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Review Article

A Comprehensive Review on Potential and Prospects of Traditional Medicinal Plants for Management of Coronavirus Disease (COVID-19)

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ABSTRACT

Coronavirus disease (COVID-19) has emerged as the most devastating global health crisis since 1918, the era of the influenza pandemic. This outbreak was triggered by the coronavirus SARS-CoV-2 that measures less than a millionth of an inch but has sent chills all across the globe. The obnoxious disease first became an epidemic in late December 2019 in Wuhan, China, that aggressively spread to the entire world, causing WHO to announce it as a global pandemic. Several features of the disease were uniformly found worldwide, including the consequential symptoms - difficult breathing or shortness of breath, acute hypoxemic respiratory failure, extreme level of fatigue, chest pain, and /or multi-organ failure leading to death. As of August 2022, the present prevalence of the disease is with a daily positivity rate of 2.71 per cent. An estimated 6 million deaths have been recorded worldwide. With no promising vaccines since its outbreak, and no control over this holocaust even after robust global mass vaccination efforts (vaccine boosters), people turned to indigenous methods, especially medicinal plants, as a lookout for immunization against the disease. According to the latest developments, herbal plants like *Ocimum* and *Azadirachta* have acted as promising plants. This review article highlights how few traditional medicinal plants can help create (on a mass scale) vaccines against the deadly coronavirus. We have identified ten significant plants based on the Indian traditional knowledge system and summarized their role in combating the disease. The study also focuses on the modifications of the active constituent from these plants and the underlying processes which can be coaxed together to find a better, reliable cure for the pandemic.

Keywords: COVID-19, immunomodulation, traditional medicinal plants, respiratory infections, SARS virus, bioactive compounds

INTRODUCTION

Prevailing catastrophic pandemic, COVID-19 clearly reflects that we are in a perilous position and just like the earlier pandemics, the mystery of the spread of the first virus to humans remains obscure. There is a flood of data that establishes Coronaviruses association with cattle and camels, but only a few studies suggest the origin of this new strain to Asian pangolins and bats species (Andersen et al., 2020). The discovery of the first human Coronavirus dates back to the 1960s by June Almeida who saw a round gray dot encircled by spikes that was responsible for the ‘complicated’ common cold. Later, scientists came across a similar group of viruses,

which they baptized after their crown-like appearance (with spikes) (Shereen et al., 2020). Etymologically, the name 'coronavirus' roots in the Latin word corona which refers to crown or wreath. The electron microscope resolved the structure like a dot with huge round projections that created an image of a halo-like the sun's corona (Morens et al., 2020). The advent of these viruses has destroyed humanity and civilisations. The outbreak of SARS in 2002 in Southern China resulted in over 8000 cases, and 774 deaths, spreading across 28 countries (Huang, 2004). Fever, headache, and respiratory issues like coughing and breathlessness were among the symptoms of this illness. Around 25,000 persons were infected with the same respiratory muddles, which led to renal failure in 858 of them. The positive sense -RNA virus of genome size 26 to 32 Kb killed millions of people and disrupted world economics.

The analysts have traced the virus SARS CoV-2 existence to Wuhan, China (2019) which originated in bats (Lotfi et al., 2020). The nagging concern now is that how an animal infecting sickness came into human beings? There are numerous hypotheses associated with it. Transference of death from animals to humans was witnessed at one of Wuhan's open-air 'wet markets' (Zhu et al., 2020). Also, few markets were involved in trading wild and prohibited animals like Cobras, Wild Boar, and raccoon dogs. Since markets are hubs for crowds and chaos, viral swaps between different animals are possible. It also aids in mutational processes bringing alterations that begin infecting and spreading. Another factor to consider is that during the onset of the pandemic bats were not sold in the Wuhan markets (Li et al., 2021). The next in line of suspicion were pangolins or the scaly anteaters. These creatures are sold illegally in a few Chinese markets. Being contagious, it soon spread across the globe, infecting people who had no direct contact with animals (Zhang et al., 2020).

