

Ayurvedic approaches for the Treatment of COVID - 19 - A Review

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Abstract

Coronavirus disease (COVID -19) is apparently a respiratory illness exacerbated by a family of viruses known to infect the respiratory tract, the lungs and it can spread from animal to individual, individual to individual, during coughing and sneezing or physical contact. Cough, cold, fever and sore throat are its common symptoms. Traditional medicine has gained expanded worldwide attention. Efforts are currently taking place to monitor and maintain traditional herbal medicine. The traditional Indian medicine, Ayurveda, continues to remain the oldest but nevertheless living traditions. Though India has indeed been significant in enhancing its interventions, more comprehensive research and evidence base are still needed. Greater adverse effects, paucity of therapeutic option for several chronic illnesses, rising cost of new drugs, microbial resistance as well as emerging diseases are some reason for increased public interest in complementary and alternative medicine. This review focuses on using herbs to manage coronavirus, raising awareness of the increasing spread of infection, public understanding about how to defend themselves against viral diseases and reducing the overuse allopathic medicines

Keywords - Respiratory virus, COVID – 19 prevention, Alternative therapy, Herbal medicine

I. INTRODUCTION

Corona virus disease 2019 (COVID-19) is delineated as infection caused by a novel corona virus presently known as severe acute coronavirus 2 syndromes. SAR -CoV-2; erstwhile termed 2019 -n(CoV), that was first identified in Wuhan City, Hubei Province, China as an outbreak of respiratory disease.¹ It was revealed initially to the WHO on 31 December 2019. On 30 January 2020, WHO declared the COVID-19 outbreak to be a global health emergency. The WHO claimed COVID-19 a worldwide pandemic on March 11, 2020, its first such designation since H1N1 Influenza was revealed a pandemic in 2009.³SARS-CoV-2 disease was referred to as COVID-19 by the WHO, an acronym derived from 'Coronavirus disease 2019.' The names were chosen to stop denigrating the underpinnings of the virus in contexts of population groups, geography or affiliation with animals.⁴The International Committee on Virus Taxonomy made a public statement on 11 February 2020 confirming legal categorization for the novel virus Severe acute respiratory syndrome corona virus 2 (SARS-CoV-2).⁵ The novel coronavirus disease has no specific treatment. Many of the symptoms are, however, being treated and perhaps treatment depending on the clinical conditions in patients. Supporting care for infected persons can indeed be pretty effective.⁶

In recent decades, herbal preparations have become increasingly important due to safety alternative to synthetic drugs as it is considered unsafe to human health and the environment. Plant drugs are predicted to contribute for as much as 25 % of total drugs in established nations such as the United States, while in fast emerging countries such as China and India, the share is as much as 80%. Being one of the most evolved and commonly practiced sciences in India, Ayurveda are amongst Siddha, Unani and folk (Tribal)

medicines. Unlike many illnesses COVID -19 is an RNA virus infectious disease

II. VIROLOGY OF SARS-COV-2

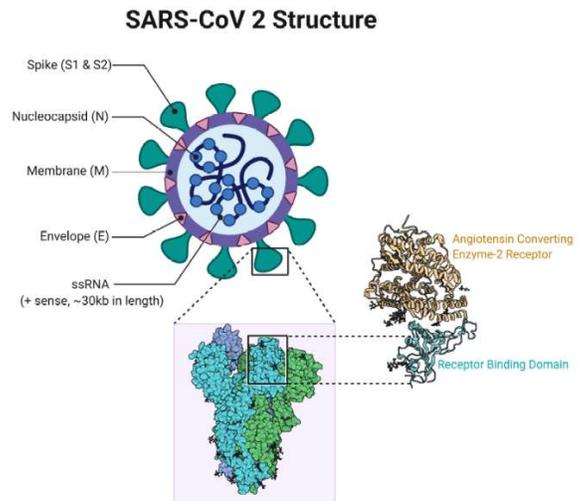


Fig .1 Structure of respiratory syndrome causing human coronavirus

SARS-CoV-2 particles are spherical and have spikes known as proteins as shown in Fig 1. The size is of 26 to 32 kilo bases. Coronavirus for an RNA virus was its largest. Such viruses are pleomorphic enveloped cells, and the positively sensed RNA in the virus is single stranded. The corona virus encodes five protein structures in their genome. They are:

