

# SARS-CoV-2, Virology and Pathogenicity and phytomedicinal immunomodulators to curb covid-19 pandemic

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## Abstract

The new coronavirus, COVID-19 has sent the world into a medical and economic crisis and if not contained can cause unprecedented damage to the human population. COVID-19 is a new pathogen and a new coronavirus that poses a global threat to healthcare system worldwide and has already devoured many lives in different parts of the world. Till date, there is no specific vaccine or effective antiviral therapy against COVID-19 disease. The only way to prevent oneself is to maintain social distancing, maintain proper hygiene and simultaneously enhance the individual's immune response by incorporating immune boosters in daily diet, as health supplements and prophylaxis. Phytotherapy (herbalism) means usage of plants or herbs as medication to treat or prevent diseases and has a lot of potential. This phytomedicinal therapeutic approach proves to be cheaper and safer alternative and reduce the incidence of drug resistance and may modulate the immune system in preventing viral diseases. This traditional therapy has less side effects and bestow a general good health. It may suppress viral replication and reduce the clinical signs of viral diseases and can be promoted as immunomodulator. COVID 19 has been shown to engage the host cell ACE2 through its spike protein receptor binding domain (RBD) and natural phytochemical from plants have distinct effects on viral RBD and host ACE2 receptor complex. The present paper aims to present a comprehensive study of certain medicinal herbs to increase the immune potential and a promising option in the fore-front in healing COVID-19 ailments, concurrent with ICMR prescribed allopathic treatments.

**Keywords:** Covid-19; SARS Virus; Virology; plants, phytochemical.

## INTRODUCTION

The world has witnessed one of the most deadly pandemic affecting almost majority of the countries in the world in the year 2020. This disease outbreak started from a local seafood market in Wuhan, Hubei province, central china. The full length genome sequence obtained from some patients were found identical to SARS-CoV and the 2019-ncov is 98% identical at the whole genome level to a bat coronavirus. (Peng Zhou et al 2020). The world health organization has recognized this pathogen as a coronavirus disease (Covid 19) on February 11, 2020 and the International Virus Classification Commission has designated the novel coronavirus as Severe acute respiratory syndrome Corona virus 2 (SARS-CoV-2) (E. de Wit et al 2016). The WHO has announced Covid 19 as the Public health emergency of international concern (PHEIC) on 30 January 2020 (Wee SL et al 2020) and a pandemic on 11 March. (World Health Organization (WHO) 2020). In the past two decades, two large scale pandemics, SARS and MERs have already been caused by coronaviruses (Drosten, C. et al 2003 and Zaki, A. M 2012) SARS CoV-2 has emerged as a highly pathogenic coronavirus into the human population. Global coronavirus cases have surged to more than 51 crores with deaths approaching 6257152 and approximately 46 crores people have recovered as reported by worldometers on 29 April 2022. (<https://www.worldometers.info/coronavirus/>)

The virus spreads through close contact via small droplets produced by coughing, sneezing and talking. It can also spread through touch of contaminated surface and then touching the eyes, nose and mouth (Centres for disease control and prevention (CDC) 2020). Covid 19 affects the respiratory tract in humans. The infection starts with mild flu-like symptoms or no symptoms and in severe cases causes death due to ARDS and pneumonia. Individuals with cardio vascular diseases, diabetes, hypertension, carcinoma and respiratory diseases are at a higher risk of having Covid 19 and it also aggravates with age. Individuals with lesser immune, children below the age of 12 and old age patients are at high risk of contamination. Vaccine

development is proving to be a challenging process, but it is the most promising approach to combating a pandemic. The development of vaccines has been accelerated as a result of lessons learned from earlier SARS and MERS outbreaks and the advancement of technology. The most promising method of containing any pandemic is vaccination; however, developing vaccines can be challenging. The development of vaccines has been accelerated thanks to lessons and experiences learned from previous SARS outbreaks and MERS outbreaks and advances in technology( Md. Tahsin Khan et al 2021) The mortality and infection caused by covid 19 has badly affected US, Italy and taking a toll in India. India has now more than 44 crores cases of covid 19 and is the second most affected country in the world{<https://www.worldometers.info/coronavirus/>}.Despite this, fatality rate(at less than 3%) in India is among the lowest of the severely affected countries{<https://www.worldometers.info/coronavirus/>}. This is a silver lining health advantage which India must sustain and build on. The present paper emphasizes the various advantages of some common indian spices of medicinal importance (e.g.,*Curcuma longa* i.e., haldi ), Ginger (*Zingiber officinale*), Pure Ashwagandha (*Withania somnifera*), Giloy(*Tinospora cardifolia*) and many more(Table1), widely used in indian cooking and as a supplementary medicine as a tool to enhance immune system.