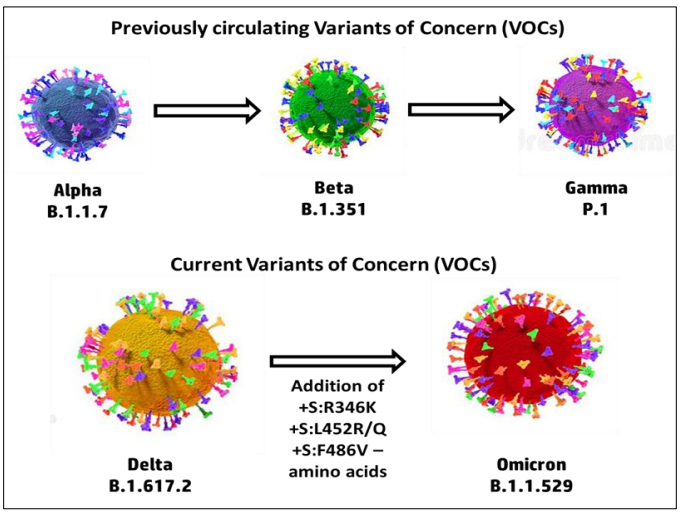

Figure 1: Evolution of coronavirus from Alpha to the present-day Omicron variant. Various factors are believed to be responsible for the evolution of Alpha to Omicron variants. However, the comparative appraisal has indicated that such evolution is associated with: i) Incremental transmissibility or destructive shift in COVID-19 epidemiology; ii) Escalated virulence or development in clinical disease manifestation; and iii) Reduction in the efficacy of public health and social bars or known diagnostics, vaccines, and therapeutics.

Source: Adapted from https://www.dreamstime.com/illustration/coronavirus-variants.html

When infected people talk or cough, they spread the virus unknowingly, releasing tiny drops of water laden with viruses. The escalating transmission worldwide transformed the disease into a pandemic. It causes mild respiratory symptoms resembling cold and flu, or pneumonia in extreme cases. Largely, it attacks the lungs and the respiratory system. This has led to a

great challenge owing to its rapid increase to an epidemic scale in a very short period with high morbidity and mortality rates. The Health Ministry has stated that the recovery percentage is 98.54 percent wherein the patients experiencing mild to moderate respiratory congestion recover without any special treatment. In a few cases, with co-morbidities like cardiovascular disorders, sugar imbalance, asthma, and chronic obstructive pulmonary disease (COPD), they are at risk to develop serious illnesses. The SARS CoV-2 virus has genetic lineages that are referred to by scientists as 'variants' owing to genetic changes in viruses (Guo et al., 2020) which might act differently. Figure 1 illustrates the evolution of coronavirus from Alpha to the present-day Omicron variant with its change occurring slowly to become Beta, Gamma, Delta, and finally Omicron. This evolution depends on various factors but during the comparative assessment, it has associations with the rise in transmissibility or destructive shift in COVID-19 infection, escalation in virulence or diminishing efficacy of public health and social bars or known diagnostics, vaccines, and therapeutics.

Given the plethora of benefits the Indian traditional medicines provide and the dearth of targeted therapeutics, these medicinal plants can be explored as an alternative to find their effectiveness against this disease (Singh et al., 2021). Slowly it is being realised that traditional medicinal herbs and plants grown in India have the prospect of creating a barrier for the mutant strains of coronavirus. Over centuries these have been used as important sources of medicine. Traditional medicines have been recognised as a major source of treatment by WHO which claims that around 80% of the world population counts on medicinal plants for treatment (Khan et al., 2021). Since mythological times, the Himalayan Terrain has produced indigenous medicines for procurement. Many therapeutic companies are looking for traditional methods for the cure. The use of such medicines depends on factors like their availability, knowledge, and social acceptance. Plants produce secondary metabolites like terpenes, alkaloids, phenols, etc. as a response to self-defense. These metabolites can act as ingredients for herbal medicines. For instance, medicinal plants like *Mentha piperita* L. and *Camellia sinensis* help in Adenovirus inhibition (Ahmad et al., 2021). There are innumerable plants that can help achieve this aim, a few of them that have already proved their worth are - *Nigella sativa, Vernonia amygdalina, Azadirachta indica, Eurycoma longifolia,* etc. (Ahmad et al., 2021). Although modern modalities have been very well thought out in the current situation, traditional medicines have also been widely used in the epidemic. Needless to say, quality checks and standardisations of medicinal botanical products also need to be highlighted. However, in the present scenario, ethnopharmacological research must be given an equitable chance among the masses to see what they are capable of.

