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REVIEW ARTICLE **OPEN ACCESS**

Traditional Herbal Plants for Coronavirus Disease 2019 Management: A Narrative Literature Review

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ABSTRACT
Coronavirus-19 (COVID-19) is a new infectious disease that has been declared a worldwide pandemic by the World Health Organization (WHO). The first case was discovered in China in December 2019, and the infection quickly spread to the rest of the world in short span of time. COVID-19 is caused by acute respiratory syndrome coronavirus 2 (SARS-COV-2), is a member of beta-coronaviruses family. The vast majority of people infected with COVID-19 may experience mild to moderate symptoms such as cough, dyspnea, fever, and viral pneumonia, and recovered without special therapy, however some of the infected patients required emergency treatment to recover from COVID-19. As there is no specific treatment options are available for the infection, hence there is a great need of treatment alternative that can decrease the severity of the disease in emergency circumstances. Traditional Chinese medicine and a variety of herbal medications have been shown to be useful in treating coronavirus infection. This article discusses the advantages of a few herbal medications that are commonly used to treat respiratory illnesses. The current review summarizes updated published works of literature on the effects of traditional Indian medicinal plants against COVID-19 infection.
Keywords: *COCID-19, Coronavirus, SARS- CoV- 2, Herbal plant, Alternative medicine, Health emergency*

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INTRODUCTION

Coronavirus disease-19 (COVID-19) is a highly infectious disease which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) [1]. It was initially discovered in December 2019 in Wuhan, Hubei Province, China, and rapidly spread around the globe. According to the worldometers.info/coronavirus, the United States currently has approximately 35,283,075 COVID-19 cases, with India (31,332,159) and Brazil (19,632,443) following closely behind [2]. The disease spreads speedily mostly through intimate contact with infected people via respiratory droplets from sneezing or coughing. In addition, there are two other routes to spread the virus: touch and aerosol transmission [3]. The most prevalent symptoms of COVID-19, in mild or moderate cases, are also typical to other respiratory infections, according to an observational study and documentation conducted across several health institutions in Europe. Headache, loss of smell, nasal airway blockage, cough, weariness, muscular discomfort or myalgia, rhinorrhea or runny nose, loss of taste, sore throat, and fever are among the most common [4]. Fatigue, confusion, muscle discomfort, diarrhoea, nausea and vomiting, headache, sore throat, and loss or altered sense of taste or smell was among the COVID-19 symptoms upon admission [5]. SARS-CoV-2 can infect people of practically any age or race, but it is far less prevalent in children under the age of 14 and typically goes unnoticed in young people [6]. COVID-19 symptoms are more severe in those who are older and have comorbidities, and allergy diseases, asthma, and chronic obstructive pulmonary disease (COPD) are significant risk factors [7].

Since the World Health Organization (WHO) declared a COVID-19 outbreak, multiple studies have been conducted to unravel the therapy possibilities and combat the disease utilizing diverse approaches and modalities. Chloroquine is a widely used medicine that has been shown to inhibit viral replication in vitro study [8]. In addition, a combination of hydroxychloroquine and azithromycin has been proven to have a strong synergistic effect in lowering viral load and promoting early recovery [9] For severe disease, the use of steroids, passive antibodies, and selective cytokine blockade is also suggested [10]. Yet, as of now, there are no specific antiviral drugs or vaccines verified to be effective against SARS-CoV-2, hence the emphasis is being laid on preventive measures and symptomatic treatment [11]. In this context when

there was no effective coronavirus therapy, experts began seeking for alternatives, and major impacted countries such as China and India began to employ herbal drugs or alternative remedies. Coronavirus sufferers in China have begun to receive traditional Chinese treatment (TCM). TCM treatment was discovered to be beneficial in reducing the communicable disease during the SARS 2003 outbreak, and as a result of that experience [12]. TCM is also used in SARS-CoV-2 [13]. Herbal remedies were helpful in decreasing the spread of COVID19 illness during the coronavirus outbreak in 2019-2020[14-16]. After being treated with traditional Chinese herbal medication, the first patient with COVID-19 pneumonia was able to leave the hospital [17]. With the evidence of successful control of COVID signs and symptoms the Chinese Guideline on the diagnosis and treatment of COVID-19 now includes TCM [18]. A substantial numbers of COVID-19 cases were successfully treated with TCM [19].

