ISSN: 2322 - 0902 (P)
ISSN: 2322 - 0910 (O)

International Journal of Ayurveda and Pharma Research

Review Article

RETHINKING ON USING OF TRADITIONAL INDIGENOUS MEDICINAL PLANTS FOR THE MANAGEMENT OF COVID-19 IN INDIA- A REVIEW

Halavath Ramesh*, M.F.Valan

*[1]Research Scholar, Department of Chemistry, Loyola College (Autonomous), University of Madras, Chennai, India.

Article info

Article History:
Received: 28-06-2021
Revised : 09-07-2021
Accepted: 09-08-2021
Published: 25-08-2021

KEYWORDS:
COVID-19, Ayurveda, SAR-CoV-2, Anti viral, Medicinal plants, Traditional medicine.

ABSTRACT

Novel corona virus first began in Wuhan, china, in December 2019, and it rapidly expanded globally. Corona virus disease 2019 (COVID-19) is a new infectious disease caused by severe acute respiratory syndrome corona virus 2 (SARS-CoV-2) that belongs to the corona virus family. With no specific and effective antiviral therapy for CoVID-19, new or repurposed antiviral are urgently needed. For traditional medicinal treasure India is well recognized all over the world. There are more than 3000 authorized plants in India that hold prodigious medicinal potential. The traditional systems of medicines viz. Ayurveda, Siddha, Unani, western herbal medicine, traditional Chinese medicine and homeopathy have roots in medicinal herbs. In view of the significant morbidity and mortality associated with this pandemic, many research activities are ongoing globally to explore possible therapeutic regiments or prophylactic agents. Ayurveda the traditional system of Indian medicine can offer prophylactic or therapeutic solutions for COVID-19. Traditional Indian Medicines has lot to offer in the management of COVID-19. Many research documents suggested that ethno pharmacological information on the medicinal plant species used by herbalists against corona virus disease. Herbal medicine are achieving attention because of the extensive therapeutics like potent antiviral, immunomodulatory, anti-inflammatory, and anti-oxidant properties and certain natural compounds might be effective for the treatment of COVID-19 based on general concepts from previous experiments. These articles discusses some herbal agents extracted from various plants, including *Cinchona*, *Curcuma longa*, *Nigella sativa, Azadirachta indica, Tinospora Cordifolia, Allium sativum, Oxylum indicum, Punicagranatum, Cocos nucifera* and some more plants, Herbal medicine, phytochemical which are considered for the treatment of COVID-19. This review will open an area for the development of novel natural herbal formulations as an alternative therapy that can be used for the preparation of immunopotentiator, development of herbal/Ayurvedic antiviral drugs, designing anti-microbial / anti viral materials and prevention and treatment of COVID-19.

INTRODUCTION

A novel corona virus induced pneumonia which was later called corona virus disease 2019 (CoVID-19) has rapidly increased to an epidemic scale and affected whole human population globally (WHO, 2020a). India is known for its traditional medicinal systems Ayurveda, Siddha and Unani. Ayurveda is the world's oldest medical system that can manage any disease without side effects.

Access this article online	
Quick Response Code	
	https://doi.org/10.47070/ijapr.v9i7.2001

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 formulation and immunity booster may show us the path to come up with a broad spectrum antiviral product, which is the needed of the hour. Medicinal plants are significant source of synthetic and herbal drugs. Medicinal plants have been used for the treatment of diseases since antiquity. The traditional systems of medicines viz. Ayurveda, Siddha, Unani, western herbal medicine, traditional Chinese medicine and homeopathy have roots in medicinal herbs. Ayurveda, the ancient healing system flourished in India in the Vedic era. The classical texts of Ayurveda, Charaka Samhita and

Sushruta Samhita were written around 1000 B.C. Ayurveda is considered to be the mother of all systems of healing. It is defined as a science of life and teaches us what is harmful and what is useful for health. Ayurveda has survived as a science since centuries. Traditional medicine is playing a key role in meeting global health care needs. Natural products from medicinal plants may act as suitable weapons to combat various diseases. In India, a majority of people rely upon traditional Indian medicine to treat diseases due to less cost, easier availability and without any side effect. These medicines are made by herbal plants.

The corona virus diseases 2019 (COVID-19) pandemic, caused by severe acute respiratory syndrome corona virus-2 (SARS-CoV-2) is the most important health issue internationally.[18] With no specific and effective antiviral therapy for CoVID-19, new or repurposed antiviral are urgently needed. Globally, researchers are working hard to discover effective antiviral agents, immunity modulators and vaccines, but an effectively remedy is not yet in sight. Pathogenic micro-organisms such as viruses, bacteria, fungi and other parasites can cause serious diseases leading to pandemic such as Covid-19 caused by corona virus.[36]

India possesses almost 8% of the estimated biodiversity of the world with around 126,000 species; there are about 400 families of flowering plants in the world, at least 315 of these can be found in India. Currently, about 45,000 species (nearly 20% of the global species) are found in the Indian subcontinent: 3,500 species of plants are of medicinal value; 500 medicinal plant species are used by the contemporary Ayurvedic industry, 80% of the medicinal plant species are procured from wild areas and 10% of medicinal plants involved in active trade are obtained from cultivation in farms. The western Himalayan region provides about 80% of herbal drugs in Ayurveda, 46% of Unani, and 33% of allopathic systems, 50% of drugs recorded in the British Pharmacopoeia are related to medicinal plants growing in this region.[1]