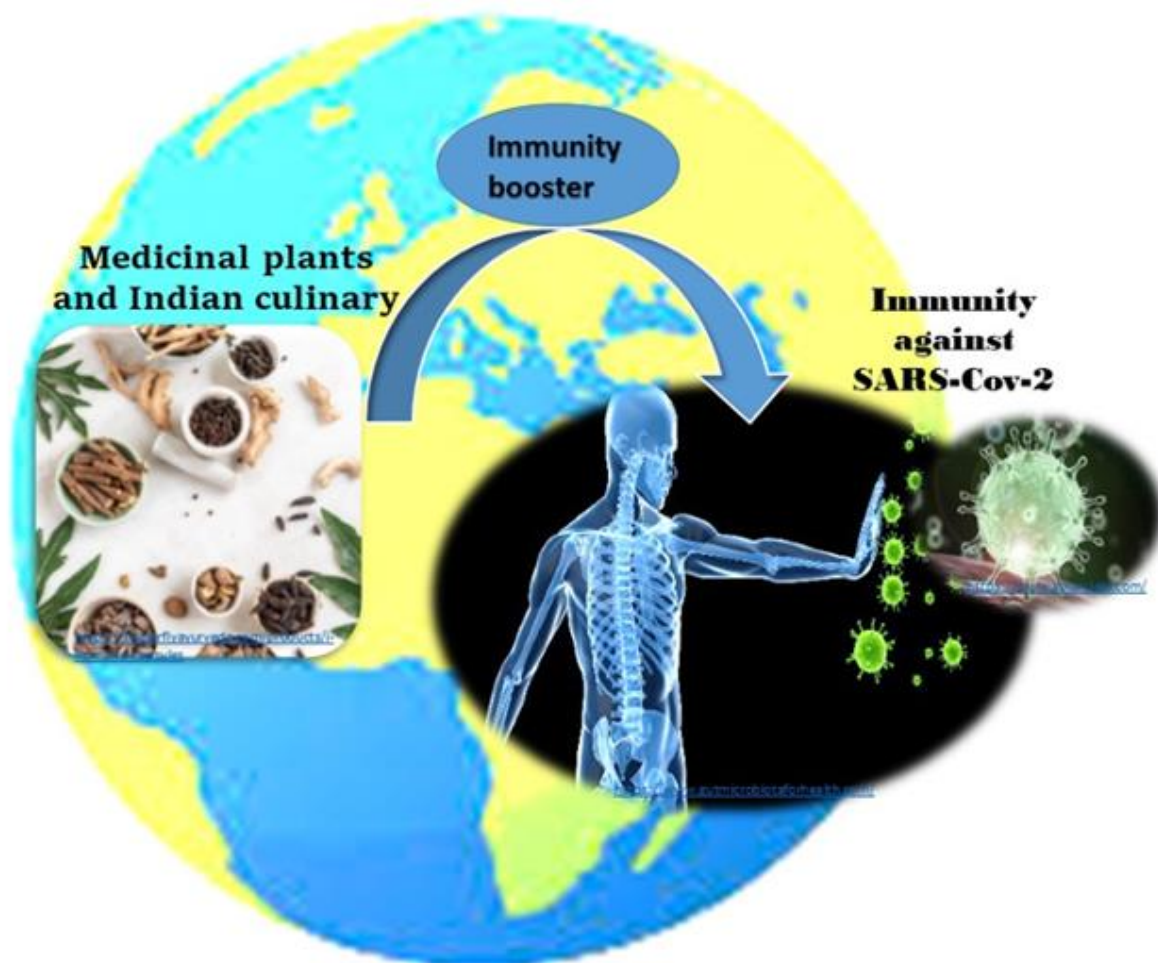


Figure 1

## Virology

SARS CoV-2 is a strain of Severe acute respiratory syndrome related coronavirus and is supposed to be of zoonotic origin{ Cui, J et al 2019 and Benvenuto D et al 2020 }. SARS-CoV-2 of the family coronaviridae is a member of the subgenus Sarbecovirus (beta-CoV lineage B{ Cui, J et al 2019}). Four Coronavirus genera ( $\alpha, \beta, \gamma, \delta$ ) have been identified so far and the viral

genome of patients in china shows the presence of  $\beta$  Co V strain in all of them { Phylogeny of SARS-like betacoronaviruses 2020}. Coronaviruses are large and roughly spherical enveloped viruses with spikes that mediate coronavirus entry into host cells. Each SARS-CoV-2 virion is 50–200 nanometres in diameter . It is a positive-sense single-stranded RNA (+ssRNA) virus, with a single linear RNA segment. Its RNA sequence is approximately 30,000 bases in length and are one of the largest among RNA viruses.

SARS-CoV-2 has four structural proteins, known as the S (spike), E (envelope), M (membrane), and N (nucleocapsid) proteins as well as several accessory proteins of unknown function. The Nucleocapsid protein holds the RNA genome, and the S, E, and M proteins together create the viral envelope. { Wu C et al 2020}. The spike protein is the protein responsible for allowing the virus to attach to and fuse with the membrane of a host cell { Wu C et al 2020}. Its S1 subunit catalyzes attachment, the S2 subunit fusion { Aronson JK 2020}. SARS- CoV -2 just like other SARS-CoV requires the angiotensin –converting enzyme2 (ACE2) { Peng Zhou et al 2020} as a receptor to enter cells.. The binding of the virus with host cell receptor determines the pathogenesis of infection { W.Li et al 2003}.

### Coronavirus entry and replication

The virus access host cell via (ACE2) found abundantly in type II alveolar cells of the lungs. The envelope spike (s) glycoproteins of coronaviruses bind to its cellular receptor ACE2 (Angiotensin- converting Enzyme-2) to mediate infection of their target cells. (W.Li et al 2003). After the virus enters the cell, the viral Rna genome is released into the cytoplasm and the viral genome begins to replicate and is translated into enveloped glycoproteins which are inserted into the ER (Endoplasmic reticulum) or golgi membrane. The nucleocapsid is formed by combination of genomic rna and nucleocapsid. The vesicles in the ERGIC-(Endoplasmic reticulum-Golgi intermediate compartments) fuse with the plasma membrane to release the virus. The entry of the virus in the cells trigger the antigenic peptides (Human Leukocyte Antigen –HLA) in humans and the virus specific cytotoxic T lymphocytes actively recognize them. The antigen stimulate the specific B and T cells and the body starts producing IgM an IgG antibodies as in common viral infection. The latest report states significant reduction in number of CD4+ and CD8+T cells in the peripheral blood of SARS-CoV-2 (Huang C et al 2020).

### Pathogenesis and “Cytokine storm”

SARS-CoV-2 infection primarily affect the lungs by directly affecting the surfactant producing Type II alveolar cells by killing them as a result of which the lungs become flooded by fluids, pus and dead cells. The common symptoms are cough, fever, chill, headache and severe bodyache , trouble tasting and smelling and difficulty breathing. Covid -19 can also present symptoms like GI disorders and Liver abnormalities (Eurekalert.org 2020).

