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Reconsidering Traditional Medicinal Plants to Combat COVID-19

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ABSTRACT

COVID – 19 is a deadly disease, caused by a novel coronavirus (SARS-CoV-2) that is rapidly spreading across the globe and causing many fatalities. WHO (World Health Organization) has declared this disease as pandemic. Currently the disease has no treatment available in the form of medicine or vaccine. Ayurveda is an ancient Indian system of medicine, been practiced in India for nearly 5000 years and relies majorly on plants for its formulations. These herbal formulations and immunity boosters may show us the path to come up with a broad-spectrum antiviral product, which is the need of the hour. In this review, we have selected plants like *Phyllanthus spp., Andrographis paniculata*, *Curcuma longa, Zingiber officinale, Glycyrrhiza glabra, and Withania somnifera* with reported antiviral properties. While others like *Tinospora cordifolia* and *Emblica officinalis* that have immunity boosting properties. The exact mechanisms of action for all the plants may not be clear as per modern medicine, but their history of safe use is in place.

Keywords: COVID -19, antiviral, immunity–booster.

Introduction

We are presently facing the biggest threat to humanity, COVID-19 caused by novel corona virus (SARS-CoV-2). The common symptoms include cold, cough, fever and difficulty in breathing. This disease spreads through the salivary droplets or sneezing or coughing fluid by infected person. The two ways in which this virus spreads are, direct physical contact and indirect contact with the surface on which the infected droplets fall. In recent times due to advanced means of transport, there is an increase in international and domestic travel; hence, the outbreak and spread of infectious viral diseases to different continents, countries, and the dangers associated with it are much larger. The development of COVID-19 has forced the requirement for therapeutic alternatives to improve and cure this new pandemic.

Nearly 80% of the people are dependent on traditional plants for their primary health (according to a WHO report). Our traditional or the ethnobotanical knowledge could help us find an alternative approach to search for possible antiviral drug molecules. Ayurveda or the traditional Indian system of medicines has described the use of plants, which have a number of compounds and secondary metabolites that are useful for drug formulations. This system of medicine believes in using certain herbs, decoctions and plant-based formulations to build immunity. Our body can fight infections in a better way with increased immunity. Several compounds extracted from plants are known to have antiviral activity. In this article we have tried to compile literature available for plants with reported anti-viral properties and their use as traditional medicine.

Listed below are few plants with reported antiviral properties (Table 1).

Table 1: Plants with antiviral properties (Ruwali P. *et. al.* 2013)

Virus Name	**Name of the plant with antiviral properties**
Human Immunodeficiency Virus	*Phyllanthus amarus, Tinospora cordifolia*
Influenza Virus	*Emblica officinalis*
H1N1, H9N2, H5N1	*Andrographis paniculata*
H1N1, H6N1	*Curcuma longa*
Dengue virus	*Andrographis paniculata*
Respiratory Syncytial virus	*Glycyrrhiza glabra*
Herpes Simplex Virus	*Phyllanthus urinaria,*
Herpes Simplex Virus 2	*Withania somnifera*

Among those listed above, majority of the plants have an established cultivation system in India. Plants like *Curcuma and Zingiber* are cultivated in India since ancient time. *Phyllanthus* and *Andrographis* are cultivated commercially at an affordable price (Kuttan R. 2011).