Ayurveda, a traditional Indian medical system is widely plasticized in Indian society since ancient time. The medicinal system of Ayurveda is divided into two categories: natural Ayurveda (Sahaja) and acquired Ayurveda (Yuktikrut). To decrease the progression of communicable disease pathogenesis, drugs like Sanjeevani vati (an antipyretic and diaphoretic ayurveda medicine) and Chitrakadi vati (a potent digestive medicine), as well as a combination of Guduchi (Tinospora cordifolia), Shunthi (Zingiber officinale), and Haridra (Curcuma longa), are employed [20]. Sanjivani vati is commonly used to treat communicable disorders, infection-related fevers, sannipataj jvara, colds, coughs, and indigestion. It also helps to build and revitalise the immune system [21]. Several antiviral medicinal plants, such as Hyoscyamus niger, Justicia adhatoda, and Verbascum thapsus, have been utilized to treat influenza virus infections in Asian countries [22]. *Rasayana* functions as an antioxidant, anti-stress, anti-inflammatory, anti-microbial, vaccination adjuvant, and confers disease protection [23]. Herbal and medicinal plants such as Garlic (Allium sativum), turmeric (Curcuma longa), Carom also known as Indian Borage or Ajwain (Trachyspermum ammi) are some ayurvedic remedies that can be used as disinfectants to prevent COVID-19 [24]. In the light of current scenario and growing global worries about the COVID-19 outbreak, awareness and knowledge of natural resources with antiviral properties is crucial for designing a COVID-19 management strategy. Hence, the current study summarizes available research on various herbal plants with antiviral characteristics in general, as well as COVID-19 specifically.

MATERIAL AND METHODS

A literature search was undertaken using computerized searches of PubMed, Scopus, Google Scholar, and other resources to find and extract pertinent content. The antiviral medicinal plants were chosen based on their use in traditional medicine, published scientific phytochemical studies, and/or their effectiveness against upper respiratory tract infections, SARS or MERS or COVID-19. This brief overview summarizes the findings of recently published studies, clinical trials, the World Health Organization's COVID-19 update, and the authors' opinion.

TRADITIONAL HERBAL MEDICINES

Here we present some herbal medicines that have been demonstrated potential activity against upper respiratory tract infections, SARS or MERS or COVID-19.

Allium sativum L.

Because of its many uses, *Allium sativum L.*, also known as garlic, is considered an indispensable herb. It can be used as a frequent element in medicine prescriptions or as a typical spice in family feasts. The organosulfur chemicals diallyl thiosulfonate (allicin), diallyl sulphide (DAS), diallyl disulfide (DADS), diallyl trisulfide (DATS), E/Z-ajoene, S-allyl-cysteine (SAC), and S-allyl-cysteine sulfoxide are the most active components of garlic (alliin) [25-28]. Amino acids (alanine, arginine, aspartic acid, asparagine, histidine, proline, alanine, valine), monoterpenoids (citral, geraniol, alfa and beta-phellandrene, and others), peptides, minerals, flavonoids, and vitamins are among the various chemical components found [29]. For thousands of years, garlic has been used as a treatment for common colds, influenza, and other illnesses [30]. Freshly crushed seed garlic, either with or without honey, can aid in immune system improvement. Numerous researchers have documented various types of biological properties of garlic such as anti-inflammatory [31], antioxidant [32], immunomodulatory [33], antimicrobial activity [34], etc, which could be attributed to the presence of a variety of bioactive sulphur-containing substances such as sulphoxide, proteins, and polyphenols [13]. Garlic and its organosulfur compounds (OSCs) have been shown in preclinical studies to have antiviral action against a variety of human, animal, and plant pathogenic viruses by inhibiting viral RNA polymerase, reverse transcriptase, DNA synthesis, and immediate-early gene 1 (IEG1) transcription, as well as downregulation of the extracellular signal-regulated kinase (ERK)/mitogen activated protein kinase (MAPK) signalling pathway [35]. The immunomodulatory effects of garlic and its OSCs have been linked to the relief of viral illness. Garlic has

also been shown in clinical investigations to have a prophylactic impact in the prevention of widespread viral infections in people by increasing the immune response [35].