- Spike (S) – It is situated just outside of the virion, and so it gives a classic shape to the virion. S proteins including the HE proteins help the virus to enter the human cell. It binds to the ACE 2 receptor protein. It has the appearance of a crown, which is why naming the Corona Virus
- Membrane (M) – They are glycosylated inside the unit Golgi. The proteins M play a major role in cell virion redevelopment. N proteins form complexes via attaching to genomic RNA and M proteins

activates the development of viruses associated with this matrix in the Endoplasmic Reticulum-Golgi apparatus-intermediate compartment (ERGIC)⁷⁻¹⁴

- Envelope (E) – They enable binding to the virus membrane. It plays a crucial role in cellular assembly and morphogenesis of virions. The viral envelope comprises E proteins.¹⁵⁻¹⁷
- Nucleocapsid (N) – They are phosphoproteins responsible for binding to helix, and have a versatile viral genome RNA structure. It plays a significant role in the virion genome RNA. It plays a vital role in the transcription and replication of Coronavirus in the virion structure¹⁸⁻¹⁹
- Hemagglutinin Esterase (HE) - Hemagglutinin is a peploma that plays a significant role in hemagglutination

Both envelope and N proteins are distributed in all virions but only certain beta corona virus has HE. Furthermore, the virus particles are believed to be clustered together because of the interactions between these proteins.²⁰⁻²³

III. CORONA VIRUS ENTRY AND REPLICATION

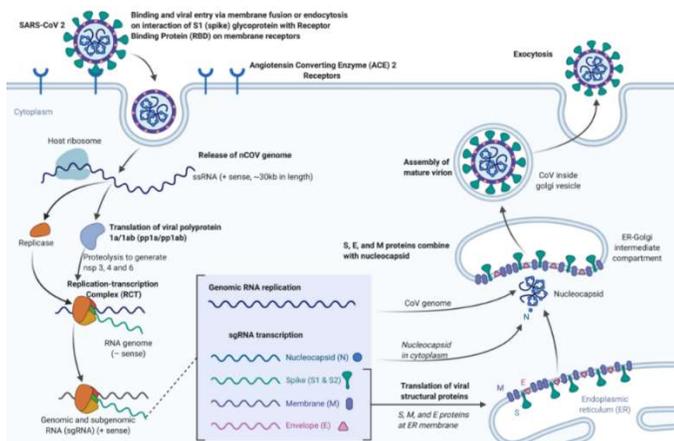


Fig. 2 The life cycle of SARS-COV-2 in host cells

SARS-CoV-2 growth cycle in host cells starts when 8 proteins entangle to the cellular receptor ACE 2. The conformation alterations in the S protein facilitated viral envelope fusion with the cell membrane via the endosomal pathway alongside binding to the receptor. The SARS-CoV - 2 releases RNA back into the host cell. Viral proteinases convert RNA with genome into polyproteins. A cascade of sub genomic m RNAs is formed by polymerase via discrete transcription then later transferred into appropriate viral proteins. Viral proteins as well as the RNA genome are then fully integrated into virions in the E.P, as shown in Fig 2

- When SARS-CoV-2 is penetrated into the alveolus it begins to infect and replicate type 2 alveolar cells
- Infected type 2 alveolar cells produce pre-inflammatory cytokines that then activate the immune response. Individuals may experience mild symptoms, including coughing, nausea and body aches. Macrophages release IL-1, IL-6 and TNF- α . IL-6 triggers vasodilatation and causes to reach more immune cell into the alveolus. It also tends to increase capillary permeability, allowing plasma to leak into alveolus as well as interstitial spaces.
- Neutrophils generate reactive oxygen species as well as proteinases which devastate infected cells.
- Such dead cells come into contact with plasma to form a protein-rich fluid which builds up throughout the alveolus, causing breathing difficulties and pneumonia. Fluid deposition and surface lining dilution contribute to alveolar collapse, which increases gas exchange, leading to hypoxemia as well as acute respiratory distress syndrome.
- If the immune system spirals out of control, inflammation could even be distributed throughout

most of the circulatory system, leading to systemic inflammatory response syndrome also regarded as cytokine storm. This systemic inflammation can cause septic shock wherein the blood pressure drops frighteningly and organs are no longer conditioned, leading to multiorgan damage and death.²⁴⁻²⁵