MEDICINAL PLANTS LISTED BY AYUSH AGAINST CORONA VIRUS

Since the beginning of civility, the use of medicinal plants has been chronicled for treating various ailments. The usage of traditional medicines relies on the availability of herbs as well as their knowledge (Adithya et al., 2021). A thorough understanding of plants' secondary metabolic pathway, ecology, and taxonomy is important for drug development strategies. Medicinal plants not only help in alleviating the symptoms of COVID-19 patients but also provide promising raw materials for potent antiviral drugs (Khan et al., 2021). Plants produce a large number of secondary metabolites as a means of self-defense, induced by stress conditions. These metabolites extracted from plants are important ingredients in herbal medicines. India has a unique medicinal system which is one of the ancient systems of medicinal practice. Many medicinal plants are indigenous to India and are reported as potential antiviral, antiallergic, and immunomodulators (Ahmad et al., 2021). Some of these include; *Azadirachta indica, Ocimum sanctum, Zingiber officinale, Ocimum basilicum, Saccharum officinarum, Piper longum, Andrographis paniculata, Cyperus rotundus, Tinospora cordifolia, Carica papaya, Cinnamomum Verum, Withania somnifera,* and *Berberis aristata.*

Table 1: List of traditional Indian medicinal plants prescribed by AYUSH against coronavirus with their detailed information of Botanical and vernacular names, family, parts used, chemical constituents, their respective therapeutic uses, pharmacological principles, and important formulations

Botanical Name	Vernacular Name	Family	Part used	Chemical constituents	Therapeutic uses	Pharmacological Principle	Important formulations for commercial use	References
Andrographis paniculata (Burm. f.) Wall. ex Nees	Kalamegha, Nilavembu, Kirayat	Acanthaceae	Whole plant	Andrographolide neoandrographolide, deoxy andrographolide	Fever, sore throat, Gastrointestinal infections, Respiratory infections	Antipyretic, antiviral, immunobooster, hepatoprotector	Bunimbadi Churna, Bhunimbadi Kasaya	Mussard et al., 2019; Kesharwani et al., 2022; Okhuarobo et al., 2014
Justicia adhatoda Medick	Vasa, Adhathoda, Adusa	Acanthaceae	Leaf, flower, root	Vasicine, Vascine, beta sitosterol, Vasicinol, Carotene, Vasicolone.	Fever, cough, skin diseases, anaemia, diarrhea	Bronchodilator, haemostatic	Vasarishtam, Vasavalehya.	Kesharwani et al., 2022; Ghosh et al., 2021;
Azadirachta indica A. Juss	Neem, Nimba, Vembu	Meliaceae	Leavesroot bark, stem bark	Azadirachtin, Nimbin, Nimbandiol, Nimbidin, Sitosterol	Diabetes, fever, skin diseases,	Antimicrobial, Antiinflammatory, Antiarthritic, Antidiabetic, improves cardio vascular activity.	Nimba haridrakhanda, Nimbadi churna, Pancha nimba churna	Sarah et al., 2019; Alzohairy et al., 2016; Kesharwani et al., 2022
Clerodendrum serratum (L.) Moon	Bharngi, Kavali, Babhanaiti	Verbinaceae	Root	Hispidulin, scutellarein, uncinatone, pectolinarigenin	Cough, fever, rhinitis	Antihistamine, Antipyretic	Bharngyadi kashaya, Bharngi guda	Wang et al., 2017; Kesharwani et al., 2022
Cinnamomum verum Presl	Tvak, Dalchini, Lavangapatta	Lauraceae	Stem bark	Cinnamaldehyde, eugenol, benzaldehyde, caryophyllene, cinnazeylanin	Cough, indigestion, rhinitis, cardiac ailments, headache	Anticomplement activity, antiallergic activity	Eladi rasayanam, sitopaladi choorna, samasarkara choorna	Kesharwani et al., 2022; Singh et al., 2021

