinks given to the patients in Guangdong and Zhejiang before they were tested positive.

### Approach

In China the combination of modern and herbal medicine used to treat the admitted patients. Patients were recovered with the diseases due to combined effects of given therapy. On the basis of in vitro studies Institute of China discovered oral liquid that can mitigate the COVID-19 infection in Shuanghuanglian. The use of herbal medicine is supported by many researchers discussed above. Since, preclinical or scientific testing is not possible in such a short time period. In current status of corona outbreak it appears inappropriate and impulsive to advocate any substitute therapies for SARS COV2 which becomes endemic. Therefore, without any clinical testing recommendation of unproved medicines for COV2 by health authorities can be misleading and dangerous. By using herbs in treating viral infection as a medicine in different dose ration have given better results in this scenario.

### Discussion

In China various natural products were used as herbal medicines to mitigate the COV2 effect. Out of them 13 natural compounds were tested positive for treating COVID-19, which is also present in traditional Chinese medicine. Afterwards, out of these 13 compounds 2 or more were constitutes of 125 Chinese herbs, in which 26 herbs are basically used to treat breathing respiratory infections caused by the virus.

Additional 22 medicinal herbal extracts were also assayed, having the capacity to reduce mouse hepatitis virus. Herb extracts decreases mouse intracellular viral RNA and proteins expression when used EC50 (from 2.0 - 27.5 micron/ml) obtained from *Cimicifuga rhizoma*, *Meliae cortex*, *Coptidis rhizoma*, *Phellodendron cortex* and *Sephorasubstrata radix*. These extracts inhibited MHV production to a great extent so can be used as anti corona virus drugs. Flavonoid

extracted from the Litchi seeds can be used for treatment of SARS-COV because it inhibits viral protein synthesis).

Table 1: Plant species and their products used to treat viral diseases.

<i>Name of plant</i>	<i>Plant product obtained from it</i>	<i>Effect</i>	<i>References</i>
<i>Dioscorea spp.</i> <i>D. batatas</i> , <i>D. ecne</i> , <i>D. alata</i> L., <i>D. pseudojaponica</i> , or <i>D. alata</i> L. var. <i>purpurea</i>	Plant extract	used to treat viral diseases such as infection by a coronavirus (e.g., SARS), orthomyxovirus (e.g., influenzavirus), an adenovirus, a herpesvirus	(Yang <i>et. al.</i> , 2009).
saikosaponins (A, B2, C, and D) <i>Bupleurum</i> spp., <i>Heteromorpha</i> spp., and <i>Scrophularia scorodonia</i>	Triterpene glycosides	Exert antiviral activity against HCoV-22E9 by preventing the early stage of HCoV-22E9 infection and viral attachment and penetration at target site	(Cheng <i>et. al.</i> , 2006).
<i>Lycoris radiata</i> , <i>Artemisia annua</i> , <i>Pyrrhosia lingua</i> and <i>Lindera aggregata</i>	Extracts of plants	Anti-SARS-CoV effect	(Li <i>et. al.</i> , 2005)
<i>Houttuynia cordata</i>	Water extract of plant	Antiviral mechanisms against SARS-CoV by inhibiting the viral 3CL protease and blocking the viral RNA-dependent RNA polymerase activity	(Lau <i>et. al.</i> , 2008)
<i>Isatis indigotica</i> and <i>Torreya nucifera</i>	Myricetin, scutellarein, and phenolic compounds	Reduce SARS-CoV enzymes activity	(Lin <i>et. al.</i> , 2005; Ryu <i>et. al.</i> , 2010; Yu <i>et. al.</i> , 2012).
<i>Gymnema sylvestre</i> R. Br. (Asclepiadaceae), <i>Pergularia daemia</i> (Forsskal) Chiov. (Asclepiadaceae), <i>Sphaeranthus indicus</i> L. (Asteraceae), <i>Cassia alata</i> L. (Caesalpiniaceae), <i>Evolvulus</i>	Direct plant parts	Virucidal activity in vitro assay against MCV (Mouse corona virus) and also anti-HSV activities	(S. Vimalanathan <i>et. al.</i> , 2009).

<i>alsinoides</i> L. (Convolvulaceae), <i>Clitoria ternatea</i> L. (Fabaceae), <i>Indigofera tinctoria</i> L. (Euphorbiaceae), <i>Abutilon</i> <i>indicum</i> G. Don. (Malvaceae), <i>Vitex trifolia</i> L. (Verbenaceae), <i>Clerodendrum inerme</i> (L.) Gaertn (Verbenaceae), and <i>Leucas aspera</i> Spr. (Lamiaceae).			
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Herbal drinks also used in large amount in Hubei for isolated and quarantined citizens suspected to be infected with the virus. In Shanghai, the patients who were treated with combined treatment found negative within 7 or 8 days (for the corona virus) in comparative to without herbal drink, it could take more than 10 days, declared by Zhang, a member of the national expert in a press conference. In Guangzhou, all of the 58 patients recovered with herbal drink and allopathic treatment including the medical staff treating them.

Simultaneously, researchers and Chinese Academy of Sciences in Shanghai confirmed a list of 12 - 15 herbs that have antiviral activity against COVID-19. By the use of bioinformatics Computer-aided drug design (CADD) technology was used to know their interaction with herbs after the knowledge of complete genome sequence of COV2.

COVID-19 patients were cured with traditional Chinese medicine (TCM) or with combination of herbal and allopathic medicine in Jinyinshan Hospital in Wuhan. These patients were treated by Traditional Chinese Medicine doctors from Beijing's Xiyuan and Guanganmen Hospitals and they were also looking after the patients in Wuhan since the outbreak, both under the China Academy of Chinese Medical Sciences, as reported by Xinhua (Deng-hai Zhang., *et. al.* 2020; Coghlan ML., *et. al.* 2015; Guangdi L and De Clercq E 2020; Sheahan TP., *et. al.* 2020; Holshue ML., *et. al.*2020).

In India a huge potential of herbal drugs are available which is need to explore for their effective use so pharmaceutical companies should conduct their research based on natural products for drug discovery. Academic world also change their dimension to harvest their potential to harbor natural products and their derivatives by using their potential for the treatment of new diseases caused by viral infection in future.

### Conclusion

According to Acharya Balkrishna, Managing Director, Patanjali Ayurved, the deadly COVID-19 virus can be combated by the combined use of herbs such as ashwagandha, giloy and tulsi. Natural phytochemicals in ashwagandha, giloy and tulsi indeed have potentials to combat covid-19 and its pathogenicity. This study may provide a preventive strategy to the medical science practitioners as well as common people across the globe by increasing the innate immunity of the body to combat COVID-19.

Finally, it can be concluded that natural products and herbal medicines can be used with allopathic treatment to treat corona virus because till date there is no confined drug and vaccine is available in world. In spite of social distancing, restricted travelling and quarantine there is no any effective treatment of COVID-19 to stop viral infection. Infected person is supported by life support system under proper observation. When herbal medicines are used with modern available treatment, they can produce better result for corona infected patients. Further more

research required to know the chemical composition of herbal medicines and mode of interaction of these herbs against viral particles. It is also need to explore in detail virus attachment process and protein synthesis in target tissues so they can be inhibited by the drug administration. We also have to work in the direction of identification of new viral particles by sequencing their genome and open new avenues to the development of effective vaccine against the viruses.

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### **Conflict of Interest**

The author declares no conflict of interest.

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