In the research of phytomedicine, it is common to observe multiple pharmacological properties from a single plant. It is now well understood that a single plant may contain a wide range of phytochemicals, making ethnopharmacology research both full of possibilities yet challenging (Süntar, 2019). Overall, these selected interventions of interest discussed here can be broadly categorised into those with 1) antiviral, 2) anti-inflammatory, 3) immunomodulatory effects.[30-32]

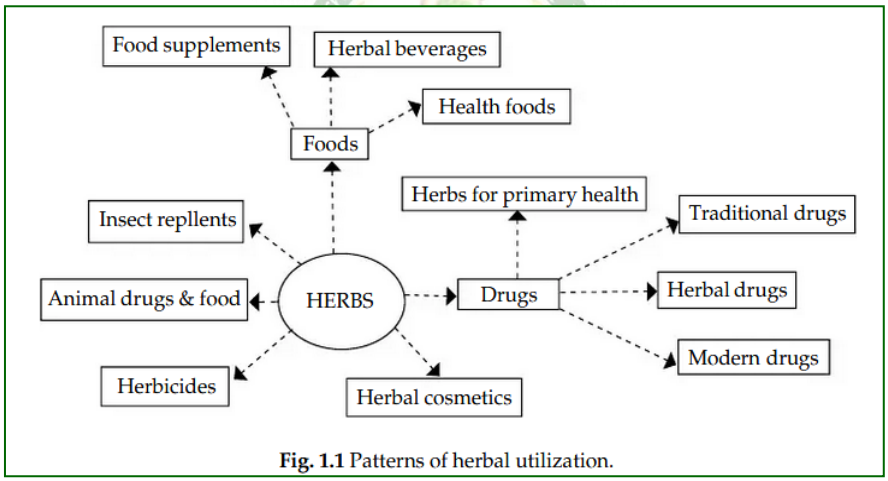

Fig. 1.1 Patterns of herbal utilization.

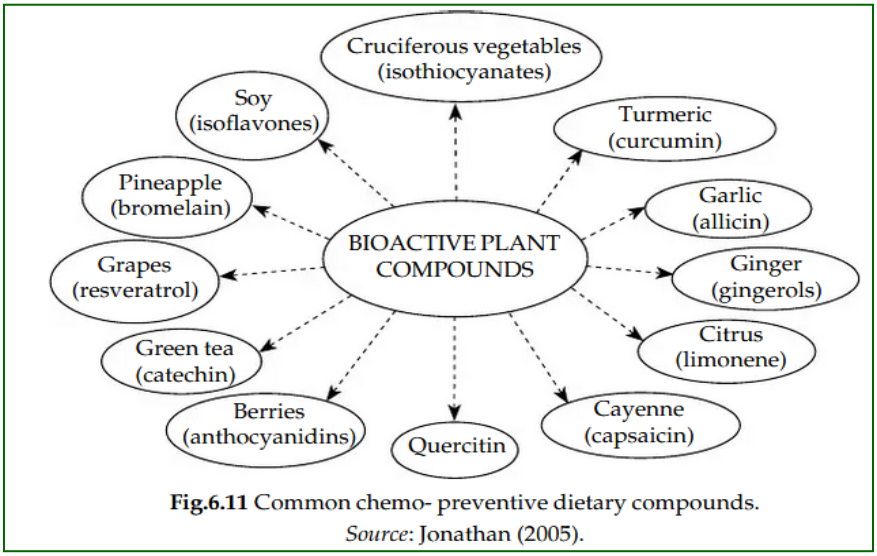

Fig.6.11 Common chemo- preventive dietary compounds.
Source: Jonathan (2005).

In this relevance, medicinal plants can act as potential healing agents that can help people to fight against this infection by boosting their immune system or by posing viricidal effect. And thus, can contribute in reducing mortality rate related to SARS-CoV-2 infections. In the present review, we have discussed briefly about different traditional medicinal plants and their bioactive components, phytochemical structure and herbal medicine that help in strengthening our immune system and also play key role in combating microbial infections including COVID-19.[4]

Potential Indian Medicinal Plants for the Management of COVID-19

Nearly 80% of people are dependent on traditional plants for their primary health (according to a WHO report). Our traditional or the ethano-botanical knowledge could help us find an alternative approach to search for possible antiviral drug molecules.[5] Ayurveda or the traditional Indian system of medicines the has described the use of plants, which have a number of compounds and secondary metabolites that are useful for drug formulations. There is plenty of data supporting the effectiveness of herbs in treating the viral infection.

***Nigella sativa* L. (Black cumin seeds)**

Nigella sativa (Black seeds) from the family ranunculaceae, have been found in several ancient sites. *Nigella sativa* (black cumin seeds) is Miraculous Healing Power plant. Black cumin (*Nigella sativa* L.) is considered as a miracle herb due to its wonderful power of healing. The *Nigella sativa* seeds have been widely used for the treatment of different biological damage and ailments. Seeds exhibit a wide spectrum of biological and pharmacological activities which include antihypertensive, antidiabetic, diuretics, anticancer, immuno-modulatory, analgesic, antioxidant, anti-microbial, anti-inflammatory, spasmolytic, broncho-dilator, hepatoprotective, pulmonary protective, nephroprotective, gastroprotective, antioxytocic, and anticonvulsant properties etc.