Botanical Name	Vernacular Name	Family	Part used	Chemical constituents	Therapeutic uses	Pharmacological Principle	Important formulations for commercial use	References
Tinospora cordifolia (Wild.) Miers	Giloe, Amrida valli, Guduchi	Menispermaceae	Stem, leaf, aerial root	Tinosporin, Tinosporide, Cordifolide, Phenyl prophyl glycoside	Fever, cough, wheezing, brain tonic	Antipyretic, Antioxidant, Immunomodulator, Antiinflammatory, Antistress	Amrithadi kashayam, amritarishtam, Amritadhi guggulu, Balaguduchyadi tailam	Upadhyay et al., 2010; Kesharwani et al., 2022
Withania somnifera (L.) Dunal	Aswagandha, Winter cherry, Amukara	Solanaceae	Root, leaf	Withaferin A, withanine, withanolide WS-1, withasomniferin A	Fatigue, weakness, insomnia, tumors	Antimicrobial, Antibacterial, Antioxidant, Immunomodulator, Antiinflammatory, Antimalarial, cardio protective, neuro protective, hepato protective, Adaptogenic, Antidiabetic.	Aswagandha churna, Aswagandha arishtam	John, 2014; Mishra et al., 2000; Dutta et al., 2019
Ocimum tenuiflorum L.	Sacred basil, tulasi, tulsi	Lamiaceae	Root, leaf, seed	Bornylacetate, Cadinene, eugenol, eugenol methyl ether, methyl chavicol, limonene	Intermittent fever, viral hepatitis, toxic disorders, cough, worms	Antiviral, Antifungal, Antibacterial Antispasmodic	Surasadigana kashayam, tumburvadi yoga	Bano et al., 2017; Kesharwani et al., 2022; Siva et al., 2016
Zingiber officinale Roscoe	Ginger, Sonth, Adrak	Zingiberacea	Rhizome	citronellol, gingerol, zingiberenes, zingiberol, zingerone, gingerols, gingerenone	Fever, dyspnoea, cough, heart ailments, reduced appetite, diarrhoea	Antibacterial, Antihistaminic, Antioxidant, Antiinflammatory, Hypoglycaemic,Bio availability enhancer	Ardhraka rasayana, ardhraka khandavalehya, nagaradi kashaya	Munda et al., 2018; Mao et al., 2019; Kesharwani et al., 2022

Majority of these plants are an integral part of Indian conventional formulations which are already in use for aeons. As modern medications are limited in developing countries, herbal medicines have very well sustained their popularity (Adithya et al., 2021). Therefore, to combat the effects of COVID-19, novel treatment methods can be evolved by conventional practices of medicinal plants. The Indian traditional technique of medicine, Ayurveda, Yoga and Naturopathy, Unani, Siddha, and Homeopathy (AYUSH) is based on some of the oldest practices that transpired in the common era which present a way of living and establishing concepts of disease prevention and promotion of good health. Various formulations of AYUSH have manifested as antiviral, anti-asthmatic, and immunomodulatory activities. Nonetheless, their accountability in the treatment of COVID-19 still needs to be ascertained. But these approaches have been used by hospitals as per their specialisation (Ahmad et al., 2021). Many experimental studies have revealed that compounds extracted from various parts of medicinal plants (Table 1) like roots, leaves, bark, and fruits help in treating common to rare infections. So, medicinal plants could prove to be of great importance, where modalities lack behind.