Phyllanthus

In India, 12 species of *Phyllanthus* belonging to Phyllanthaceae family, have been used extensively in traditional medicines. This traditional knowledge is now being supplemented with modern research to know the exact mechanisms involved and their mode of action. Almost all species of *Phylllanthus* genus contain phyllanthin which has reported antiviral activities (Naithani *et al.* 2010). *Phyllanthus* also has compounds like corilagin, geraniin, gallic acid, hypophyllanthin, ellagic acid, phyltetralin, niranthin, catechin, quercetin, astragalin, and chebulagic acid, which may have therapeutic potential in the treatment of immune related diseases (Ibrahim J. 2019). In a study by Lee C. D. *et. al.* (1996) it has been reported that transcription and replication of hepatitis B virus m RNA is down-regulated by *P. amarus*. Ethanolic extract of *P. niruri* revealed strong inhibition against Hepatitis C virus (HCV). It has also shown enhanced anti-HCV activity of simeprevir (NS3 protease inhibitor) with increased action up to 4-fold compared to a single treatment of simeprevir (Wahyuni T. S. 2019). Cocktail of aqueous and ethanolic extracts of *Phyllanthus* (*P. amarus, P. niruri, P. urinaria,* and *P. watsonii*) exhibits robust activity to inhibit dengue virus with more than 90% reduction in infection (Lee *et. al.* 2013). Mehrotra *et. al.* (1991) tested alcoholic, chloroform, butanolic, hexane and aqueous extracts of *P. amarus* on HbsAg, HBeAg and HBV-DNA from HBV positive serum samples in-vitro, which was later screened using ELISA technique to confirm the positive results. Out of the 5 extracts, butanol extract was found to be the most effective against the tested antigens.

Emblica officinalis

Phyllanthus emblica Linn. or *Emblica officinalis* Gaertn., commonly known as Indian gooseberry or Amla, is an important medicinal plant belonging to family Euphorbiaceae. Almost all plant parts are medicinally important, but fruit is the most widely used in the Indian system of medicine as diuretic, restorative, hair tonic, laxative, anti-pyretic, ulcer preventive, liver tonic and for common cold & fever. The fruit is very rich in vitamin C content and helps to boost immunity. Pentagalloyl glucose, found in the amla fruit can inhibit Influenza A virus replication via two mechanisms: prevention of virus adsorption and suppression of virus release (Dasaroju S. 2014).

Andrographis paniculata

Andrographis paniculata is commonly known as Kalmegh (King of Bitters, Creat, or Chireta) and widely used in Ayurvrdic medicines. It belongs to the family Acanthaceae. It is traditionally used in the treatment of

various ailments like cough, cold, viral fever and liver disorders (Shah A. 2013). A diterpenoid, Andrographolide, extracted from *Andrographis paniculata* has anti-inflammatory properties. A brief mechanism of action of andrographolide is depicted in fig. 1. It is the main bioactive compound extracted from the stem and leaves of *Andrographis paniculata*. It has shown potential against a variety of viruses like Influenza A virus (H9N2, H5N1 and H1N1), Hepatitis B and C virus, Herpes simplex virus, Epstein-Barr virus, Human papillomavirus, Human immunodeficiency virus, and Chikungunya virus (Gupta S. 2016).