Many active compounds have been isolated, identified and reported so far in different varieties of black seeds. The most important active compounds are thymoquinone, thymohydroquinone, dithymoquinone, and thymol etc. *N. sativa* could be used as an adjuvant therapy along with repurposed conventional drugs to manage the patients with COVID-19. Thymoquinone (TQ), the main active ingredient of black seed oil, is an easy, cost-effective natural source of anti-inflammatory, antioxidant, immune stimulant, antibacterial, anticoagulant, and antiviral properties. TQ use may thus be expected to improve COVID-19 comorbidities and to protect against certain antiviral drug-induced side effects and toxicities. TQ appears to be a promising therapeutic option for managing COVID-19 and its complications, and clinical trials in COVID-19 patients to examine the beneficial effects of TQ are thus highly recommended. It has also shown to decrease the replication of SARS-CoV in-vitro in cell cultures.

Azadirachta Indica

Azadirachta indica, commonly known as neem, is a tree in the mahogany family Meliaceae.[8] *Neem* fruit, seeds, leaves, stems, and bark contain diverse phytochemicals, In addition to azadirachtin and related limonoids, the seed oil contains glycerides, diverse polyphenols, nimbolide, triterpenes, and beta-sitosterol. *Neem* leaves has been already known for its antiviral and antibacterial properties around the world. Since Meliacinan hydride and other compounds are derived from *Neem* leaves, ingesting. Neem leaves extract powder or crude *Neem* leaves contain might inhibit the COVID-19 virus by prevent it from replicating.[8] Also neem leaves are known to reduce blood sugar levels and also they act as ACE inhibitors. *Neem* is one of the most popular herbs in the world of Ayurveda. It has an array of medicinal properties that help keeping you away from common infections. The study found a reduced risk of COVID-19 infection in participants receiving *Neem* capsules, which demonstrates its potential as a prophylactic treatment for the prevention of COVID-19 infection. The anti-inflammatory and antiviral effects of neem make it a potential agent for COVID-19 prophylaxis.

Tinospora Cordifolia

Tinospora Cordifolia (common name *Guduchi*) is a miraculous plant that belongs to family menispermaceae. *T.cordifolia* are capable of inhibiting the SARS-CoV-2 main protease with high binding efficiency.[9] *T.cordifolia* has several therapeutic properties. It has been reported for various biological activities including jaundice, reheumatism, urinary, disorder, skin diseases, diabetes, anemia, inflammation, allergic condition, anti-periodic, radioprotective properties, etc. Tinospora herb has heart-shaped leaves and is been used and advocated in Indian medicine for ages. Drinking fresh Giloy juice helps to improve immunity. It enhances the activity of macrophage (the cell responsible for fighting foreign bodies as well as microorganisms) and thus helps in early recovery.[9] *Guduchi Ghanavati* (extract of *Tinospora Cordifolia*), one of the safe Ayurveda herbal medicines, has been recommended and is used widely by the Indian population to improve immunity during the pandemic.

Garlic (*Allium sativum*)

Garlic is a functional food, whose antimicrobial effect was known for a long time.[6,10] Garlic is one of the most efficient natural antibiotics against the wide spectrum of viruses and bacteria. Garlic (A.sativum L.) was reported for abdominal, discomfort, diarrhea and respiratory tract infections and antimicrobial drugs,

anti-oxidant, anti-inflammatory, and anti-stress properties, anti-cancer, cardiovascular disease, anti-diabetic property, immunity booster and antimicrobial effects etc. The most important phytochemical of sulfur constitutes (~82%) of garlic thiosulfinates (allicin), S-allyl cysteine sulfoxide (alliin) etc. Decreasing the rate of viral infection caused by SARS-CoV-2 may be contributed to the presence of organ sulfur (e.g.allicin) and flavonoid (e.g., quercetin) compounds in aqueous extracts and essential oils of garlic. Many research results suggested that natural garlic essential oil is considered as a valuable resource recommended for preventing SARS-CoV-2 invasion into the human body.[6] The compounds in the garlic essential oil inhibit the ACE2 protein, leading the virus to lose the host receptor and attacking the PDB6LU7 protein- the main protease of SARS-CoV-2 at the same time. The synergistic interaction of 17 bioactive substance of the garlic essential oil exhibited good inhibition on the ACE2 protein (host receptor of virus) and the PDB6LU7 protein of virus.[26]