The acute manifestation of SARS-CoV-2 is ARDS (Acute Respiratory Distress Syndrome), a common immunopathological event for SARS-CoV-2, SARS-CoV, and MERS-CoV infections. The immune effector cells release large amounts of pro-inflammatory cytokines (IFN- $\alpha$ , IFN- $\beta$ , IL- $\beta$ , IL-6, IL-12, IL-18, IL-33, TNF-  $\alpha$ , TGF  $\beta$ , etc.) and chemokines (CCL2, CCL3, CCL5, CXCL8, CXCL9, CXCL10) in an uncontrolled manner . This leads to hyper-immune response or Cytokine storm (C. Castilletti et al 2005). Cytokine storm. Or “Hypercytokinemia” leads to ARDS. Most patients have mild symptoms and good prognosis. So far, a few patients with 2019-nCoV have developed severe pneumonia, pulmonary oedema, ARDS, or multiple organ failure and have died (Wu F et al 2020). Till date few potential and promising vaccine have been found and approved by WHO, AstraZeneca/Oxford vaccine, Johnson and Johnson, Moderna, Pfizer/BionTech, Sinopharm, Sinovac, COVAXIN, Covovax, Nuvaxovid, CanSino (<https://www.who.int/emergencies/diseases/novel-coronavirus-2019/covid-19-vaccines/advice>). Beginning in early December 2020, the first mass immunisation programme was launched. On December 31, 2020, the Pfizer/BioNtech Comirnaty vaccine was added to the WHO Emergency Use Listing (EUL). The State Institute of India and SK Bio, respectively, produced the SII/Covishield and AstraZeneca/AZD1222 vaccines, which were administered for EUL on February 16, 2021. In June 2021, Bharat Biotech and the National Institute of Virology (NIV) of the Indian Council of Medical Research (ICMR) jointly developed Covaxin, an indigenous Covid-91 vaccine. The vaccine effectiveness of the Covaxin against symptomatic COVID-19 infections has been shown to be 77.8%. Two doses of the immunisation, spaced 28 days apart, are required. Johnson & Johnson created the Janssen/Ad26.COV 2.S, which was scheduled for EUL on March 12, 2021. Beginning in early December 2020, the first mass immunisation programme was launched. Beijing Bio-Institute of Biological Products Co Ltd, a division of China National Biotec Group, is the company that makes the Sinopharm vaccine

Additionally, a number of allopathic medications have a number of side effects that are hazardous to the heart, kidneys, and diabetic patients despite initially being beneficial in treating the infection. Another treatment option for the Covid-19 virus is plasma therapy, which isolates plasma from the blood of patients who have recovered from viral infections. As a result, various

preventive actions must be taken, mostly using alternative medications made from herbal plants to strengthen the immune system and combat COVID-19

### Medicinal spices as immunity booster

There have been few successful vaccine candidates approved; however, given the rapid rate of virus mutation, vaccine efficacy against mutated strains is unknown. (Arpana Parihar et al 2022, E. Andreano 2021, D. vanEgeren 2021, A. Khan et al 2021). A new strain of SARS-CoV-2 was responsible for the second wave of the pandemic. These strains, first reported in the UK (N501Y), South Africa (K417N-E484K-N501Y), and Brazil (K417T-E484K-N501Y), have higher infectiousness, associated mortality, and morbidity (Arpana Parihar et al 2022). As a result of the current scenario, new candidate drugs with a maximum therapeutic potential that exhibit fewer side effects are crucial to be considered. Plant-based phytochemicals are bioactive molecules that are promising candidates owing to their low side effects and high therapeutic value (Arpana Parihar et al 2022). The flavonoids and non-flavonoid phenols, terpenoids, and alkaloids have been studied as potential antiviral agents because of their inherent properties, which include antioxidants, immunomodulators, and anti-inflammatory roles which may reduce the severity of infection and disease symptoms and enhance the patient's immune response (Arpana Parihar et al (2022 b) The present paper represents the phytomedicinal approach to Covid -19 where the use of certain immunomodulators has been emphasized. Phytomedicines have good efficacy and lack of side effects and hence are promising and can be suggested as complementary therapy (Table 1). SARS-CoV-2 infection depends on the interaction between the virus and individuals immune system. The individuals immune system factor depends on several factors like genetics, age, gender, nutritional status and neuroendocrine-immune regulations. Use of some common spices which are also of medicinal importance like Curcuma long, Zingiber officinale, Pure Ashwagandha (*Withania somnifera*), Giloy (*Tinospora cardifolia*) and many more enhance and boost our immune (Figure 1) response to various acute viral infections and may have promising results. We have selected Curcuma long, Zingiber officinale, Pure Ashwagandha (*Withania somnifera*), Giloy (*Tinospora cardifolia*) because of easily availability of these plants.

Table 1: List of plants suggested for SARS-CoV-2

Plant species	Family	Chemical composition	Mode of action	Traditional uses	Reference
Glycyrrhiza glabra L	Fabaceae	Glycyrrhizin, glycyrrhetic (Glycyrrhetic) acid, the aglycone of glycyrrhizin, isoflavonoids, chalcones, coumarins, triterpenoids, sterols, lignans, amino acids, amines	Viruses such as hepatitis, herpes, influenza, and SARS are significantly inhibited by glycyrrhizin and its analogs. An antiasthmatic flavonoid, Liquiritigenin, was found to be present in root extracts	laxative, emmenagogue, contraceptive, galactagogue, anti-asthmatic, antitussive, and antiviral agent	(Umashankar . V et al. 2021)  (Sharma V et al.2017)  (Khare, CP 2007)

Tylophora indica	Asclepiadaceae	tylophorine, tylophorinine, and tylophorinidine	By inhibiting JAK2-mediated NF-kB activation, Tylophora alkaloids can suppress viral RNA replication. Unlike tylophorine, derivatives of this chemical can inhibit the action of MHV, TGEV, and SARS-CoV	Cancer, respiratory infections, bronchial asthma, whooping cough, and anaphylaxis.	(Umashankar . V et al. 2021)  (Shahzad A et al 2016)  (Yang C-W et al 2017)  (Yang C-W et al 2010)  (Yang CW el al 2017)  (Yang C-W et al 2020)
Justicia adhatoda L.	Acanthaceae	alkaloids, anthraquinones, flavonoids, phenols, saponins, and tannins	Many viruses can be directly interfered with by aqueous and methanolic extracts of leaves. Vasicine alkaloids have antiviral activity	asthma, chronic bronchitis, and other problems including fever, swelling, asthma, pneumonia, malaria, tuberculosis, cough, and cold	(Umashankar . V et al. 2021)  (Sharma MP et al 1992)  (Singh B et al 2020)  (Amber R et al 2017)