MEDICINAL PLANTS WITH ANTIVIRAL/IMMUNOMODULATORY ACTIVITIES

Figure 2: Plants and herbs that can potentially help in fighting COVID-19. a) Turmeric, *Curcuma longa* (perennial herb with branched rhizome); b) Ashwagandha, *Withania somnifera* (Annual herb); c) Holy Basil, *Ocimum sanctum* (perennial herb); d) Ginger, *Zingiber officinale* (perennial herb with aromatic rhizome); e) Embelic, *Phyllanthus emblica* (small deciduous tree); f) Garlic, *Allium sativum* (perennial herb); g) Creat, *Andrographis paniculata* (annual herb); h) Heart leaved moonseed, *Tinospora cordifolia* (climbing shrub); i) Black pepper, *Piper nigrum* (perennial climber); j) Black cumin, *Nigella sativa* (annual herb)

Curcuma longa

Family: Zingiberaceae

English name: Turmeric

Curcuma longa is a spice (more commonly available as Turmeric) that has gained worldwide acceptance for its medicinal properties. It is a major source of polyphenol curcumin. It has several benefits which are attributed to its antioxidant and anti-inflammatory effects (Hewlings & Kalman, 2007). Turmeric is grown extensively in India, particularly on a large scale in Tamil Nadu, Maharashtra, and West Bengal. It is widely used in Ayurveda and Siddha. Curcumin is the natural polyphenolic compound found in *C. longa*. It exhibits properties like antimicrobial, antiviral, and anti-inflammatory (Chopra et al., 2021). Curcumin helps in relieving pain and congestion and in patients with sinusitis, it improves the breathing process (Benzie & Wachtel-Galor, 2011). It acts as an antithrombotic agent and aids in cleaning mucus in the lungs, facilitating an adequate supply of oxygen to the body (Rocha & de Assis, 2020). The antiviral activity is well documented. Studies confirm its inhibitory actions against flock house virus, herpes simplex virus, respiratory syncytial virus, and vesicular stomatitis virus (Moghadamtousi et al., 2014). *Curcuma longa* extract (Alpha-turmerone) also brings about an immunomodulation in human peripheral blood mononuclear cells (PBMC) (Singh et al., 2021) triggering the release of various cytokines. Water and ethanolic crude extract of *C. longa* inhibits replication of viruses as evident by upregulation of TNF-α as well as IFN-β mRNA expression (Ahmad et al., 2021).

***Withania somnifera (*Ashwagandha)**

Family: Solanaceae

English name: Winter Cherry, Indian ginseng

For ages ashwagandha has been known for its antiviral and immunomodulatory properties. Root of *W. somnifera* contain alkaloids withanine, somniferinine, pseudowithanine, and withaferin-A (Khare, 2008). *Withania somnifera*, Ashwagandha was first studied in mice with myelosuppression with three compounds. After the induction, there was a significant increase in all the blood cell counts and hemoglobin concentrations (Ziauddin et al., 1996). Thus, it showed how Ashwagandha could help in hemolytic antibody responses toward human erythrocytes. Withaferin-A compound exerts its potent antiviral actions against SARS CoV- 2 by suppressing RNA polymerase with escalated binding energy than hydroxychloroquine and many other drugs (Ahmad et al., 2021). It is also used in the treatment of the common cold, gynecological disorders, and infertility issues (Logeswari et al., 2020). Withaferin -A increases macrophages nitric oxide synthase activity and restores immune homeostasis (Chopra et al., 2021) It is used as an anti-inflammatory in medicines for the treatment of swelling, tumors as well as a sedative (Adithya et al., 2021). The root extracts of *Withania* in their aqueous form halts the release of anti-inflammatory cytokines (Ahmad et al., 2021). Withanolides in its different form, Withanolide _G, Withanolide_I and Withanolide_M, are a group of bioactive compounds which are potent immune boosters (Khanal et al., 2022).