Oroxylum Indicum

Oroxylum indicum belongs to the family Bignoniaceae and is also known as *Arthro-phyllum reticulatum* Blume ex Miq. *Oroxylum indicum* (*O.* indicum) is a medicinal plants widely used as drugs or component of drugs for treatment of various diseases., *Oroxylum indicum* (*O. indicum*) and *Begonia roxburghii* (*B. roxburghii*) are medicinal plants widely used as drugs or component of drugs for treatment of various diseases. The experimental and molecular docking studies have revealed that active constituents of Sonapatha including oroxylin A, baicalein, and chrysin have the potential to act against the COVID-19 infection by blocking the ACE2 receptors and attenuating the activity of enzyme main protease, which aid in the replication of SARS-CoV-2 in humans. Pharmacologically, it has been found to possess anti-microbial, anti-diabetic, anti-hyperlipidemic, hepato-protective, analgesic and anti-inflammatory, anti-carcinogenic, immunomodulatory, nephro-protective, anti-tussive cardioprotective, anti-allergic, anti-bronchitic, anti-rheumatic activities (Ahad et al. 2012). Flavonoids, alkaloids, glycosides, essential oils and phenolic compounds have been reported as an important phytoconstituents (Lawania et al. 2010). Flavonoids such as baicalein, baicalin, chrysin, oroxylin-A, scutellarin, acacetin, hispidulin, isorhamnetin, and Isoquercetin, quercetin-3-o-α-l-arabinopyranoside 1-(2-hydroxyethyl) cyclohexane-1,4-diol, api-genin, 2,5-dihydroxy-6,7-dimethoxy flavones, 3,7,3′,5′-tetramethoxy-4′-hydroxyflavone, pterocarpans, etc., has been isolated previously (Ahad et al. 2012; Deka et al. 2013). Other chemical constituents such as Prunetin, β-Sitosterol, Stigmasterol glucoside, Ellagic acid, Triter-pene Carboxylic acid, Ursolic Acid, Lupeol, p-Coumaric Acid, Napthquinones, Anthraquinone, Phenylethanoid glycosides, and Cyclohexylethanoids are also extracted from this plant.[23]

Justicia adhatoda

The leaves of *Justicia Adhatoda* contain phytochemicals such as alkaloids, tannins, saponins, phenolics and flavonoids. The most important is vasicine, a quinqzoline alkaloid.[44] Bromhexine,a serine protease inhibitor with mucolytic properties available over the counter in Europe, was originally derived from Justicia adhatoda. The leaves of *Justicia adhatoda* commonly known as *Vasaka* (*Vasaka* plant) also contains different alkaloids like vasicolinone, vasicoline, vasicine. These alkaloids are well known for their anti tuberculosis activity. Furthermore, extracts from justice *Adhatoda* leaves have also reported to exhibit antiviral activity against influenza virus and But whether these alkaloids from the leaves of justicia adhatoda exhibit any anti viral activity against SARS-CoV-2 by inhibiting the enzymatic/ proteolytic activity of Mpro is far from clear.

Houttuynia Cordata

Houttuynia cordata Thunb. (Saururaceae) (HC) is a traditional Chinese medicine (TCM) used for hundreds of year to relieve lung-related symptoms such as lung abscess, phlegm, cough and dyspnea and is effective in treating pneumonia, infectious disease, refractory hemoptysis as well as malignant pleural effusion. The major bioactive phytocompounds including flavonoid, alkaloid, as well as essential oil, have been reported from various parts of *H. cordata* which possesses antimicrobial, hepatoprotective, anti-inflammatory, antioxidative, anticancer, anti-diabetic, anti-obesity and antiviral properties. *Houttuynia cordata* was one of the most important ingredients of the herbal formulation used for the treatment of Severe Acute Respiratory Syndrome (SARS) outbreak of Southern China in 2003. Several scientific studies also reveal that the extract of *H. cordata* has the potential to inhibit replication of the various viral strains including SARS coronavirus (SARS-CoV), Chikungunya, Herpes simplex viruses, dengue virus serotype 2 (DEN-2), Influenza neuraminidase, pseudorabies herpes virus (PrV), Human noroviruses (HuNoVs), murine coronavirus and dengue virus infection and also possess innate immune modulation activities. Many clinical trials on effect of Quercetin for Prophylaxis and treatment of COVID-19.[24] *Houttuynia cordata* was used in traditional Chinese medicine, including by Chinese scientists in an attempt to treat SARS and various other disorders.

***Curcuma Longa* L.**

Turmeric is a flowering plant, *Curcuma longa* of the ginger family, Zingiberaceae, the roots of which are used in cooking. Curcumin, as a potential agent, could

be considered to treat COVID-19.[2,3] Curcumin, as an active constituent of rhizomes of *C. longa* (turmeric), is a hydrophobic polyphenol. Curcumin is the major yellow pigment extracted from turmeric, which can be used as chemotherapeutic agent for colon, skin, oral and intestinal cancers. Curcumin has several pharmacological effects such as antioxidant, anticancer, antibacterial, antiviral, and antidiabetic effects as well as anti-inflammatory activity.[3] Curcumin prevented the replication of SARS-CoV and inhibited 3Cl protease in Vero E6 cells. Also, it significantly has an inhibitory activity against the cytopathogenic effect of SARS-CoV in Vero E6 cells. Curcumin is a nutraceutical that could be a new treatment option to combat the COVID-19 pandemic.[2] Scientific evidence suggests that curcumin could have a potential role to treat COVID-19.