Camellia sinensis L	Theaceae	theaflavin, theaflavin-3-gallate, theaflavin-3'-gallate, and theaflavin-3,3'-digallate	Influenza A and B viruses were found to be ineffective against theaflavin di-gallate in in vitro studies. Researchers have shown that water-soluble phenols such as tannic acid and flavin-3-3'-digallate inhibit the 3-chymotrypsin-like protease (3CLpro) of the SARS Coronavirus. Hence, it can be considered as a starting point for molecules against the SARS-CoV-2	inflammation, possess antimicrobial effects, and are used in the treatment of respiratory diseases such as asthma	(Umashankar . V et al. 2021)  (Chattopadhyay D et al 2007)  (Palit P et al 2021)
Ocimum Tenuiflorum L.	Lamiaceae	df apigenin, linalool, ursolic acid, tulinol A-G and dihydro-dieuginol B	Tusinol A-G and dihydro-dieuginol B exert inhibitory effects on SARS Coronavirus Main Protease (Mpro) and Papain-like Protease (PLpro)	common cold, headache, stomach ailments, inflammation and heart disease	(Umashankar . V et al. 2021)  (Pattanayak P et al 2010)  (Shree P et al 2020)
Syzygium Aromaticum (L.) Merr. & L. M. Perry	Myrtaceae	sesquiterpenes, monoterpenes, hydrocarbons, and phenolics along with Eugenyl acetate, eugenol, and $\beta$ -caryophyllene	The high concentration of eugenol in clove essential oil makes it highly effective when treated with HSV or HCV because of its ability to inhibit viral replication.	dental, digestive, and respiratory disorders, including asthma	(Umashankar . V et al. 2021)  (Shah B et al 2012)
Berberis vulgaris L.	Berberidaceae	berberine, oxyaconthine, berbamine, brolicin, and columbamine	protective effects on LPS-induced lung injury via activating Nrf2	fever, cough, liver disease, depression, hyperlipidemia, hyperglycemia and bleeding	(Liang, Y et al 2019)
Paulownia tomentosa (Thunb.) Steud	Paulowniaceae	geranylated flavonoids (tomentin A-E)	inhibit the papain-like protease as a vital enzyme for SARS-CoV-2 propagation	bronchitis, especially by reducing coughing, asthma, and phlegm	(Cho, J. K et al 2013)

<i>Stephania tetrandra</i> S. Moore	Menispermaceae	Tetrandrine, fangchinoline, cepharanthine, bisbenzylisoquinoline, Sanguinarine, palmatine, berberine, chelidonine, jatrorrhizine, ipecac alkaloids, and emetine	anti-HCoV activities, anti-SARS-CoV-2 agents	arthralgia caused by rheumatism, wet beriberi, dysuria, eczema and inflamed sores	(Kim, D. E et al 2019) (Bleasel, M. D. et al 2020) (Wink, M. et al 2020)
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By raising the survival percentage (challenge test) lysozyme, phagocytic index, and phagocytic activity, cinnamon zeylanicum essential oil and powder demonstrated significant immune-stimulatory action.(Tamam et al 2017 and Kuntal das 2022). Throughout the world, black pepper (Family: Piperaceae) is one of the most commonly used spices. Colds, coughs, and throat infections are well treated with the fruit. There are also other constituents present such as (-)-kusunokinin, piperamide, piperamide-B, piperamide, and (-)-kusunokinin that contribute to the therapeutic potency of piperine.(Kunatal Das 2022 and Takooree H 2019)

#### Curcuma longa

Curcuma longa (Family Zingiberaceae), also known as turmeric or haldi, a perennial, rhizomatous plant is a common ingredient in indian culinary and widely used as a health supplement in Asia. Turmeric holds an important position in Indian pharmacopeia and has many therapeutic applications such as blood purifying, wound healing and inflammatory disorders. The key active constituent of C. longa is curcuminoids , a mixture of curcumin (60-70%), demethoxycurcumin(20-27%) and bismethoxycurcumin(10-15%)(Figure 2).Curcumin , a polyphenol product interacts with different cellular and molecular targets and possess anti-cancer, anti-inflammatory and immunomodulator properties (Yue GG et al 2010). Curcuminoids modulate the proliferation and cellular response of various cell types such as T cells, B cells, macrophages neutrophils, NK cells and dendritic cells (Momtazi-Borojeni AA et al 2018). The immunomodulator properties of curcumin interact with molecular components involved in the inflammatory processes, such as cytokines and various transcription factor with their downstreaming signaling pathways(Momtazi-Borojeni AA et al 2018). Curcumin has also been found to inhibit the production of inflammatory cytokines involved in NF-κB activation (Selvam C et al 2005) and also inhibits IL-1β,IL-8, monocyte inflammatory protein-1 (MIP-1α), monocyte chemotactic protein -1(MCP-1) and TNF- α (Weber WM et al 2006).