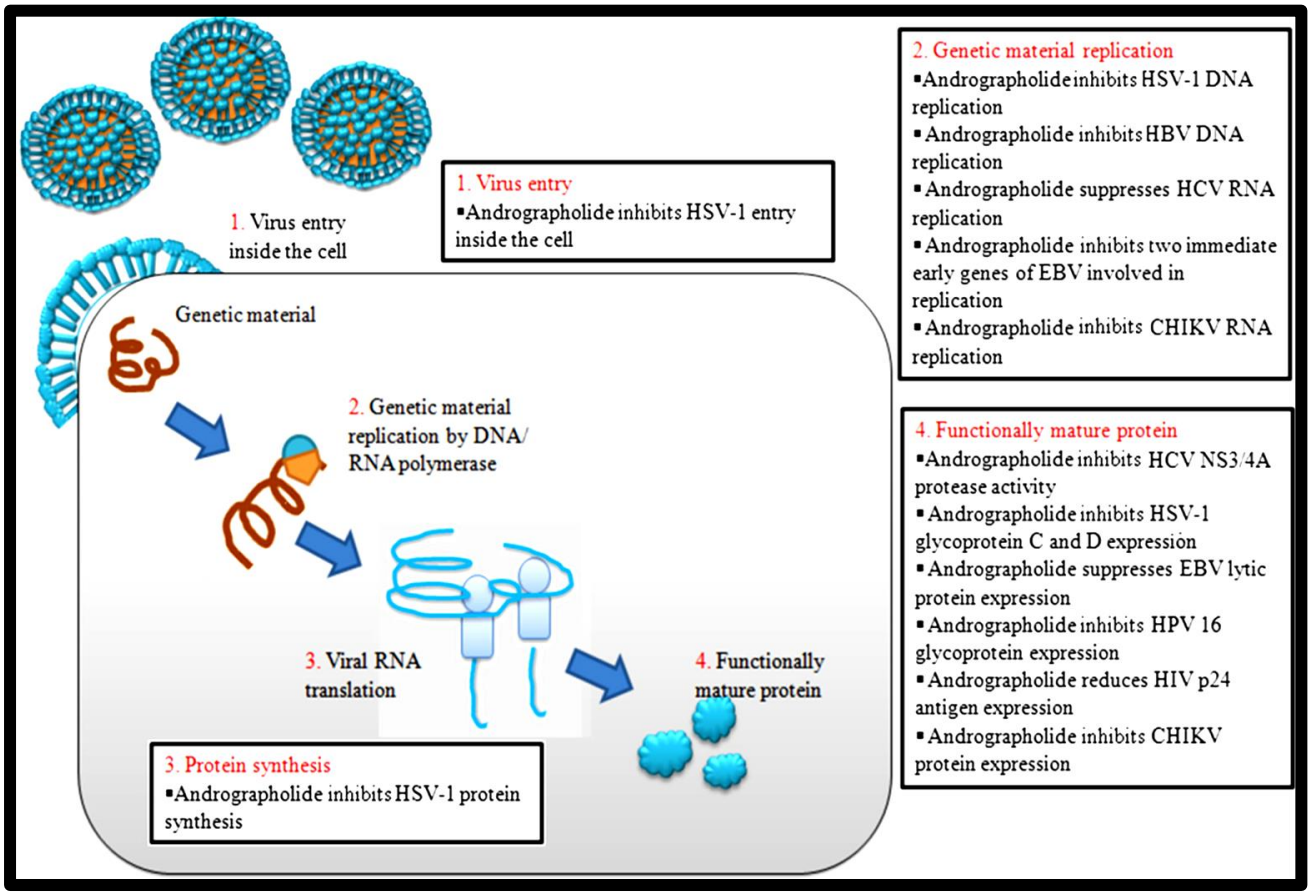

Fig. 1: Inhibitory effects of andrographolide on the viral life cycle. (Gupta S. 2016).
HSV: Herpes simplex virus, HBV: Hepatitis B virus, HCV: Hepatitis C virus, EBV: Epstein-Barr virus, CHIKV: Chikungunya virus, HPV: Human papillomavirus, HIV: Human immunodeficiency virus

Curcuma longa

It belongs to family Zingiberaceae which is native to India and commonly known as Turmeric. In Indian food preparation, it is commonly used as a spice and a coloring agent. It is known to have antioxidant, anti -inflammatory and anti-tumor properties (D. Qaiser *et al.* 2018). It is also used to boost immune system. The rhizomes of this plant contain Curcumin (diferuloylmethane), which is the main active component. According to Zandia K. *et. al.* (2010) curcumin and its new derivatives (gallium-curcumin and Cu-curcumin) have remarkable antiviral effects on HSV-1 in vitro. Antiviral activity of curcumin was reported against a number of different viruses that include, hepatitis virus, influenza virus, zika virus (ZIKV) or chikungunya virus (CHIKV), human immunodeficiency virus (HIV), herpes simplex virus 2 (HSV-2) and human papillomavirus (HPV) (Mazumder A. *et. al.* 1995, Praditya D. *et. al.* 2019; Dimas P. 2019. In a study by Chen D-Y *et. al.* (2010) it has been proven that curcumin directly acts against infection by viral particle (H6N1 and H1N1) which was indicated by inhibition of haemagglutination without developing resistance to curcumin.