IV. MODE OF TRANSMISSION

Respiratory infections can be spread by droplets of varying sizes: when the droplet particles are $> 5-10 \mu\text{m}$ in diameter, they are alluded to as respiratory droplets and are then regarded to as droplet nuclei if they are $< 5 \mu\text{m}$ in diameter.²⁶ COVID-19 virus is highly contagious, transmitted among humans through respiratory droplets as well as contact routes as per current evidence.²⁷⁻³² The airborne transmission was not mentioned in an observation of 75,465 COVID-19 case scenarios in China. Droplet transmission occur when an individual is in frequent proximity (within 1 m) with a person of respiratory symptoms (e.g. coughing or sneezing) and is thus at risk of exposure to highly contaminated respiratory droplets via his / her mucosa (mouth and nose) or conjunctive (eyes). Transmission can sometimes appear via fomites around the infected individual in the direct vicinity.³³ Consequently, COVID-19 virus transmission can occur through direct contact with infected persons and indirect contact through surfaces in the immediate surroundings or with items used with the afflicted person (e.g., stethoscope or thermometer). There is also some substantiation that infection with COVID-19 may lead to bowel infection that is present in feces. Only one study has, nevertheless, developed the COVID-19 strain from a single stool sample to date. To date, hardly any findings of fecal–oral COVID-19 virus transmission have indeed been released.

V. SIGNS AND SYMPTOMS

- Most common symptoms: fever, dry cough, tiredness
- Less common symptoms: aches and pains, sore throat, diarrhea conjunctivitis, headache, loss of taste or smell, a rash on skin, or discoloration of fingers or toes
- Serious symptoms: difficulty breathing or shortness of breath, chest pain or pressure, loss of speech or movement.³⁴

VI. DIAGNOSIS

Advanced diagnosis is based via extensive molecular examination of respiratory samples (throat swab / nasopharyngeal swab / sputum / endotracheal aspirates and bronchoalveolar lavage); Virus can indeed be identified in the stool, and blood in severe cases. It is important to remember that perhaps the currently available multiplex PCR panels do not include the COVID-19. Commercial tests are also not available at present. In a suspected case in India, the relevant sample will be sent to the specified reference laboratory in India or to the National Virology Institute in Pune.

Other laboratory study is generally not accurate. The count of White Cells is normally non-specific. There may be lymphopenia; serious illness has been associated with a lymphocyte count < 1000 . The count of platelets is probably regular or slightly weak. The CRP and ESR are significantly augmented by procalcitonin levels. A high level of procalcitonin may indicate a co-infection with the bacteria. Extreme amounts of ALT / AST prothrombin, creatinine, D-dimer, CPK and LDH can always be associated with serious disease. The Chest X - Ray (CXR) generally shows bilateral infiltration but can be common in initial disease. The CT is much more precise and sensitive. CT imaging typically

reveals ground glass distortion infiltrations and sub-segment consolidation. It is also anomalous in asymptomatic patients who have no clinical evidence of lower involvement in the respiratory tract. In fact, irregular CT scans were used to diagnose COVID-19 with negative molecular diagnosis in suspicious cases; most of these cases showed positive molecular tests after frequent trials.³⁵

VII. PREVENTION

To prevent COVID-19 from spreading:

- Clean your hands quite frequently. Use water and soap, or maybe a hand rubbing which contains alcohol
- Keep up a safe distance from someone coughs or sneezes.
- Do not touch the eyes, mouth or nose
- When you sneeze or cough, close your mouth and nose with your bent elbow or a tissue
- If you fall sick, stay at home
- If you've had a fever, cough and breathing difficulties, seek immediate medical attention. Call on ahead of time
- Consider the local health authority guidelines.³⁴