Ocimum sanctum

Family: Labiatae; Lamiaceae

English name: Sacred Basil

Grown throughout India, *Ocimum sanctum* or Tulsi is known for its curative properties. Intracellular multiplication of the Virus is inhibited by hydroalcoholic extract of *Ocimum sanctum*. Due to its curative properties, it is used in Ayurveda for treating innumerable health ailments like asthma, bronchitis, gastric and hepatic disorders, microbial infections

(Bahramsoltani & Rahimi, 2020). It is widely used in various formulations owing to its stress relieving properties and is proposed to treat health conditions in cancer (Balachandran & Govindarajan, 2005). Various compounds are found in *O. sanctum* like phenolics, terpenoids, phenylpropanoids, fixed oil, and fatty acid derivatives. A research study has found that ethanolic extracts of basil contain flavonoid luteolin-7-O-glucuronide and polyphenolic chlorogenic acid. These may bind covalently to the active site of residue Cys145 of the main protease of SARS-CoV-2. This binding inhibits the enzyme irreversibly when screened in silico (Mohapatra et al., 2020). The extract from *O. Sanctum* (terpenoid and polyphenol) was also found to show antiviral activity against the H9N2 virus (Ghoke et al., 2018).

Zingiber officinale Roscoe

Family: Zingiberaceae

English name: Ginger

Z. officinale shows promising antiviral, antiemetic and antibacterial properties (Singh et al., 2021). Besides this it was found to be effective against HRSV (Human respiratory syncytial virus)-induced infection in two cancer cell lines: A549 and Hep-2 (Chang et al., 2013). 6-gingerol obtained from ginger may act as a promising phytocompound for drug discovery to combat COVID-19 as it shows the maximal binding affinity with manifold targets of SARS-CoV-2 such as viral protease and RNA binding protein (Rathinavel et al., 2020). *Zingiber officinale* gives rise to phytochemical compounds that have a very good potential to reduce the viral load and shedding of SARS-CoV-2 in the nasal passages (Haridas et al., 2021). Ginger also has antioxidant properties and contributes to strengthening the body's defense system. 6-Shogaol, an important compound of ginger, helps in relieving the severity of respiratory issues (Logeswari et al., 2020). Studies reveal that in patients suffering from rhinitis allergy, the oral alcoholic ginger extract helps in the reduction of total nasal symptom scores (TNSS) (Yamprasert et al., 2020). Consumption of soft gel capsules containing *Z. officinale* active compounds boosts anti-inflammatory and immunomodulatory properties (Dall'Acqua et al., 2019). Gingerol, a volatile oil component present in the rhizome of ginger is responsible for most of the bioactivities such as anti-inflammatory and antimicrobial. Another active compound β-sitosterol is a potential candidate against colon cancer (Zhang et al., 2021).

Phyllanthus emblica

Family: Phyllanthaceae

English name: Indian gooseberry, Embelic

Phyllanthus emblica commonly known as Amla in India possess antipyretic, analgesic, antitussive, antiatherogenic, adaptogenic, cardioprotective, gastroprotective, antianemia, antihypercholesterolemia, wound healing, antidiarrheal, antiatherosclerotic, hepatoprotective, nephroprotective and neuroprotective properties. In the future, it may establish itself as an important anticancer drug ingredient as it shows promising in vitro cytotoxicity results in cancerous cell lines such as human leukemia (HL-60) and human hepatocellular carcinoma (SMMC-7721) (Chaikul et al., 2021) Ethanolic extracts of Amla exhibited an increase the level of anti-inflammatory cytokines, and reduce the level of pro-inflammatory cytokines and also acted strongly against the dengue virus with more than 90% reduction in infection (Lee et al., 2013; Chatterjee et al., 2011).

Potent Compounds like geraniin and isocorilagin obtained from *Phyllanthus emblica* are known to show immuno-stimulatory effects (Liu et al., 2012). A compound :1, 2, 4, 6-tetra-O-galloyl-β-d-glucose obtained from *P. emblica* showed antiviral potential against HSV by

inactivating HSV-1 that leads to the inhibition of early infection by suppressing intracellular growth and inhibition of gene expression of HSV-1 E and L along with the replication of DNA (Xiang et al., 2011). Almost all species of the genus *Phyllanthus* contain a rich compound called phyllanthin, known to show antiviral activities (Naithani et al., 2010) while there are many other phenolic compounds having therapeutic potential in treating immune-related diseases including catechin, hypophyllanthin, ellagic acid, geraniin, gallic acid, gallic acid, and chebulagic acid (Jantan et al., 2019).