Chinchona Officinalis

Cinchona trees are sources of the Andean mountain forests have medicinal benefits as particular components of the trees contain bioactive compounds that can heal fever. Quinine was discovered as the principal bioactive compound from Cinchona officinalis, a South American antimalarial medicinal plant. Chloroquine and hydroxychloroquine are synthetic analogs of quinine and have beenapproved for treating malaria, HIV, systemiclupus erythematosus, and rheumatoid arthritis.[25] A preliminary clinical study in France recently showed promising resultsof chloroquine and hydroxyl-chloroquine in reducing the SARS-CoV-2 viral load in COVID-19 patients.[27]

***Ocimum sanctum* (*Tulsi*)**

Tulsi is an aromatic shrub in the basil family Lamiaceae that is thought to have originated in north central India and now grows native throughout the eastern world tropics. Within Ayurveda, *Tulsi* is known as "The Incomparable One," "Mother Medicine of Nature" and "The Queen of Herbs," and is revered as an "elixir of life" that is without equal for both its medicinal and spiritual properties.[11] Within India, *Tulsi* has been adopted into spiritual rituals and lifestyle practices that provide a vast array of health benefits that are just beginning to be confirmed by modern science. Ocimum species exhibit high antiviral activity, and thus can be used as potential bio resources against COVID-19.[12] Molecular docking study of the interaction of some compounds derived from Ocimum species with SARS-CoV-2 protease is in progress in order to identify the potential inhibitors of the virus. *Tulsi* has also been shown to counter metabolic stress through normalization of blood glucose, blood pressure and lipid levels, and psychological stress through positive effects on memory and cognitive function and through its anxiolytic and anti-depressant properties. *Tulsi's* broad-spectrum antimicrobial activity, which includes activity against a range of human and animal pathogens, suggests it can be used as a hand sanitizer, mouthwash and water purifier as well as in animal rearing, wound healing, the preservation of food stuffs and herbal raw materials and traveler's health. *Tulsi* have many phytochemicals out of three compounds namely vicenin, Isorientin Ursolic acid. O. Tenuiflorum (Sanctum) Major constituents of EO (%) β-Bisabolen (20.99), 1, 8-cineole (20.78), eugenol (15.70), γ-elemene (10.47). Camphor (31.52), eucalyptol (18.85), eugenol (13.77), ocimene (7.12). [54] Eugenol (22.0), β-elemene (19.2), β-caryophylene (19.1), germacrene D (5.03). [55] Eugenol (58.20), germacrene D (11.68), cis-β-ocimene (10.79), β-caryophyllene.

***Phyllanthus emblica* (*Amla*)**

Phyllanthus emblica, also known as *Embli*. Family: Phyllanthaceae. All parts of the plant are used in various Ayurvedic medicine herbal preparations, including the fruit, seed, leaves, root, bark and flowers. These fruits are reputed to contain high amounts of ascorbic acid (vitamin C), and have a bitter taste that may derive from a high density of ellagitannins, such as emblicanin A (37%), emblicanin B (33%), punigluconin (12%), and pedunculagin. Amla is one of the most important botanical materials in Indian traditional medicine, "Ayurveda." It has been used for many diseases including diabetes, osteoporosis, liver dysfunction, and anemia, not only in India but also in other countries. Many studies demonstrated that *Amla* enhanced mitochondrial spare respiratory capacity through activation of mitochondrial biogenesis and antioxidant systems.[17]

Withania somnifera (Aswagandha)

Withania somnifera, known commonly as Ashwagandha. The main phytochemical constituents are with anolides – which are triterpene lactones – withaferin A, alkaloids, steroidal lactones, tropine, and cuscohygrine. The plant, particularly its root powder, has been used for centuries in traditional Indian medicine. Therefore, WFA demonstrates real potential as a therapeutic agent to treat or prevent the spread of COVID-19 due to the reported interference in viral S-protein to host receptor binding and its lack of effect on ACE2 expression in the lungs. Molecular docking studies have shown that *Ashwagandha* (*Withania somnifera*) can prevent the novel corona virus from binding to ACE2 and hence preventing viral entry into host cells along with reducing the expression of TMPRSS2 in certain cells.

***Geranium robertianum* (Geranii Herb)**

Geranium robertianum, commonly known as herb-Robert. Family: Geraniaceae. The active ingredients are tannins, a bitter compound called geraniin,[22] and essential oils. One of the report suggested Geranii Herba ethanol extract (GHE) and its

component geraniin showed high antiviral activity against influenza A strain as well as influenza B strain. Although several studies have reported on the antiviral activities of geraniin (GN), the main component of Geranii Herba, against herpes simplex virus (HSV), human immunodeficiency virus-1 (HIV-1), dengue virus type 2 (DENV2). But one of study reported, the compounds present in Geranii Herba could be used as possible drug candidates for the prevention/treatment of SARS-CoV-2 infection. The molecular dynamic simulation studies also proved Geranii Herba's inhibition efficiency on the SARS-CoV-2 RBD. Overall, the polyphenolic compounds that exist in Geranii Herba (Geraniaceae) couldbe suitable drugs for SARS-CoV-2 infection and also for other viral infections.