VIII. PATIENTS WITH INCREASED RISK OF COMPLICATIONS

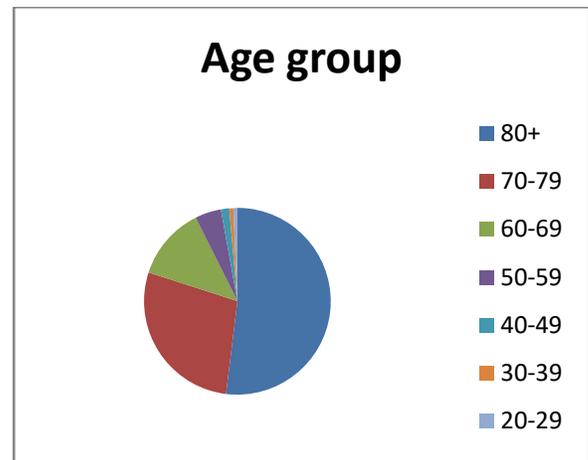


Fig 3 COVID-19 death rate by age group

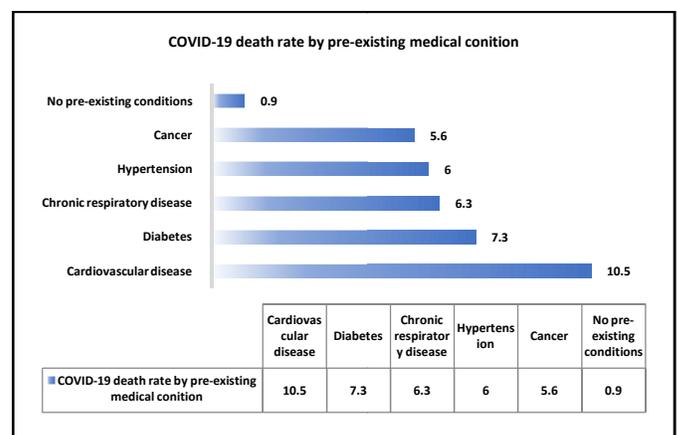


Fig 4 Preexisting medical conditions and COVID-19

IX. AYURVEDIC TREATMENT AGAINST COVID - 19

The medicine system that is deemed to be Indian in origin or medicine systems that have migrated from elsewhere to India and have been successfully integrated into Indian culture is regarded as Indian System of Medicine. In this category, India has the distinctive privilege of having six acknowledged medical systems. They are Ayurveda, Siddha, Unani and Yoga, Homoeopathy and Naturopathy.

Ayurveda supports the belief that when one's immune system is strong, even when the body is exposed viruses, one won't get influenced. While on a pandemic or an outbreak, Ayurveda highlights immunity for people living in Virus-affected areas. The Medicinal system facilitates the ingestion of special herbs or decoctions to increase people's immune system. Ayurvedic remedies include pure, natural herbs which are successful against infectious diseases. Also, the herbs help alleviates COVID -19 symptoms, and to boost the virus immune system against the SARS CoV virus.

A. *Vitex trifolia*

The *Vitex trifolia* is commonly referred to as Indian privert (Tamil- karunochi). It is the large coastal shrub, or small tree that belongs to the Verbenaceae family. It is a deciduous plant distributed in Pacific coastal areas-Asian regions including China, India, Australia and Singapore. Traditionally *Vitex trifolia* is being used for various inflammatory ailments. In Traditional Chinese medicine, dried ripe fruits are identified to treat various ailments such as eye inflammation, headache, blurred vision, rhinitis and common cold. In the traditional system, leaves are also used to treat inflammatory conditions such as rheumatic pain. The stems have been used for dysentery, the roots being used as diaphoretic, antiemetic, and expectorant. Researchers mentioned in the study that the active ingredients Viteosin-A and Vitexicarpin isolated from *Vitex trifolia* leaf, reduced inflammatory cytokines using the NF-KB pathway, a pathway involved in SARS-CoV respiratory distress as shown in Fig 5³⁶.