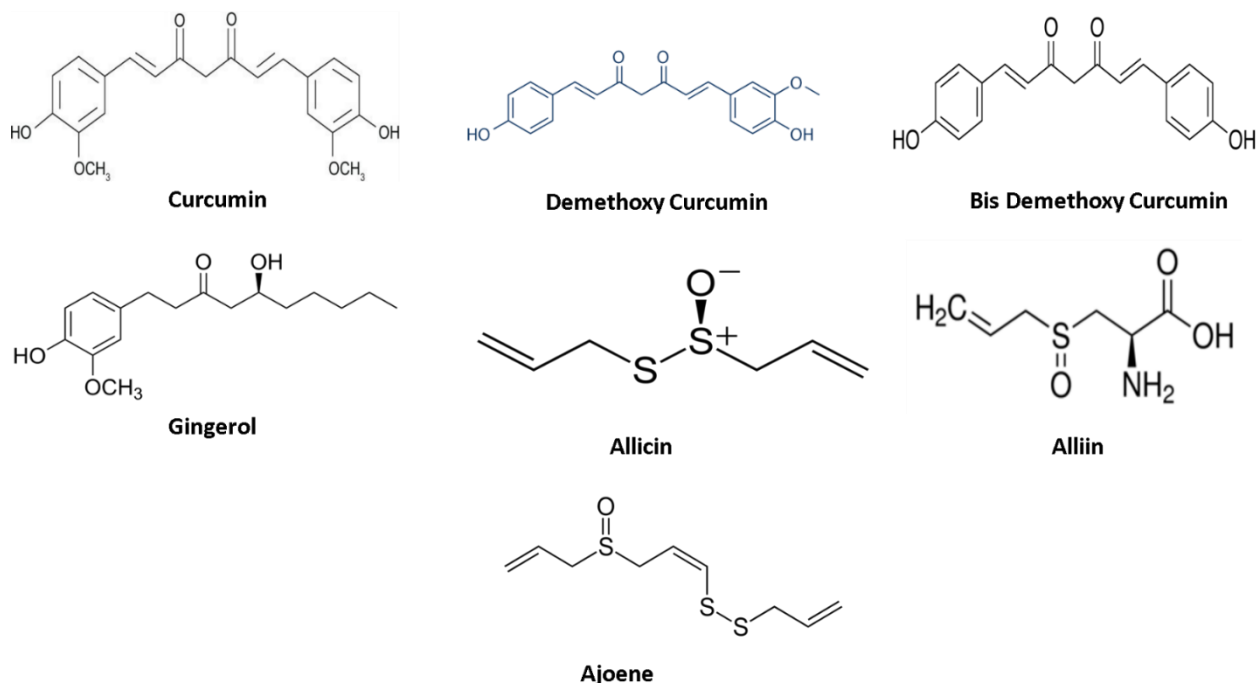


Figure 2 Curcumin, Demethoxy Curcumin, Bis demethoxy curcumin, Gingerol, Allicin, Alliin and Ajoene

In a recent non-randomized phase 2 study with seven endometrial cancer patients, curcumin phytosome was examined for immunomodulatory effects by T cell activation, and the results showed strong immune-stimulating action. (Kuntal das 2022 and Tu Figure 3 discuss about the mechanism of inhibition of SARS-CoV-2 infection by Curcuma longaerts S et al. 2019)

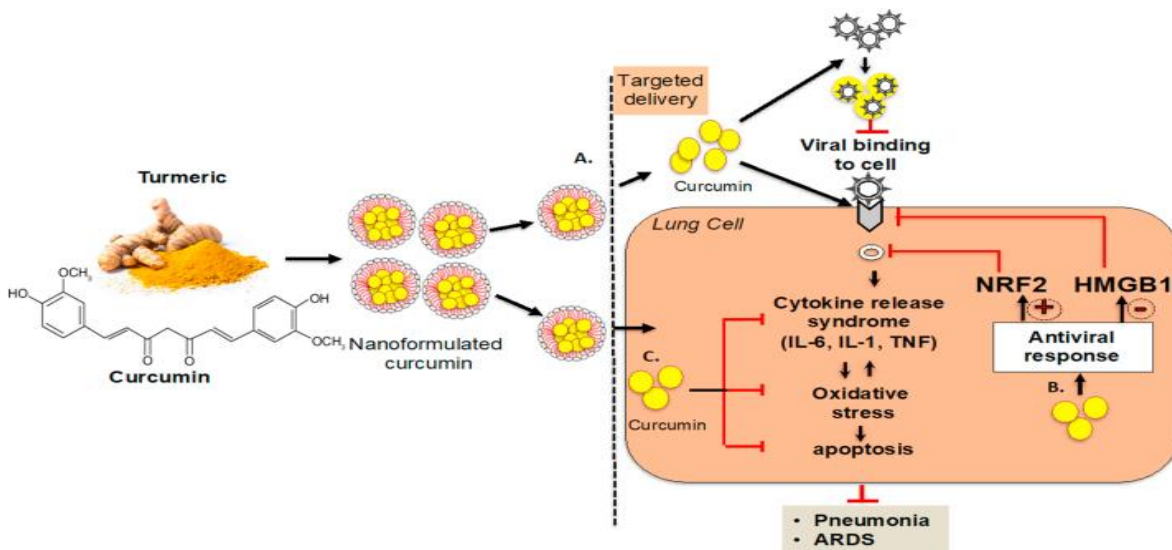


Figure 3: This schematic illustrates the potential mechanisms by which curcumin may be effective against COVID-19 (Reproduced by permission © 2021 Published by Elsevier Ltd.) (Rajesh K. Thimmulappa et al 2021)

## Ginger

Zingiber officinale (family Zingiberaceae), Ginger or Adrak a herbaceous perennial plant, commonly consumed as a spice and a herbal medicine for thousands of years (Han Y.A et al 2013). It is rich in chemical constituents like phenolic compounds,

terpenes, polysaccharides, lipids, organic acids, and raw fibers. The health benefits of ginger are mainly attributed to its rich phytochemistry especially the phenolic compounds, such as gingerols (such as 6-gingerol, 8-gingerol, and 10-gingerol), shogaols and paradols. It has been found to possess biological activities, such as antioxidant, anti-inflammatory, antimicrobial, and anticancer neuroprotective, cardiovascular protective, respiratory protective, antiobesity, antidiabetic, anti-nausea, and antiemetic activities (Zhang M. et al 2016). Ginger possesses the potential to prevent and manage respiratory disorders as crude ginger extract showed bronchodilator activity [Chrubasik S et al 2005]. The polyphenol content of ginger shows many protective roles and aqueous extracts of ginger show a significant inhibitory effect on ACE (Angiotensin converting enzyme) and lipid peroxidation (Akinyemi A. J et al 2013 and 2014). As stated earlier the spikes of SARS CoV 2 bind to its cellular receptor ACE2 (Angiotensin- converting Enzyme-2) to mediate infection of their target cells. ACE inhibitors prevent production of angiotensin II, which narrows blood vessels and release hormones which cause hypertension. Ginger also has an effect on several genes encoding cytokines, chemokines and the inducible enzyme cyclo-oxygenase -2 (Grzanna R et al 2005). The components of ginger have fewer side effects and are more effective than NSAIDs-non steroidal anti-inflammatory drugs (Grzanna R et al 2004). Studies have also shown that ginger has hypoglycaemic and anti-inflammatory effects (Charlier C et al 2003). The gingerol (Figure 2), a pungent volatile oil with sulphur-containing compounds (allicin, alliin, and ajoene) (Figure 2), and enzymes (allinase, peroxidase, and myrosinase) exhibit antibiotic properties (Fatehi-Hassanabad Z et al 2005). The allicins have fibrinolytic activity and help in reduction of platelet aggregation by inhibiting prostaglandin E<sub>2</sub>. Research has suggested that various anti-influenza agents are presented in ginger including TNF- $\alpha$ , an anti-influenza cytokine (A. Shah et al 2013). Compounds in ginger also increase levels of antioxidant enzymes, which stimulate inflammatory reactions triggered by viral infections.