*Artemisia annua (*Sweet Wormwood Plant)

Artemisia annua belongs to the plant family of Asteraceae. It has medication used to treat malaria. A. annua contains diverse phytochemicals, including polyphenols such as coumarins, flavones, flavonols, and phenolic acids which have unknown biological properties in vivo. Derivatives from the herb *Artemisia annua* have been used as traditional medicine over centuries for the treatment of fevers, malaria, and respiratory tract infections. A. annua derivatives, artesunate, is a promising novel drug to treat pulmonary fibrosis by inhibiting pro-fibrotic molecules associated with pulmonary fibrosis (Wang, Xuan, Yao, Huang, & Jin, 2015). The rationale for testing antioxidants and antifibrotic effect in *A.annua* is appealing that might play a key role in lung fibrosis. Some of the experimental studies suggested that A. annua may contribute to the identification of anti-coronavirus compounds that may successful and safe antiviral in the treatment of COVID-19. Specifically, the mode of action of *A. annua* on Spike protein of the SARS-CoV-2 is not clearly understood. Nevertheless, it has been reported to be by inhibiting the enzymatic activity of chymotrypsin-like protease (3CLpro) (Law et al. 2020). *A. annua* stimulates adaptive immunity by generating CD8 and CD4 lymphocytes responsible for the production of antibodies targeting SARS-CoV-2 and down-regulating the production of pro-inflammatory cytokines prostaglandin E2 (PGE2), TNF-α, interleukin-6 (IL-6), interleukin-10 (IL-10), thus increasing CD4 count and CD4/CD8 ratio. Notably, the outbreak of COVID-19 pandemic, its global human-to-human transmission curve, and the resultant mortality rate have beamed attention on the viability, safety, and efficacy of *Artemisia* and its derivatives as a potential therapeutic drug for the treatment of SARS-COV-2.

Trigonella foenum-graecum (Fenu greek)

Fenugreek (*Trigonella foenum*-graecum) is an annual plant in the family Fabaceae. Fenugreek is used as a herb (dried or fresh leaves), spice (seeds), and vegetable (fresh leaves, sprouts, and microgreens). Sotolon is the chemical responsible for the distinctive maple syrup smell of fenugreek. Lowering blood sugar levels, boosting testosterone, increasing milk production in breast feeding mothers, immunity boosters, manages diabetes, enhances cardiac functioning, treats gastro-intestinal anomalies. Constituents of fenugreek seeds include flavonoids, alkaloids, coumarins, vitamins, and saponins, the most prevalent alkaloid is trigonelline and coumarins include cinnamic acid and scopoletin. Fenugreek is rich in fiber, protein, and due to its valuable bioactive components has promising therapeutic and application. Anti-diabetic, antioxidant, anti-carcinogenic, hypoglycemic activity, hypocholesterolemic activity are the major medicinal properties of the fenugreek demonstrated in various studies. In a cyclophosphamide induced animal model of immuno suppression, fenugreek could prevent lymphopenia and neutropenia, and improve the cellularity of bone marrow, spleen, and thymus, proposing an immuno stimulatory effect for this plant. One of the computational studies suggested that phytochemicals from *T. foenum*-graecum showed more 3CLpro inhibitory potential compared to those from N. sativa and A. muricata. Trigoneoside IB, derived from *Trigonella foaenum*-graecum (Fenu greek) showed the highest binding affinity and stable interaction with the amino acid residues present in active sites of covid-19 proteins.

Flax seed (*Linum usitatissimum* L.)

Good for digestive system. Reduces risk of cancer, Improves blood sugar levels, flax seeds have a high amount of omega 3 fatty acids, fiber and plant compounds. A number studies on preclinical and clinical researches revealed the valuable cardiovascular effects of dietary supplementation with flax seed. The cardiovascular effects included an antihypertensive action, anti-atherogenic effects, a lowering of cholesterol an anti-inflammatory action, and an inhibition of arrhythmias (Parikh et al., 2018). Some proven research revealed that flax seeds are used to treat chronic cough and asthma. The Omega-3 fatty acid present in flaxseed may beneficial for avoiding and treating hardening of the arteries (atherosclerosis). Thus it may help to fight against COVID-19 as a immune booster.

Syzygium aromaticum (Clove)

Cloves are the aromatic flower buds of a tree in the family Myrtaceae. A major component of clove taste is imparted by the chemical eugenol. Clove (*Syzygium aromaticum* L.) is a well-known culinary spice that has been used for centuries in folk medicine in many disorders. Interestingly, traditional medicines have used clove since ancient times to treat respiratory ailments, whilst clove ingredients show antiviral and anti-inflammatory properties. Other interesting

features are the clove anti-thrombotic, immuno-stimulatory, and antibacterial effects. One of review paper expressed that the potential role of clove in the frame of anti-COVID-19 therapy, focusing on the antiviral, anti-inflammatory, and antithrombotic effects of clove and its molecular constituents described in the scientific literature.

Carica papaya

The *Papaya* is the plant *Carica papaya*, family: Caricaceae. *Papaya* skin, pulp, and seeds contain a variety of phytochemicals, including carotenoids and polyphenols, as well as benzyl isothiocyanates and benzyl glucosinates, with skin and pulp levels that increase during ripening. *Papaya* seeds also contain the cyanogenic substance prunasin. *Carica papaya* is traditionally used as herbal to treat dengue fever. Scientifically, *Carica papaya* has been studied as a serine protease inhibitor. *Carica papaya* leaves have the potential to be the SARS-Coronavirus-2 antiviral agent from herbal. This is due to the 20 compounds presenting in its leaves which have drug-like likeness structure, non-carcinogenic, non-toxic, pharmaco kinetically and pharmaco dynamically stable as predicted by *in silico* experiments.