B. *Sphaeranthus indicus*

Sphaeranthus indicus is commonly referred to as East Indian Globe thistle (Visnu- Karantai in Tamil). It is a heavily branched, strongly fragrant annual herb with winged stem and dented wings belongs to the Asteraceae

family. In Ayurvedic medicine; it is widely used in various conditions such as epilepsy, mental illness, cough, and fever. Because of its potential health, the plant has been studied primarily as an anti-inflammatory property.³⁷ A research demonstrates that an active constituent 7- hydroxyl frullanoid of *Sphaeranthus indicus* showed significant decrease of circulating MCP levels -1, TNF- α and IL- 6 through NF- KB pathway as shown in Fig 5

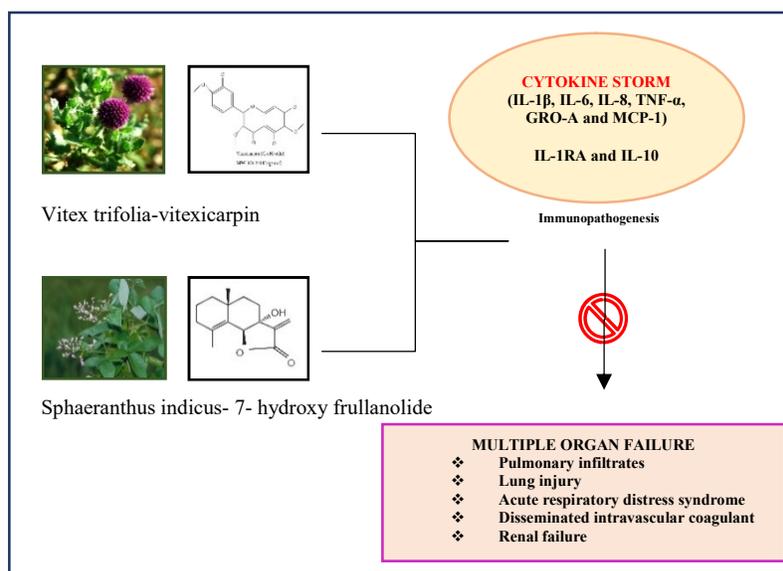


Fig 5 Reduction of cytokine storm

C. *Clitoria ternatea*

Clitoria ternatea is commonly known as butterfly pea (Kannikkodi in Tamil). It is a herbaceous perennial plant with elliptic, obtuse leaves which belong to the Fabaceae family. The plant is located primarily in regions such as India, Sri Lanka, Malaysia and Burma. It is a traditional ayurvedic medicine that has been used as a memory enhancer, anticonvulsant, and its extract have anti-inflammatory, anti-pyretic properties for decades. In addition, the therapeutic uses of this plant are scientifically validated, especially at international level, as well as several biological

functions have been reported, such as antioxidant, antidiabetic and hepatoprotective properties. In COVID-19, metalloproteinase inhibition can indeed be targeted using this plant, ADAM 17, a metalloproteinase implicated in ACE shredding, as ACE shredding is related to increased virus formation as shown in Fig 6.³⁹⁻⁴⁰