Althaea officinalis L.

Althaea officinalis (A. officinalis), sometimes known as Marsh mallow, is a member of the Malvaceae family. This medicinal herb has been utilized for therapeutic purposes since antiquity. Medicine is made from the roots and leaves of the *A. officinalis* plant. Mucilage, flavonoids, and glycosides are found in the roots of *A. officinalis*, and the coumarin scopoletin is found in the leaves [36,37]. It has medicinal potential due to the presence of important secondary metabolites. *A. officinalis* has strong pharmacological action in cough, throat irritation, stomach inflammation, anti-tumor, antiviral, and immunostimulant confirmed in vitro and in animal studies [38]. Antibacterial and anti-inflammatory properties, as well as effects on mucociliary transport, polysaccharide adhesion to buccal membranes, and cough reduction have all been observed in this plant [14]. Because *A. officinalis* has a large amount of polysaccharide, it is beneficial in reducing irritation and inflammation of the oral and pharyngeal mucosa [14].

Andrographis paniculata

Andrographis paniculata (Burm. f.) Wall. ex Nees (A. paniculata) is an important medicinal herb used all over the world. It is a member of the Acanthaceae famil*y. A. paniculata* is one of the most commonly utilized medicinal herbs in Unani and Ayurvedic medicine. In recent years, commercial formulations of this plant extract have been employed in some nations. The aerial part of *A. paniculata* is the most often utilized section, with diterpenoids, diterpene glycosides, lactones, flavonoids, and flavonoid glycosides present in the extracts. Various pharmacological activities suh as anticancer, antidiarrheal, antihepatitis, anti-HIV, antihyperglycemic, anti-inflammatory, antimicrobial, antimalarial, antioxidant, cardiovascular, cytotoxic, hepatoprotective, immunostimulatory, and sexual dysfunctions have been reported in this plant [15]. Andrographolide and the Andrographiside component in *A. paniculata* can inhibit ACE and SARS3CLpro, respectively [16]. Andrographiloids, which have been widely investigated in a variety of models, including human clinical trials, for their medicinal properties, are the main active components of this herbal plant. Furthermore, this herbal plant has been shown to have very low toxicity in both animals and people [39]. The anti-SARS-CoV-2 activity of *A. paniculata* and andrographolide was demonstrated in a study by Sa-ngiamsuntorn et al. utilizing a Calu-3-based anti-SARS-CoV-2 test. The anti-SARS-CoV-2 activity of *A. paniculata* extract and, in particular, andrographolide, as well as the favourable cytotoxicity profiles, support further development of *A. paniculata* extract and, in particular, andrographolide as a monotherapy or in combination with other effective drugs against SARS-CoV-2 infection [40].

***Commiphora molmol* Engle**

Guggulu, also known as *Commiphora molmol (C. molmol)*, is made up of oleo-gum resin collected by tapping the stem and branches of *Commiphora wightii* (Arnott) [41]. The guggul tree is the common name for this shrub. Guggulu has been used in Indian traditional medicine for thousands of years to treat arthritis, inflammation, gout, rheumatism, obesity, and lipid metabolic issues. Diterpenoids, triterpenoids, steroids, long-chain aliphatic tetrols, aliphatic esters, ferulates, lignans, polysaccharides, and a range of inorganic ions, together with low levels of sesamin and other undiscovered compounds, are phytoconstituents of guggulu [41]. Only a few researches on anti-inflammatory or antinociceptive effect have been found for this herbal remedy, which has not been scientifically demonstrated for symptoms of respiratory disease [29]. This herbal plant is thought to have medicinal properties for a variety of ailments. Immunomodulatory, anti-inflammatory, cytotoxic, antioxidant, antibacterial, hepatoprotective, anti-tumor, anti-ulcer, and analgesic effects are thought to be present in *Commiphora myrrh.* As a result of its medicinal properties, *C. molmol* can be utilized to treat a variety of disorders. This herbal plant's antiviral properties aid in the prevention of a variety of ailments. As a result, *C. molmol* may be useful in treating COVID-19 instances that are currently being treated [42].