Panax quinquefolius (Ginseng)

Ginseng is the root of plants in the genus *Panax*. *Panax ginseng* (ginseng) as traditional Chinese medicine is widely used in the treatment and health care for respiratory diseases. The use for the herbal medicines is a secular practice, and we found a most popular, but is present study is about the ginseng radix. Ginseng is an herbal medicine derived from the root of the panax, and your use is described since the first millennium, your properties are preventing many diseases, including cancer, hypertension, and others, described in the literature. The Ginseng radix is an herbal medicine be used in the treatment for the children and adults, the problems for the tract respiratory, and exists a guideline specific for the herbal medicines and the use in clinical practice.

***Scutellaria baicalensis* (Baikal skullcap)**

Scutellaria baicalensis, with the common name Baikal skullcap. Family: Lamiaceae. Several chemical compounds have been isolated from the root; baicalein, baicalin, wogonin, norwogonin, oroxylin A and β-sitosterol are the major ones. Its use in TCM is for "for the prophylaxis and treatment of hepatitis, atherosclerosis, hypertension, hyperlipidemia, type 2 diabetes, dysentery, ulcerative colitis, and respiratory disorders. Baicalein is the main active compound of *Scutellaria baicalensis* Georgi, a medicinal herb with multiple pharmacological activities, including the broad anti-virus effects. baicalein inhibited cell damage induced by SARS-CoV-2. baicalein improved the respiratory function, inhibited inflammatory cell infiltration in the lung, and decreased the levels of IL-1β and TNF-α in serum. In conclusion, oral administration of crystal form β of baicalein could reach its effective concentration against SARS-CoV-2. Baicalein is inhibit SARS-CoV-2-induced injury both *in vitro* and *in vivo.* Therefore, baicalein might be a promising therapeutic drug for the treatment of COVID-19. baicalein and the crude extract inhibit viral replication by directly targeting SARS-CoV-2 $3CL^{pro}$ in cells, and anti-SARS-CoV-2 $3CL^{pro}$ activity under complex cell environment. Previous reports analyzed that flavones isolated from Scutellaria baicalensis (baicalein, baicalin, wogonin, norwogonin, and oroxylinA) is studied as possible compounds in the treatment of SARS-CoV-2 and SARS-CoV-2-inducedacute lung injuries and these flavones as possible potent drugs against respiratory damage that occurs during SARS-CoV-2 infections, with astrong recommendation for baicalein.

***Punica granatum* (Pomegranate)**

In India's ancient Ayurveda system of traditional medicine, the pomegranate is frequently described as an ingredient in remedies. In some Hindu traditions, the pomegranate (Hindi: *Anār*) symbolizes prosperity and fertility, and is associated with both Bhoomidevi (the earth goddess) and Lord Ganesha (the one fond of the many-seeded fruit). Pomegranates have been known for hundreds of years for their multiple health benefits, including antimicrobial activity. The most abundant phytochemicals in pomegranate juice are polyphenols, including the hydrolyzable tannins called ellagitannins formed when ellagic acid and gallic acid bind with a carbohydrate to form pomegranate ellagitannins, also known as punicalagins. The antioxidants in pomegranate juice can help remove free radicals, protect cells from damage, and reduce inflammation. There are various phytochemical compounds in pomegranate that have demonstrated antimicrobial activity, but most of the studies have found that ellagic acid and larger hydrolyzable tannins, such as punicalagin, have the highest activities. Pomegranate peel extract had a higher content of dietary fiber and total polyphenols as well as a stronger antioxidant capacity. Many study observations indicated that PPEs may be successfully employed as antiviral agents against SARS-CoV2. Some research studies are investigate the in silico effects of the most abundant pomegranate peel extract constituents on the multi-step process of serious acute respiratory syndrome coronavirus 2 (SARS-CoV-2) internalization in the host cells. Binding affinities and interactions of ellagic acid, gallic acid, punicalagin and punicalin is studied on four selected protein targets with a significant and confirmed role in the process of the entry of virus into a host cell.[29]

***Cocos nucifera* (coconut tree)**

The coconut tree (*Cocos nucifera*) is a member of the palm tree family (Arecaceae) coconut oil contains lauric acid and monolaurin, which researchers believe the potential mechanisms behind its antiviral activity include "First, they cause disintegration of the virus envelope, second, they can inhibit late maturation stage in the virus replicative cycle, and third, they can prevent the binding of viral proteins to the host cell membrane. Coconut oil has also been studied in several clinical trials for its anti-HIV properties.[28] Patients on the coconut oil treatment tend to show higher levels of CD4, CD8 and T-lymphocyte counts compared to the control group. Some of the research reports suggested that the potential of coconut oil, lauric acid and its derivatives as effective and safe agents against a virus like COVID-19 and this treatment is affordable and virtually risk free and the potential benefits are enormous.[37-39]

Indian herbal medicine for Covid-19 management

***Kabasura Kudineer* (KSK)**

Kabasura Kudineer is a well known Siddha medicine that consists of a whopping 15 herbal ingredients, each of them having unique characteristic features of its own. But this *Churnam* is extensively aimed for boosting the lungs, improving respiratory mechanism and treating infectious conditions like cough, cold, fever and other respiratory infections.[13] Therefore, some reports suggested that the analysis of 145 phytocompounds from *Kabasura kudineer* against the structure of SARS-CoV-2 3CLpro through structure –based in silico molecular docking and to identify potent anti-COVID-19 natural compounds. *Nilavembu Kudineer* (NVK) exhibits a rich concentration of diterpenoids, lactone, diterpene, glycosides, flavonoids.[14-15] The herbal drug which contains nine ingredients mixed in equal proportion in powdered form, it has scientifically proved effective against different types of fevers, including dengue and chickungunya.[21]

Platycodonis Radix

Platycodonis Radix, the root of *Platycodon grandiflorum* (Jacq.) A. DC., is a well-known edible herbal medicine. It is used for different types of diseases like to diffuse the lung, soothe the throat, asthama, bronchitis, pneumonia, pulmonary, tuberculosis, cough, and inflammatory diseases.