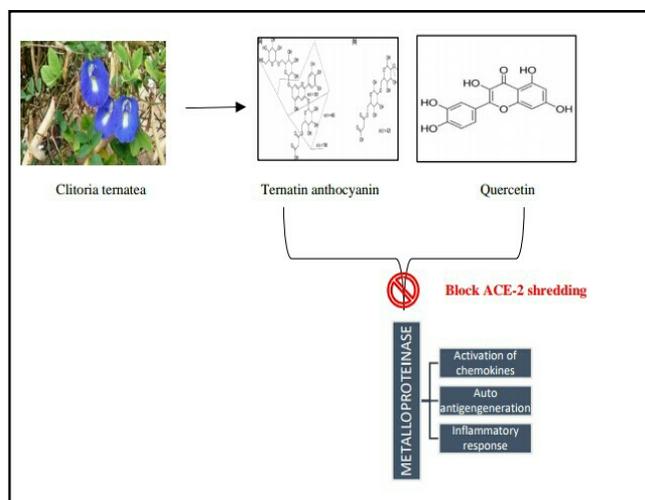


Fig. 6 Inhibition of Metalloproteinase

D. Glycyrrhiza glabra

Glycyrrhiza glabra is frequently referred to as Licorice (Adhimadhuram -Tamil). It is a flowering plant belonging to the Fabaceae family of beans, from which a sweet aromatic flavoring can be extracted. It is used to treat gastritis and anterior respiratory infections with herbal remedies. A study indicates that the phytoconstituents derived from this medicinal plant, Glabrin B, Shinflavanone, Glycyrrhetic acid, Shinpterocarpin, Glabrin, Hispaglabdrin A and Liquiritinapioside have the ability to bind to vital SARS-CoV-2 proteins which are incredibly important for viral replication as shown in Fig 7. The plant may hinder the viral

prevalence by interfering with viral entry and even its multiplication in the infected persons.⁴¹

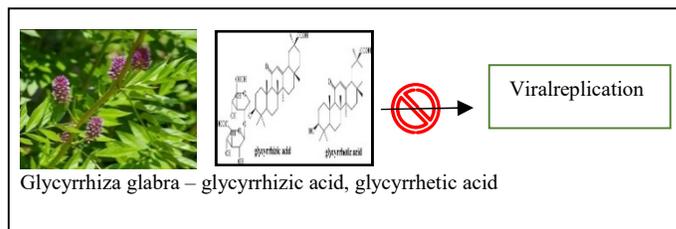


Fig. 7 Inhibition of viral replication

E. Allium sativum

Herbaceous bulbous plant of Amarylidaceae family. Historically, garlic is often used to treat illness, and some of its therapeutic properties have been confirmed such as hypoglycemic, anticancer and antimicrobial activity. It is a versatile food widely appreciated for its anti-inflammatory properties and immunomodulatory effect.⁴²This might be satisfactory preventive measure towards COVID-19 infectious disease to strengthen components of the immune system and suppress the production and secretion of proinflammatory cytokines and also adipose tissue obtained from hormone leptin having proinflammatory nature. Thus the, allitridin as well as allicin extracted from garlic can be beneficial as a therapeutic agent battling against COVID 19 as shown in Fig 8.⁴³⁻⁴⁶

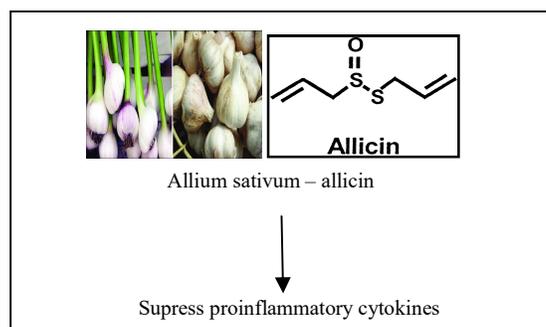


Fig. 8 Supression of inflammatory response

F. *Clerodendrum inerme*

Clerodendrum inerme is typically referred to as Vanjai (in Tamil Cankankuppi). It is straggling branched shrub that belongs to the Verbenaceae family. It occurs mainly in coastal India's mangrove forest, and is distributed globally in Australia. It has immense activities such as that of the antioxidant, antimicrobial, febrifugal, and uterine stimulant. Its own roots and leaves are being used to treat rheumatism and skin infection. The two-systemic antiviral resistance inducing CIP-29 and CIP-34 proteins obtained from plant leaf provide ribosome inactivating tendencies and block the SARS-CoV-2 translation of proteins as shown in Fig 9.⁴⁷