Figure 4 discuss about the mechanism of inhibition of SARS-CoV-2 infection by Zingiber officinale

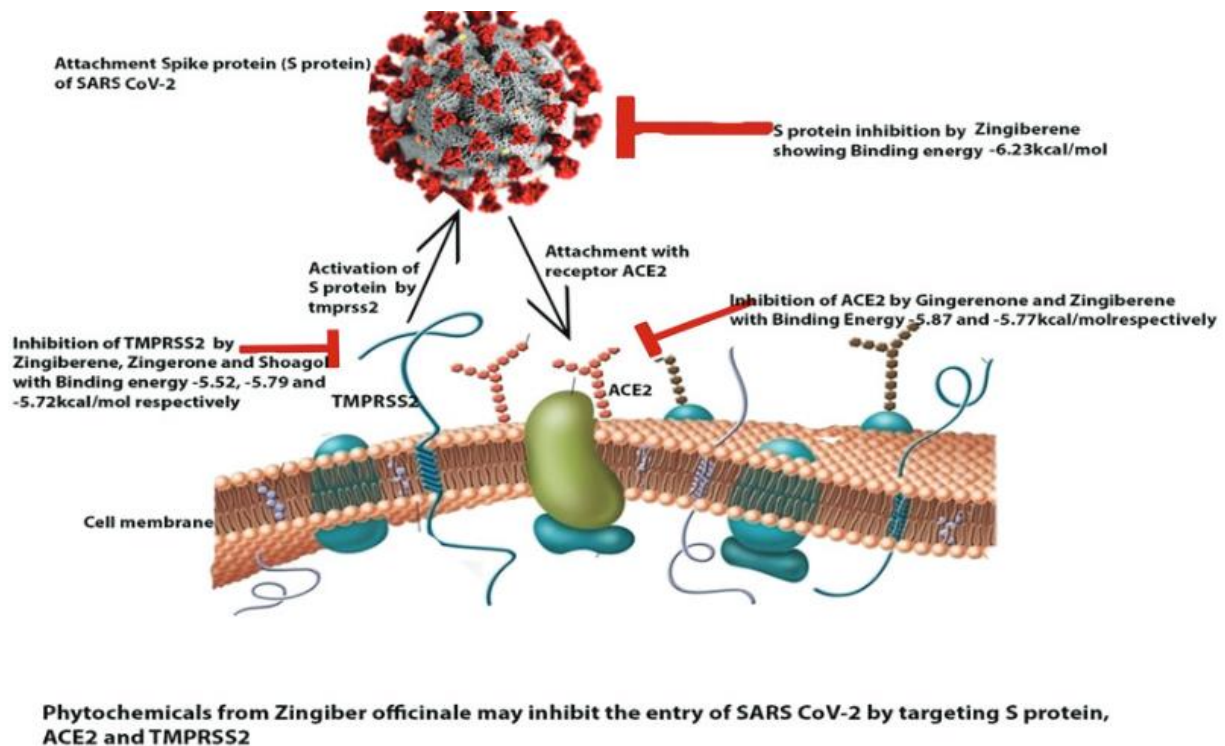


Figure 4: Phytochemicals act at the site of entry of viral proteins ( Ankita Singh Chakotiya and Rakesh Kumar Sharma 2020)

Pure Ashwagandha (*Withania somnifera*)

Ashwagandha (*Withania somnifera*) is a well-known medicinal plant that has been used in traditional medicine for over 3,000 years. Many ailments, including arthritis, impotence, amnesia, anxiety, cancer, and cardiovascular diseases, and others, are treated using this plant extract and its medicinal components.

A spike protein receptor binding domain (RBD) on COVID-19 has been shown to bind ACE2 on host cells. Natural phytochemicals derived from *Withania somnifera* have been shown to affect ACE2 receptors and viral RBDs in distinct ways. Withanone (Figure 5), a compound from the *W. somnifera* plant, docked very well in the binding interface of the ACE2-RBD complex on simulation and moved slightly toward the interface center. The electrostatic component of the binding free energy of the ACE2-RBD complex was dramatically reduced by withanone. At the interface, two salt bridges were discovered; the addition of Withanone destabilised these salt bridges and reduced their occupancies. We believe that disrupting the electrostatic connections between the RBD and ACE2 would prevent or weaken COVID-19 entrance and infectivity. It shows that natural phytochemicals may be feasible possibilities for regulating COVID-19 entrance into host cells, and *W. somnifera* may be the first plant to be considered in these directions. (Balkrishna, A et al 2020 and [https://www.patanjaliresearchinstitute.com/pdf/covid19/Patanjali\\_Proposal\\_to\\_Battle\\_COVID-19\\_\\_1\\_.pdf](https://www.patanjaliresearchinstitute.com/pdf/covid19/Patanjali_Proposal_to_Battle_COVID-19__1_.pdf))

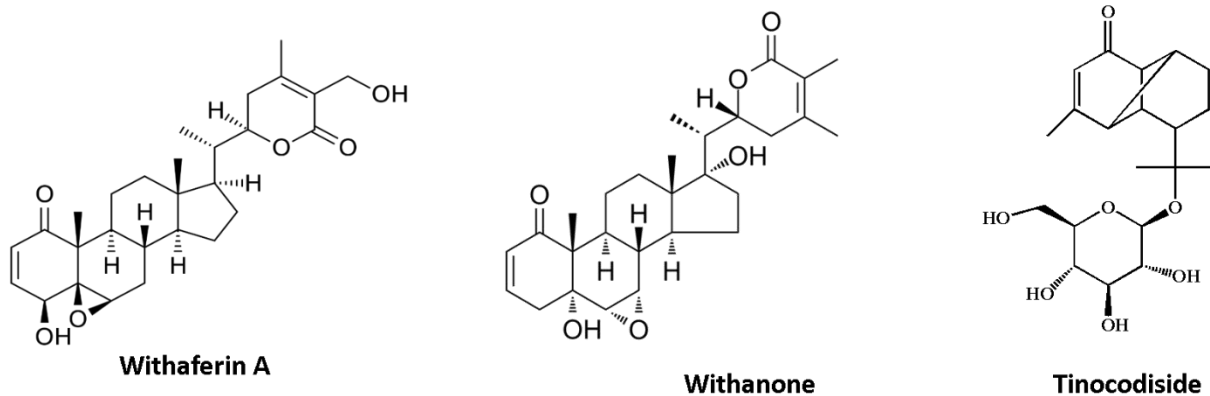


Figure 5: Withaferin A, Withanone and Tinocodiside

Giloy(*Tinospora cardifolia*)