***Cymbopogon citratus* (DC.) Stapf**

In tropical areas, the herb Cymbopogon citrates (***C. citrates)***, Stapf (Lemon grass) is commonly utilized. Aromatherapy uses the essential oil of this plant. Terpenes, alcohols, ketones, aldehydes, and esters are the most common chemicals found in Cymbopogon citratus**.** Essential oils containing Citral, Citral, Nerol Geraniol, Citronellal, Terpinolene, Geranyl acetate, Myrecene, and Terpinol Methylheptenone are some of the phytoconstituents of this plant. Other phytoconstituents include luteolin, isoorientin 2'-O-rhamnoside, quercetin, kaempferol, and apiginin, which are flavonoids and phenolic compounds [43]. Cymbopogon citratus has been found to have anti-amoebic, antibacterial, antidiarrheal, antifilarial, antifungal, and anti-inflammatory properties, according to numerous studies. Antimalarial, antimutagenicity, antimycobacterial, antioxidants, hypoglycemic, and neurobehavioral properties have all been investigated [43,44]. This is a well-known natural treatment. Because the formulations of C. citratus have an anti-inflammatory effect on the respiratory system, they may be useful for symptomatic relief of respiratory illnesses [29]. Traditional healers employ this medicinal herb as an immune booster [45]. The

essential oil of lemon balm has antiviral action against the influenza virus. Lemon balm oil contains active components that can stop the influenza virus from replicating [46]. The herb *C. citratus* is used to treat respiratory infections [47]. It has antiviral property hence may be effective for Covid-19 [48].

***Ocimum sanctum* (Tulsi)**

Tulsi is the common name for *Ocimum sanctum (O. sanctum)*. Tulsinol (A, B, C, D, E, F, G) and dihydrodieuginol-B, which inhibit COV-19 primary protease and papain-like protease, are found in *O. sanctum*. Pain, diarrhoea, cough, and fever, all of which are common COV-19 symptoms, are treated with O. sanctum. O. sanctum boosts the body's immunity and helps to build a defence mechanism against viruses and germs [49]. Kumar et al. found that methyl eugenol, oleanolic acid, and ursolic acid have good binding activity against SARS-CoV-2 surface spike glycoprotein and RNA polymerase. Epoxyazadiradione, Gedunin, Methyl eugenol, Oleanolic acid, and Ursolic acid were found to have high binding activity against SARS-primary CoV-2's protease. Natural compounds from tulsi and neem had higher binding efficacy than the conventional medications Lopinavir/Ritonavir and Remdesivir. Tulsi and neem natural chemicals have a significant binding activity against SARS. -CoV-2 targets factors involved in viral attachment and replication, making it useful in the treatment of SARS infections. -CoV-2. [50].

***Withania Somnifera* (Ashwagandha)**

In its latin name, Ashwagandha is known as *Withania Somnifera*. It's a shrub that grows in India's arid regions. Gujarat and Haryana, Madhya Pradesh, Punjab, and Uttar Pradesh are among the states where it is widely grown [51]. Ashwagandha's natural product Withaferin A is separated (Withania somnifera). It aids in the treatment of a variety of illnesses, including the common cold, gynaecological disorders, and even infertility. It has antiviral activity against a variety of viruses, including COVID-19 [52]. Natural phytochemicals may likely be realistic possibilities for reducing COVID-19 entry into host cells, according to a study by Balkrishna et al., and W. somnifera may be the top choice among herbs in these directions to curb COVID-19 infectivity [53].

***Azadirachta indica* (Neem)**

Azadirachta indica, sometimes known as Neem, has a wide spectrum of chemicals, some of which have medicinal promise. Antipyretic, fungicidal, antihistamine, and antiseptic effects have been demonstrated for nimbin (triterpene). Nimbin (triterpene) possesses anti-inflammatory and antioxidant properties that aid to reduce damage by lowering reactive oxygen species generation. Flavonoids in neem act as inhibitors of prostaglandin production, endoperoxides, and enzymes implicated in inflammation such as protein kinases and phosphodiesterases. Oil extracts are the most commonly utilised form of neem, and in-depth phytochemical study has verified the presence of large levels of triterpenes, flavonoids, and saponins, while other components like catechins and nimbins appear to be present in less concentrations. Limonoids, tannins, alkaloids, terpenoids, reducing sugar, catechins, sterols, and gallic acid are among the other metabolites discovered in neem extracts [54]. Neem is an immunomodulator with antiviral characteristics. It can suppress viruses at an early stage and has antiviral qualities. All of these characteristics make neem an excellent choice for inhibiting COVID-19 because it can stop the virus at any stage [55]. In a study conducted by Nesari et al., it was discovered that taking neem capsules lowered the incidence of COVID-19 infection, demonstrating its promise as a prophylactic medication for COVID-19 infection prevention. Clinical trials should be conducted to further investigate the findings [56].