***Chyawanprash* (CP)**

Chyawanprash (CP) is an Ayurvedic health supplement which is made up of a super-concentrated blend of nutrient-rich herbs and minerals. Hence, the idea is that taking this Ayurvedic formulation may help in boosting immunity against infections, including COVID-19 disease. A study on *Chyawanprash* as an immunity booster against Covid-19 has shown 'encouraging results', a Delhi government-run Ayurvedic hospital has claimed.

'Coronil and Swasari', is a medicine to combat and prevent the spread of the deadly coronavirus, which has killed 14,011 people till date. He claimed it to be the first Ayurvedic medicine against Covid-19, the respiratory disease caused by SARS-CoV-2 virus. The Yoga Guru claimed that the medicine, has been prepared by the combined efforts of Patanjali Research Centre and NIMS, has shown 100 percent favourable results during clinical trials on affected patients, at Patanjali Yogpeeth.

Rasayan churna

Rasayan churna is the herbal formulation of in powder of *Amalaki* (Emblica oficinalis), *Guduchi* (Tinospora Cordifolia), and *Gokshura* (Tribuluster–restris) in equal quantity which should be taken with ghee and honey. From literally study from various recourses it is found that *Rasanyan churna* have property anti-depressant, anti-xylotic, immuno-modulatory, anti-diabetes, anti-hypertensive, anti-inflammatory, anti-toxic effects, anti-arthritic, anti-cancer effects, anti-microbial effect, and anti-oxidant which can be useful in preventive aspect of Covid-19 in all phase like normal individual, also can be used in asymptomatic patients and symptomatic patients, clinical study can be performed for the same to evaluate the result.[40]

Phytochemical that can help in fight against COVID-19

Plant life is an excellent source of organic compounds like alkaloids, flavonoids, phenols, chalcones, coumarins, lignans, polyketides, alkanes, alkenes, alkynes, simple aromatics, peptides, terpenes, and steroids. These phytochemicals possess antibacterial, antiviral, anticancer, antioxidant, and antidiabetic activities. The structures of these bioactive compounds could be useful toward the elaboration of anti-COVID-19 formulations. Phytochemicals have been used as antiviral agents against several viruses since they could inhibit several viruses via different mechanisms of direct inhibition either at the viral entry point or the replication stages and via immunomodulation potentials.[35] Recent evidence also suggests that some plants and its components have shown promising antiviral properties against SARS-CoV-2.

CONCLUSION

The SARS-CoV-2 has become an emergency problem due to non-availability of approved vaccines or drugs for its treatment. Many natural medicinal plant herbs that have been reported to work as an immunity booster against other viral infections and to treat the anti-inflammatory activities and it also examined against Covid-19. Afetr China, the Indian subcontinent has a famous heritage of traditional

medicine. Since these botanical plants having low cost, minimum toxicity and almost found everywhere in country, it has potential to enhance immunity to fight against COVID-19. In the prevention of covid-19, the phytoconstituents need to have anti-inflammatory, antioxidants, antiviral activity and effects on cardiovascular targets in lieu of rennin-angiotension system being involved in covid-19, with ACE-2 as the major target. Such herbal formulation medicine used as antiviral activities, without side effects, used for the evidence based protocols.

In the present review, a total of 22 medicinal plants and their biodiversity, phytochemical structure and management of herbal medicine are discussed, that are edible and traditional plants. They have potential antiviral activities on the basis of previous reported studies. Many of them contain phytochemical compounds that act as an anti-corona viral activity. Keeping in view the potential of AYUSH medicines and medicinal plants of India, the herbal drug, manufacturers, and the national and global research organizations should develop necessary strategies for furtherance of preclinical and clinical research on these promising therapeutic leads.

ACKNOWLEDGMENTS

We thank Dr. M.F.Valan Assistant Professor and Scientist (LIFE), Research Supervisor, Department of Chemistry, Loyola College, Chennai. This work is supported by funding support from NFST (National fellowship & Scholarship for higher studies of ST students), RGNFST (201819-NFST-TEL-00990) awarded to Halavath Ramesh.

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Cite this article as:
Halavath Ramesh, M.F.Valan. Rethinking on Using of Traditional Indigenous Medicinal Plants for the Management of CoVID-19 in India- A review. International Journal of Ayurveda and Pharma Research. 2021;9(7):53-63. https://doi.org/10.47070/ijapr.v9i7.2001

Source of support: Nil, Conflict of interest: None Declared

***Address for correspondence**
Halavath Ramesh
Research Scholar,
Department of Chemistry,
Loyola College (Autonomous),
University of Madras, Chennai,
India.
Email:
halavathramesh39@gmail.com