Allium sativum L.

Family: Liliaceae

English Name: Garlic

Allium sativum commonly known as garlic is cultivated in all parts of India and its beneficial properties are known to humans for ages. Pre-clinical studies on garlic have demonstrated that it has antiviral potential against different human, animal, and plant pathogenic viruses by blocking viral entry into host cells, inhibiting viral RNA polymerase, reverse transcriptase, and immediate early gene transcription. With higher concentrations of sulphur- based compounds such as Ajoene, S-allyl cysteine, vinyldithiin and non-sulphur compounds like flavonoids, saponins, garlic has an incredible taste and pungent smell (Bahramsoltani & Rahimi, 2020). It acts as an immunomodulator by activating natural killer cells and macrophages (Gunathilake & Rupasinghe, 2015). It induces the secretion of cytokines and increases CD8+ and CD4+ cells (Donma & Donma, 2020). Serine-type protease and a bioactive compound found in *Allium* form H-Bonds in the active sites which suppress the outbreak of COVID-19. It may thus act as a preventive measure against COVID infection (Khubber et al., 2020).

Andrographis paniculata

Family: Acanthaceae

English Name: Creat

In India, *Andrographis paniculata* is commonly known as Kalmegh and Kariyat. It is an annual herb that is cultivated throughout India and is used in Ayurvedic medicines. Phytochemical compounds extracted from this plant include diterpenes, flavonoids, xanthones, and andrographolide and the plant extracts containing these compounds have various biological qualities such as antimalarial, antidiabetic, anti-inflammatory, antiprotozoan, and immunomodulatory. It is thus widely used in the treatment of illnesses including colds, coughs, liver disorders, leprosy, bronchitis, dyspepsia, and viral fever (Bahramsoltani & Rahimi, 2020). Andrographolide extracted from *Andrographis leaves and stems* has antiinflammatory properties. It is known to show potential against viruses such as Herpes simplex virus, Epstein-Barr virus, HIV, and Chikungunya virus (Gangal et al., 2020; Rahman, 2020). It has also been reported that *Andrographis* inhibits the enhanced concentrations of caspase-1, NOD-like receptor protein-3, and interleukin-1β molecules, which are intricated in the SARS CoV-1 mechanism (Singh et al., 2021).

Tinospora cordifolia

Family: Menispermaceae

English Name: Heart leaved moonseed

Commonly known as giloy, *Tinospora cordifolia* thrives best at higher peaks in India. It has various properties like antipyretic, anti-inflammatory, anti-allergic, and diuretic (Gangal et al., 2020). Biologically important phytochemicals obtained from *T. cordifolia* include steroids,

lactones, alkaloids, glycosides, polysaccharides, diterpenoids, and flavanoids which have immunomodulatory functions (Yates et al., 2022). It is known to have potential against inflammation and oxidation (Reddi & Tetali, 2019), diabetes (Sharma et al., 2015), and cancer and helps in maintaining immune balance (Bahramsoltani & Rahimi, 2020). Recent studies have shown that natural compounds obtained from *Tinospora* including Tinocordiside, Magnoflorine, Berberine, and Isocolumbin, have great binding affinity to targets of SARS CoV-2 which are responsible for virus attachment and replication. The validity of these natural products is reported to be equivalent to or even better than some important antiviral drugs like Remdesivir and Favipiravir. This makes *Tinospora* a potential herb in the management of COVID-19 (Singh et al., 2021). Its antiviral properties against H1N1 and Chikungunya are well documented (Sagar & Kumar, 2020). *T. cordifolia* possesses immunomodulatory properties owing to the presence of active compounds such as cordifolioside, syringin and magnoflorine (Sharma et al., 2012).