Zingiber officinale

Commonly known as ginger (belonging to family Zingiberaceae) and a very popular spice as well as a main ingredient in many traditional and folk medicines. It reduces cold & cough, has anti-inflammatory, anti-nausea and good digestive properties (D. Qaiser *et al.* 2018). The roots or rhizomes of this plant contain a pungent volatile oil component (Gingerol) along with compounds containing sulphur (allicin, ajoene, and alliin), and enzymes (allinase, myrosinase and peroxidase). Chopra R. N. *et. al.* (1956) reported presence of TNF-*a* (anti-influenza cytokine) in ginger. Kharisma V. D. (2018) reported that the active compound β-sitosterol contained in the *Zingiber officinale* are predicted to have a potential as NNRTIs (antiviral agent) on HIV-1.

Tinospora cordifolia

Tinospora cordifolia, commonly known as Guduchi or Giloy, is an Indian native herbaceous vine belonging to family Menispermaceae, extensively used in Ayurveda. It has anti-diabetic, anti-allergic, anti-inflammatory, anti-pyretic, diuretic and immunomodulatory properties. According to a study by Sharma D. N. and Sharma A. (2015) *Tinospora cordifolia* boost immunity in children and has application as an adjuvant to vaccination. According to a study conducted by Kalikar M. V. *et. al.* 2015 HIV positive patients treated with *Tinospora cordifolia* extract showed lesser symptoms and reduced counts in TLC, neutrolphils and eosinophils thus confirming the anti-HIV property.

Glycyrrhiza glabra

It is commonly known as Licorice in English or Yashtimadhu in sanskrit and Mulathi in Hindi. The roots of this perennial herb belonging to family Fabaceace, are used worldwide for the treatment of cold and cough since immemorial time. Roots are extensively used as expectorant and in the treatment of upper respiratory tract infections with main active compounds as glycyrrhizin and glycyrrhetinic acid. In vitro studies of root extract confirmed the antiviral activity against SARS related coronavirus, HIV-1, respiratory syncytial virus, vaccinia virus, arboviruses and vesicular stomatitis virus (Fiore C. *et. al.* 2008 and Feng Yeh C. *et. al.* 2013).

Withania somnifera

It is commonly known as Ashwagandha in Sanskrit belonging to Solanaceae family. In ayurvedic preparations it is used as a general tonic and to boost immunity. Misra B. (2004) reported that *Withania somnifera* contains alkaloids (anaferine, anahygrine, isopelletierine and anahygrine) saponins and steroidal lactones (withaferins and withanolides) as biologically active compounds. Grover A. *et. al.* (2011) reported a hypothesis on the mode of action of withaferin A against Herpes Simplex Virus. According to them Withaferin A inhibits the DNA polymerase enzyme of the virus which doesn't allow viral replication.

Conclusion

The selected medicinal plants referred here are used in Indian traditional medicine, offer an effective solution or may help in the discovery of new drug molecules. The extracts or formulations of these plants work as a potential antiviral remedy. They also have phytochemicals and other metabolites that offer a plethora of immunity boosting properties. Resulting in improved immune system of human body to fight against infectious diseases like COVID-19.

The genus *Phyllanthus* is enriched with many phytochemicals like flavonoids, phenylpropanoids, triterpenoids, and diterpenoids. Almost all species of *Phylllanthus* contain phyllanthin which has reported antiviral activities and also significant immunomodulatory effects. Fruits of *Emblica officinalis* are rich in vitamin C and have strong anti- oxidant properties. It has been used in Ayurvedic preparations like

Chyawanprash and is known to boost immunity and encourage general well-being. Curcumin a diferuloylmethane, belonging to the class of natural phenols is the main component of turmeric which shows antiviral activity against many viruses. Andrographolide the main bioactive compound in *Andrographis paniculata* shows antiviral activity against many viruses including those causing respiratory diseases. Glycyrrhiza glabra is used as an expectorant, antitussive and demulcent since ancient times, hence it may help to give symptomatic relief to COVID-19 patients experiencing breathlessness.

Holistic approach with above selected plant formulations will help to build immunity to combat infectious diseases like COVID-19, in addition to having antiviral, anti-inflammatory effect in human being. Further studies will help to explore the possibility of combined therapies with other naturally derived substances or standard therapeutics resulting in development of broad-spectrum antidote for prevention and control of viral diseases.

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Conflict of Interests

The authors declared that no conflict of interest exist regarding this publication.

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