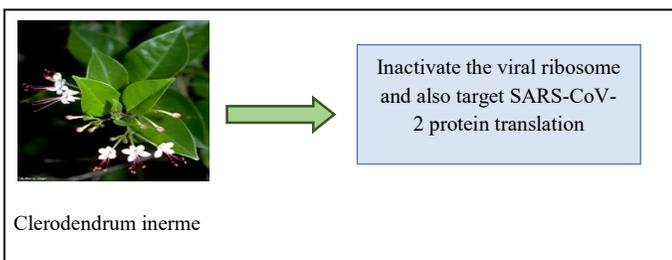


Fig. 9 Inactivation of viral ribosome

G. *Strobilanthes cusia*

Strobilanthes cusia popularly known as Assam indigo or Ryukyu Ai is an evergreen shrub from Japan, Taiwan, China as well as the Indochina Peninsula. The plant is harvested from the wild for local use as medicinal products and colorants.⁴⁸ The leaves and roots are anti-inflammatory, depurative and febrifugal. A concoction can be used when treating rashes induced by epidemic mumps, sore throat, erysipelas and fever. The leaves were indeed lithotrophic, diuretic and astringent. Additionally, *Strobilanthes cusia* stopped the transcription of the viral RNA genome and reported to induce papain like targeting protease activity. A study identified tryptanthrin as the key active ingredient in

Strobilanthes Cusia leaf that behaved independently against HCoV-NL63 in a cell-type way. The findings state that tryptanthrin has antiviral ability against the infection with HCoV-NL63 as shown in Fig 10.⁴⁹

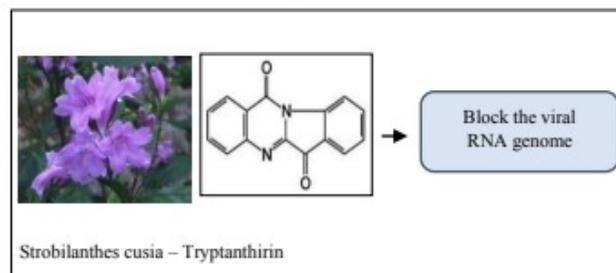


Fig. 10 Blocking of viral RNA genome

H. *Withania somnifera*

Withania somnifera, Ashwagandha is indeed a tonic herb that belongs to the Solanaceae family; it is suggested to promote strength and stamina, enhance immune function and help the body combat imbalances caused by mental or physical stress, poor nutrition, sleep deprivation or environmental toxins.⁵⁰ Its active compounds include anaferine, ambhygrine, beta-sisterol, chlorgeric acid, cysteine, cuscohygrine, pseudotropine, scopoletin, somniferidine, coidhaferine α , withanine, withananine and withanolides. Studies examined, Ashwagandha along with some other ayurvedic plants found that it would have no harmful effects as well as activated the immune system. The researchers targeted the main SARS - CoV-2's protein splitting enzyme, known as the main protease or Mpro, which plays a significant role in viral replication mediation. It is an ideal drug target for this virus and since humans actually don't have this enzyme, drugs that target Mpro are likely to have low toxicity. They found that withanone, a natural compound derived from Ashwagandha, can interact and block Mpro's activity as shown in Fig 11.⁵¹

I. *Andrographis paniculata*

Andrographis paniculata (Kalmegh in Hindi) is an herbaceous plant in the Acanthaceae family that is originally from India and Sri Lanka. This is often referred to as "Indian Echinacea" since it is assumed to have almost the same properties as Echinacea. Andrographolide, the extract's main constituent being involved in its pharmacological operation. Research on the cellular processes and targets modulated by andrographolide treatment of immune cells have been conducted. Andrographolide has been found to increase the symptoms and shorten the cold period in clinical trials. *Andrographis paniculata* also decreased symptoms of the cold such as weakness, sore throat, nasal congestion, headache and swelling of lymph nodes.^{52- 53} *Andrographis paniculata* possesses anti-inflammatory, antipyretic, and anti-viral and immunostimulatory functions and reports have also shown that taking andrography supplements helps alleviate symptoms, resulting in faster recovery and avoids complications of HcoV by acting against Mpro's as shown in Fig 11.⁵⁴

