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Review on Herbal Drugs Used in COVID 19

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ABSTRACT

COVID-19 is a pandemic infection declared by the World Health Organization (WHO) on March 12, 2020¹, this pandemic has created a global health crisis posing an unprecedented public health emergency. The cause pandemic of coronavirus disease 2019 (COVID-19) is due to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Herbal Drugs & some dietary fibers, macro & micronutrients have been prescribed by traditional healers for various diseases. Thus, the aim of this review is to present main herbal products, their source, characteristics, and potential activity concerning COVID-19. Throughout the globe number of deaths and people being infected are increasing daily. Effective management to address this infection is still evolving and attempts are being made to integrate traditional interventions along with standard of care. Herbal medicine can interfere with COVID-19 pathogenesis by inhibiting SARS-CoV-2 replication and entry to host cells. citrus Spp., orange (*C. Sinensis*), *Allium sativum*, *Allium Cepa*, *Menthapiperita*, *Glycyrrhiza glabra*, and *nigella sativa* are the most desirable herbal drink or fruit that can introduce effective adjuvant components in COVID-19 management are some of the antiviral medicinal plant species¹. Some recommended measures from the Ministry of Ayush such as Spices like Haldi (Turmeric), Jeera (Cumin), Dhaniya (Coriander) are also focused in this article.



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INTRODUCTION

On March 12, 2020, the occurrence of coronavirus disease (COVID-19) has been stated as a pandemic by the World Health Organization (WHO)¹. It is a severe acute respiratory syndrome caused by corona virus 2 (SARS-CoV-2), which had not formerly affected humans. More than 230,953,959 patients are infected and about 4,734,427 deaths were reported due to COVID-19 worldwide as on September 2021.⁵

COVID-19 induces an inflammatory immune response. Release of inflammatory cytokines in cases of COVID-19 leads to a dysregulation of cytokine storm and immunity, acute respiratory distress syndrome and multiorgan dysfunction. Presently, various types of vaccine is available to prevent the COVID-19 pandemic but deliverability is still a challenge especially for developing countries. Remdesivir is a recently approved antiviral drug available with limited supply which was developed by U.S.-based Gilead Sciences and approved by the FDA. An NIH-sponsored trial of remdesivir that involved dozens of sites in the United States. Different findings suggested that herbal medicine can reduce the severity and prevent COVID-19. India use herbal medicine with modern medicine to enhance the immunity of patients under the guidelines by Ayush Mantralaya. Curcumin has been revealed in-silico studies to prevent the entry of the SARS-CoV-2 which is causative agent for Corona or Covid -19 into cells, and viral replication⁹, while a recent experimental finding has shown that bromelain may also inhibit viral entry into cells Furthermore, potential specific antiviral agents such as the decoy mini protein CTC-445.2d , protease inhibitors, mainly against the Main protein, nucleoside analogs, such as molnupiravir, and compounds blocking the replication transcription complex proteins, such as plitidepsin and zotatifin are under investigation against COVID-19 .

Herbal medicines have also helped to alleviate the effects of infectious diseases as Covid 19, Flu Typhoid. Evidence supports that herbal medication may be effective in lowering and managing the chance of COVID-19. Currently, well-known herbal medicines with antiviral activities are being used as an additional treatment to suppress SARS-CoV-2 virus causing severe condition in Covid 19 patients, since conventional treatments are still not well succeeded. People with comorbidities or elderly patients with (immunodeficiency, digestive, and endocrine disease, cardiovascular, hypertension, HIV, respiratory (TB), cerebrovascular, etc.) are more likely to develop severe viral cases. Plant material, in addition to supportive treatment, is employed to treat such disorders. Elderly

individuals in rural areas are better educated about herbal plants that can be used to heal various ailments. COVID-19 & recently vaccines also contributed more in controlling pandemic corona attack.²

Current prevention of COVID-19

Herbal medicines could exert antiviral, relieve chronic obstructive pulmonary disease and hypoxemia, immune-regulatory and anti-inflammatory activities. Similarly, traditional medicines are used for the management of COVID-19 parallel with modern medicine and vaccinations in India. "Wet, heat, and congestion" are three types according to symptoms of patients who infected with COVID-19 in their lungs. "Wet" means the factor with sticky and heavy turbidity that can cause a long course of disease and damage the function of the body. "Hot" refers to the disease-causing element of hot, dry, and growing turbidity. "Congestion" is a causal factor that can obstruct blood flow and result in symptoms such as pain. Some medicinal herbs that are supported by relevant establishments can be used as an alternative to combat COVID-19. Some therapeutic ingredients that can be used for viral suppression include garlic, ginger, turmeric, chilly, lemon, and hot water with salt.

Treatment of COVID-19 mild infection

Symptoms of COVID 19 are fever, headache, sweat, thirst, dry cough, sore throat, red tongue tip, and floating pulse⁸. The main purpose is to clear lung heat, expel, relieve cough, regulate the patient's lungs and restore normal respiratory function. Clinically, A study has done on different herbal supplements showed that ginger, lemon/orange, vitamin C, honey, black seed have a significant impact on COVID-19 management.

Treatment of COVID-19 Severe infection

In the early course of COVID-19 management, if the infection cannot be easily controlled then respiratory failure, multiple organ failure, and death will be worsened. These infectious patients have the following main symptoms: high fever, dry cough, difficulty in breathing, sweating, chest stiffness, fatigue, nausea, bloating. *G. glabra*, *Thymus vulgaris*, *Allium sativum*, *Althea officinalis*, and ginseng are some of the preventive and supportive management of COVID-19 through tempering the immune system.