*Tinospora cordifolia* has been used for centuries as an immunostimulant and a treatment for a variety of microbiological illnesses. (<http://www.flowersofindia.net/catalog/slides/Gulbel.html>)

and Sinha, K et al 2004) Berberine, choline, columbin, chasmanthin, jatrorrhizine, palmatine, tinocordifolioside, tinosporon, tinosporic acid, tinosporin, tinosporol, tinosporaside, tembeterin etc (<https://www.drugs.com/npp/tinospora.html>)

[https://bioinfo.bisr.res.in/project/domap/plant\\_details.php?plantid=0122&bname=Tinospora%20 cordifolia](https://bioinfo.bisr.res.in/project/domap/plant_details.php?plantid=0122&bname=Tinospora%20cordifolia), Mishra, A et al 2012 and Sharma, P et al 2019 ), Giloy is widely used to treat diabetes, dyspepsia, jaundice, rheumatoid arthritis, pyrexia, inflammations, gout, cardiac debility, excess mucus, urinary problems, asthma, splenopathy, and other etiologies. (<http://www.flowersofindia.net/catalog/slides/Gulbel.html>)

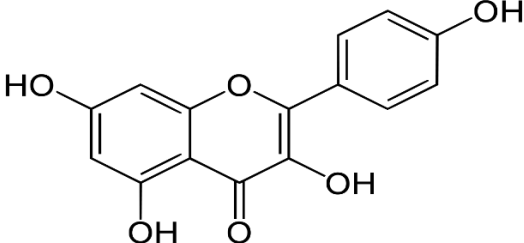
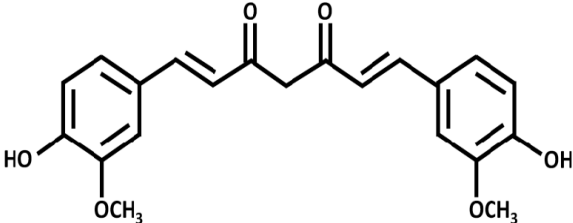
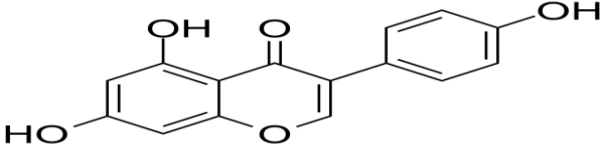
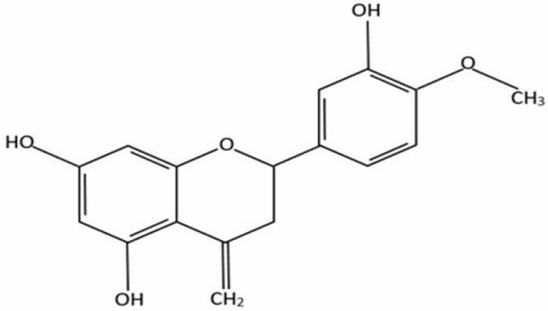
[https://bioinfo.bisr.res.in/project/domap/plant\\_details.php?plantid=0122&bname=Tinospora%20 cordifolia](https://bioinfo.bisr.res.in/project/domap/plant_details.php?plantid=0122&bname=Tinospora%20cordifolia), Mishra, A et al 2012 and Sharma, P et al 2019)

Tinosporine, tinocodiside( Figure 5), diterpenoid furano lactone, tinosporaside, cordifolide, cordifol, syringin, clerodane furano diterpene, tinosporidine, columbin, heptacosanol, b-sitosterol, and tinosporide are the principal phytochemicals found in Giloy (Tin Immunomodulatory action has been observed for cordifolioside A and syringin. Tinosporin, a diterpenoid, has been used to treat a variety of viruses, including (retroviruses) (HIV-1, HIV-2, all subgroups), HTLV, Herpes simplex Virus (HSV), and other viral diseases.

Tinocodiside, like Withanone, docks particularly well within the ACE2-RBD complex. Tinocodiside also showed favourable binding poses inside the ACE2-RBD interface with many inter reacting sites in the simulated state. Many more phytochemicals are listed in table 3 which inhibits SARS-CoV-2

There are few phytochemicals which are in clinical trial for management of Covid -19 (Table 2)

Table 2: List of Phytochemical under trial for Covid -19

Chemical family	Phytochemical	Structure	Reference
Flavonoid	kaempferol		(Javier Echeverria et al 2020)
curcuminoid	<u>curcumin</u>		(Abdurrahman Pharmacy Yusuf et al et al 2022)
Flavonoid	<u>genistein</u>		(Abdurrahman Pharmacy Yusuf et al et al 2022)
Bioflavonoid	<u>hesperidin</u>		(Abdurrahman Pharmacy Yusuf et al et al 2022)