***Tinospora cordifolia* (Giloy, Guduchi)**

Tinospora cordifolia (willd.) Hook. f. and Thomson is a climbing shrub found throughout Asia, Africa, and Australia's tropical and subtropical climates. Members of this family are high in polysaccharides, terpenes, and alkaloids, which have anti-inflammatory, immune-stimulatory (phagocytosis), anti-diabetic, and anti-oxidant properties [57]. Berberine, a component of Tinospora cordifolia, has built a solid case for acting as a potential inhibitor of the 3CLpro protein's activity and thereby suppressing viral proliferation. The findings of the study are expected to pique the interest of researchers working on new drug development for SERS-CoV-2, for which no specific treatments or vaccines are currently available [58].

***Curcuma longa* (Turmeric)**

Curcuma longa (C. longa) is a Zingiberaceae plant that is generally known as turmeric. In Indian cuisine, it is often used as a spice and a colouring agent. The main active ingredient is curcumin, which is found in the rhizomes of this plant (diferuloylmethane) [59]. Curcumin is an antiviral drug that is effective against a variety of enveloped viruses, including influenza A and respiratory syncytial virus. Curcumin has also been shown to be efficacious in in vitro experiments against SARS-CoV [60]. Chemical constituents from turmeric, such as cyclocurcumin and curcumin, and andrographolide and dihydroxy dimethoxy flavone from Andrographis paniculata, are significantly active against COVID-19 by inhibiting the SARS CoV-2 main protease enzyme, according to in silico studies, with remedial potential [61].

***Cinnamomum zeylanicum* (Cinnamon)**

Cinnamaldehyde and trans-cinnamaldehyde (Cin), which are contained in the essential oil, are the most important components of cinnamon. Procyanidins and catechins are found in cinnamon bark. Both procyanidin A-type and B-type connections are present in procyanidins. Cinnamon and berry procyanidins have also been demonstrated to have antioxidant properties [62]. Cinnamon, in combination with other ingredients (Gene-Eden-VIR), has been shown to have a variety of antiviral effects on beta coronaviruses and SARS-CoV, including inhibiting cell entry and infection, inhibiting replication, and inhibiting viral proteases, all of which improve the antiviral immune response and reduce the formation of virulent quasi-species [63].

Artemisia annua

Artemisinin is a commercially available antimalarial medicine derived from Artemisia annua (A. annua). It is one of the most promising natural compounds and an important contender for antiviral activity. Furthermore, A. annua contains sterols that have antiviral properties [64]. In ethnobotanical practise, the entire plant is widely used to cure malaria, cough, and cold [65]. In Vero-E6 cell-based cytopathic effect screening, A. annua extracts significantly decreased cytopathy caused by SARS-CoV strain BJ001 and demonstrated efficacy against SARS-CoV-2 [66]. In vivo study, artemisinins and the plant A. annua decrease inflammatory cytokines like IL-6 and TNF-. During the "cytokine storm" that many SARS-CoV-2 patients experience, these effector molecules can be problematic. Artemisinin also reduces fibrosis, which is another issue that SARS-CoV-2 survivors face and causes more long-term organ damage [67].

CONCLUSION

COVID-19 is a worldwide epidemic. There is currently no specific treatment for this infectious condition, thus many researchers are concentrating on existing medications and herbal plant source. It was attempted in this review article to enlist several herbal medicines that have been found to be useful in the treatment of COVID-19. These drugs exhibit antiviral action against COVID-19 and can help alleviate some of the symptoms of coronavirus infection. Furthermore, these herbal medications can also be used as a prophylactic to boost immune system strength, which will help people fight COVID-19 more effectively.

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COMPETING INTERESTS

The authors declare that there is no conflict of interest among the authors.

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