Piper nigrum

Family: Piperaceae

English Name: Black pepper

Amongst all the spices, *Piper nigrum* is known as the "king of spices" which has been widely explored. It has a strong smell due to the presence of its alkaloid constituents (Adithya et al., 2021). The main bioactive compound found in black pepper, Piperine is known for its diverse properties like antiasthmatic, anticarcinogenic, antihypertensive, and antitumor (Takooree et al., 2019). Piperine is also effective against viral particle proliferation by blocking the packaging of RNA inside capsid protein (Yadav et al., 2021). Researchers in a computational study has also found that piperine can inhibit SARS CoV-2. In a recent study, it was shown that the main protease of COVID-19 was inhibited by the phenolic constituents (Methysticin and Kadsurenin L) found in *P. nigrum* (Davella et al., 2022). Ayush Kwath is an important formulation recommended by the Ministry of AYUSH with the interest of health promotion. It contains four herbs, *Piper* being one of them. The extract of *Piper* enhances the efficiency of many drugs, nutrients, and vaccines (Gautam et al., 2020).

Nigella sativa

Family: Ranunculaceae

English Name: Black cumin

Nigella sativa is well known for its immense pharmacological potential and is reported to cure various ailments and disorders such as cough, fever, influenza, bronchitis, asthma, gastrointestinal problems, jaundice, conjunctivitis etc. (Forouzanfar et al., 2014). Phytoconstituents obtained from this herb include terpenes (thymoquinone, dithymoquinone, limonine, p-cymene), indazole alkaloids (nigellicine, nigellidine), isoquinoles have great therapeutic implications) (Akram & Afzal, 2016; Kazmi et al., 2019). In a study it was found that the seeds of N. sativa can act as a natural alternative to Chloroquine (Rahman, 2020) as its active component nigellimine has structural similarities with hydroxy-choloquinone and chloroquine and the main phytoconstituent responsible for its therapeutic properties is thymoquinone (Bahramsoltani & Rahimi, 2020). Considering its antiviral implication, black cumin seeds and oil have shown properties against some of the deadly viruses like HIV and Hepatitis C virus (Khazdair et al., 2021). In another study, it was shown that Zinc stops the recombinant SARS –CoV RdRp activity and as Nigellimine shares structural similarities with chloroquine, black seeds in combination with Zinc could be a great alternative for COVID-19 treatment (Rahman, 2020).

CONCLUSION

SARS-CoV-2 and its variant forms are keeping the entire world in the grip of fear and despair. It has challenged the healthcare systems and economies of many countries. Even though India and other countries have developed vaccines and other boosters in patches, it has not brought a halt for the havoc that this virus has made. The usage of herbal medicine is a potential platform for combating the deadly effects of COVID-19 virus. The bioactive fractions in the selected medicinal plants in this review provide an effective supportive measure against inflammation and the complications such as fever, cough, and respiratory pathologies associated with COVID 19. India is a hub of traditional medicinal plants and they should be extensively studied and used therapeutically in COVID-19 pathogenesis. The extract of plants like *Azadirachta indica*, *Nigella sativa*, and *Eurycoma longifolia*, *Allium sativum*, and *Althea officinalis* are potential agents for antiviral remedies and provide a broad range of immune-boosting properties to fight highly infectious diseases like COVID-19. Although a complete cure for COVID-19 has not been reported by the use of Ayurvedic medicines, they can definitely minimise the chances of viral infection by boosting the immune system thereby reducing the mortality rate. The Ministry of AYUSH, Govt. of India recommends the usage of products and formulation of medicinal plants from time to time, keeping in view the evidence of traditional systems of medicines. It also provides advisories for encouraging research based on plants. Herbal plants are low-cost, need low maintenance, and have widespread availability in our country with negligible adverse effects. Alternative medicines could be a great asset as complementary therapy to fight various diseases. Knowing their importance, individually or combined collectively with allopathic therapeutics would help to alleviate COVID symptoms.

CONFLICT OF INTEREST

The authors declare that they have no competing interests.

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