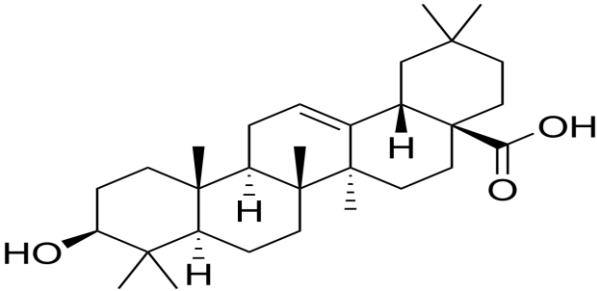
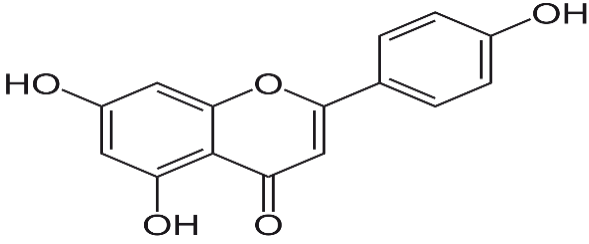
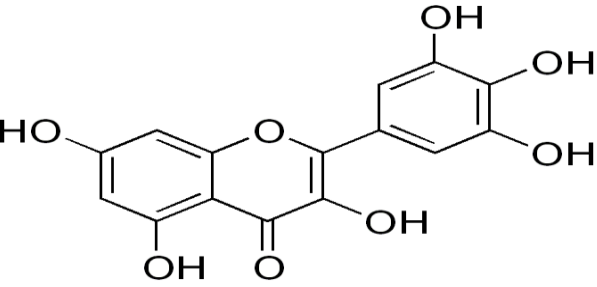
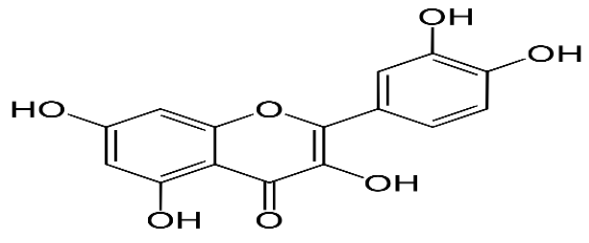
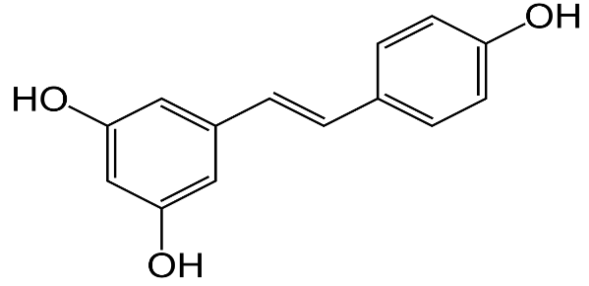
pentacyclic triterpenoid	<u>oleanolic acid</u>		Abdurrahman Pharmacy Yusuf et al et al 2022
Flavone	apigenin		(Javier Echeverria et al 2020)
Flavonoid	myricetin		(Javier Echeverria et al 2020)
Flavonoid	<u>quercetin</u>		(Abdurrahman Pharmacy Yusuf et al et al 2022)
Stilbenoid (natural Phenol)	<u>resveratrol</u>		(Abdurrahman Pharmacy Yusuf et al et al 2022)

Table 3 Phytochemicals that inhibit SARS-CoV-2

Plant Source	Phytochemical	Mechanism	References
Camelia sinensis	Betulinic acid	3CLpro	(Lung et al., 2020), (Olabisi O. Ogunrinola et al 2022)

Carapa guianensis	Limonoid	ACE2	(Khandelwal & Sharma, 2020), (Olabisi O. Ogunrinola et al 2022)
Cassia siamea	22-Hydroxyhopan-3-one	3CLpro	(Gyebi et al., 2021), (Olabisi O. Ogunrinola et al 2022)
Monodora angolensis	Annonidine F	ACE2	(Gyebi et al., 2020), (Olabisi O. Ogunrinola et al 2022)
Camptotheca acuminata D	Camptothecin	TMPRRS2	(Gyebi et al., 2020), (Olabisi O. Ogunrinola et al 2022)
Salvadora persica	Kaempferol	3CLpro & PLpro	(Owis et al., 2020; Zhang et al., 2020), (Olabisi O. Ogunrinola et al 2022)
Chamaecyparis obtusa var.	Savinin	3CLpro	(Swargiary et al., 2020), (Olabisi O. Ogunrinola et al 2022)
Myrica nagi Thunb	Myricetin	TMPRSS2	(Chikhale et al., 2020), (Olabisi O. Ogunrinola et al 2022)
Scutellaria baicalensis	Baicalein	TMPRSS2 & 3CLpro	(Da Silva et al., 2020; Liu et al., 2021), (Olabisi O. Ogunrinola et al 2022)
Camellia sinensis(L.)	Gallocatechin gallate	PLpro	(Swargiary et al., 2020), (Olabisi O. Ogunrinola et al 2022)

Abbreviations: 3CLPro, 3-chymotrypsin like protease. ACE2, angiotensin-converting enzyme 2; TMPRSS2, transmembrane protease serine 2; PLpro, papain-like protease);

## Conclusion and Future scope

COVID-19 infection is more likely to affect individuals with weak immunity and those who already have chronic illness such as cardiovascular problems, diabetes, neurological disorders etc. Therefore, enhancing immunity and controlling other illness can definitely help treating COVID-19 cases. Chinese traditional medicines in combination with allopathic treatments has been advantageous in symptomatic alleviation in COVID-19 cases. The traditional Indian Medical practices, popular as Ayurveda mentions several immunity boosting therapeutics which are very common in Indian culinary and common use. This research paper proposes benefits of certain rhizomes (Curcuma long and Zingiber officinale), Pure Ashwagandha (Withania somnifera) and Giloy (Tinospora cardifolia) in the fore-front in healing COVID-19 ailments (for their binding affinities to COVID-19 essential proteins and host protein interactions) and must be considered viable options for controlling COVID-19 entry into host cells. It has been well established in peer research that natural phytochemicals indeed have potentials to combat COVID-19 and its pathogenicity. Both curcumin and ginger can be consumed fresh, dried or ground and are available in supplement forms. Regular intake of such beneficial herbs can help reduce general body illness and boost our immune response to curb covid infectivity. Thus it has been suggested to take Curcuma long, Zingiber officinale, Giloy (Tinospora cardifolia) and Pure Ashwagandha (Withania somnifera) as a preventive measure against Covid 19 and it will boost the stiff effort of world to fight against such deadly virus. Viruses keep on mutating so its very difficult to make vaccine for each type of virus that why one need to look for many more phytochemicals as potential drugs for combat COVID-19. There are many more phytochemicals which can be potential drugs to combat COVID -19 without any side effects. So intense research require for identification of many more phytochemicals for COVID-19

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