J. *Justica adhatoda*

Justica adhatoda is an evergreen, upright shrub with few branches to many branches. *Justica adhatoda* of family Acanthaceae is a shrub used by medical practitioners from Asia and Europe. The plant was included in the traditional Indian medicinal system. This plant's leaves, roots, seeds, and bark were used in cough, colds, asthma; liquefy phlegm, bronchodilator, bronchitis, and tuberculosis. The parts of this plant are frequently used in decoction or powder form. Indian Pharmacopoeia (955) mentions Vasaka syrup and Vasaka liquid extract.⁵⁵ A vasicin derivative, bromhexine (N - cyclo - N -methyl - (2- amino - 3, 5 - dibrom - benzyl) amine hydrochloride) was shown to have liquefying mucus /

expectorant operation and act as Mpro inhibitor as shown in Fig 11. Anisotine- replicase inhibition activity of these compounds was within the range of Nano molar.⁵⁶

K. *Ecklonia cava*

Ecklonia cava is edible marine brown algae of family genus Lessoniaceae distributed in the Japanese and Korean oceans. It's being used as herbal supplement in the form of an extract called seanol, a polyphenolic extract and ventol, a rich natural agent called phlerotonin. Fucodiphlorethol G 7- Phloroeckol, 6, 6 - bieckol, eckol, 8, 8'-bieckol, 8, 4-dieckol may be isolated from *Ecklonia cava*. *Ecklonia cava* is known for its antioxidant, anti-inflammatory, antidiabetic and anti-cancer properties, it acts against Mpro, as shown in Fig 11.⁵⁷

L. *Theonella swinhoei*

The Palauan sponge *Theonella swinhoei*, member of family Theonellidae, which contains theopalauamide, an antifungal, bicyclic glycoprotein.⁵⁸ These pseudotheonamides were obtained from sea sponge *Theonella swinhoei*, and showed strong serine protease inhibitor effects as shown in Fig 11.

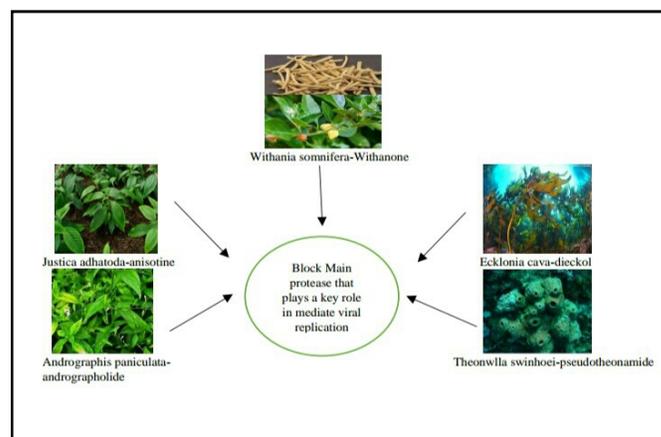


Fig . 11 Blocking of main protease

X. CONCLUSION

As many viruses survive without a preventive vaccine and successful antiviral therapies, it becomes difficult to eliminate such infectious infections. Fortunately, natural products serve as a significant reservoir of biodiversity for inventing new antivirals, identifying new structure-activity relationship, and developing successful defensive / therapeutic strategies against viral infections. Numerous natural and herbal products lead as a novel antagonist of SARS-CoV-2. Additional research should also explore the possibility of combination therapies with other natural sources or with conventional treatments, because multi-target therapy can help reduce the risk of drug-resistant viruses being produced. We conclude that natural products continue to play a significant importance and contribute to the production of antiviral medicines

LIST OF ABBREVIATIONS:

ACE – Angiotensin Converting Enzyme

ADAM 17 – ADAM metallopeptidase domain 17

ALT – Alanine Transaminase

CDK – Cyclin Dependent Kinase

CIP – CDK Interacting Protein

COVID 19 – Corona Virus Disease 2019

CRP – C Reactive Protein

CT – Computed Tomography

ESR – Erythrocyte Sedimentation Rate

GRO A – Growth Regulated Oncogene Alpha

H COV NI 63 – Human Corona Virus NL 63

IL – Interleukins

LDH – Lactate Dehydrogenase

MCP 1 – Monocyte Chemoattractant Protein 1

NF – KB – Nuclear Factor Kappa Light Chain Enhancer of Activated B Cells

PCR – Polymerase Chain Reaction

SARS COV 2 - Severe Acute Respiratory Syndrome Coronavirus 2

TNF – Tumor Necrosis Factor

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