Some herbal medicine used in COVID-19

On top of exhibiting direct antiviral effects, herbal drugs are reported as anti-inflammatory activities may have significant roles in COVID-19 treatment as the elevation of inflammatory indicators such as interleukin (IL)-6, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) has been related to severe disease with worse outcomes,

In the research of herbal medicine single plant species have much medicinal value. It is now well understood that a single plant may contain a variety of biochemicals. Generally classified as antiviral, anti-inflammatory, immunomodulatory, and mixed-effects having more than one purpose based on valuable evidence for efficacy. Some examples of herbal medicine used in the management of COVID-19 are summarized below.

Azadirachta indica (neem)¹

The leaves of neem are traditionally boiled and consumed for the management of fever-related with COVID-19, with reported anti-inflammatory effects in animal studies. Fever is the main clinical symptom of COVID-19 and to reduce it these plants have valuable outcomes. Neem leaves extracts and their metabolic constituents such as flavonoids and polysaccharides have direct antiviral effects against different viruses including Hepatitis C Virus is confirmed by the animal study and in-silico docking research. It has demonstrated that Neem-derived compounds such as nimbolin, nimocin, and cycloartenol can bind to the SARS-CoV-2 envelope, membrane, glycoproteins, and also inhibitory role has been demonstrated by molecular docking research specific to SARS-CoV-2. Its leaves have immunoregulatory properties that can increase immune response in animal studies. Zingerone, shogaols, gingerols, paradols, wickstromol, and carinol in mice immunized with the Brucella Rev-1 vaccine, subcutaneous administration of neem seed extract increased post-vaccination IFN- production. Animal study has demonstrated that neem seed extracts have abortifacient effects in pregnant women. Clinical studies have shown that it inhibits the production of human chorionic gonadotropin. According to studies, the traditional use of neem for medical purposes is based mostly on the ingestion of the leaves, which are boiled in water and drunk. One of the key issues is safety; therefore, before further research on efficacy, a clinical study should be conducted to identify safe doses of neem leaves unique to the formulation intended for usage.

Mentha piperita: ^{1,4}

Peppermint (*M. Piperita*) is the oldest herbal remedy for different diseases and condition in the world. Dry peppermint has been composed since 1000 BCE, and its importance has been described in ancient Egypt, Greece, and traditional Chinese medicine. Peppermint has essential oil and significant antibacterial and antifungal activity against Gram-negative and Gram-positive bacteria, yeast, and fungi, mainly as a result of the presence of the abundant phytochemicals menthol and menthone. However, to the best of our knowledge, a study done of Saudi Arabia stated that about 78% of non-hospitalized patients used peppermint, compared with only 22% of hospitalized patients without using peppermint supplement, due to COVID-pandemic so the use of peppermint during infection with COVID-19 was associated with lower odds of hospitalization.

Allium sativum and Allium cepa^{1, 4}

Garlic (*Allium sativum*) is indicated for respiratory disease namely cold and cough, and onion (*Allium cepa*) are commonly used as a home remedy for different disease conditions. Garlic is considered is traditional herbal medicinal product used for the relief of cold symptoms. Moreover, the British Herbal Pharmacopoeia considers that garlic products are indicated for recurrent colds and whooping cough. Fresh garlic: 2.0–4.0 g average daily dosage is preferable to use a commercial preparation with defined composition and an adequate dose. This herbal medicine has antiviral activity this has been experimentally proven. Onion, which is used in traditional medicine to treat various conditions and infections, was obtained to destroy the avian influenza virus (H9N2). But the preparation process is critical, as boiled or fried onions are ineffectual. Onion is a strong choice for managing COVID-19 patients, according to researchers, because of its anti-inflammatory, antithrombotic, and antiviral properties. It is mostly used for its immunomodulatory, antimicrobial, antioxidant, anti-inflammatory, anticarcinogenic, antihypertensive, antithrombotic, antidiabetic, antimutagenic, and prebiotic activities. Active metabolites of garlic can be classified into two, such as sulfur-containing and non-sulfur-containing compounds. Allicin and allin are the major sulfur-containing compounds, while the principal sulfur-free active compounds include flavonoids and saponins. Garlic's ability to inhibit the SARS-CoV-2 was perceived in silico by forming hydrogen bonds between amino acids with the binding site of the main structural protease of SARS-CoV-2 and its bioactive parts that protease being responsible for viral production. Usually, COVID-19 patients have reduced

the number of T helper cells, if we take garlic leads to a significant upregulation in the T helper cells, cytotoxic T cells, and NK cells, as well as downregulation of the levels of leptin, leptin receptor, TNF- α , IL-6, and proliferator-activated receptor gamma (PPAR- γ). So, it could be one possible option for the management of COVID-19 because of the ability to modulate cytokine secretion, immunoglobulin production, phagocytosis, and macrophage activation.

***Glycyrrhiza glabra*^{1,4}**

Glycyrrhizin, also called glycyrrhizic acid (GLR), is a triterpenoid saponin mainly isolated from the roots (*Glycyrrhizae Radix*) of the plant *Glycyrrhiza*. GLR effectively inhibited the replication of two clinical isolates of SARS-associated coronavirus (FFM-1 and FFM-2). The drug was found to inhibit the cytopathic effect of the virus with an EC₅₀ of 300 mg/ml while being non-cytotoxic to the host cells. GLR inhibited virus replication but also the penetration and adsorption of the virus into cells. The mechanism of action at the origin of this activity was not known at that time but a drug-induced production of nitrous oxide synthase was mentioned, signifying that nitrous oxide could be accountable for the inhibition of virus replication. GLR also showed activity when it was tested against 10 clinical isolates of SARS coronavirus in infected Vero-E6 cells but the activity was limited in time. The rapid metabolism of the drug limits the drug exposure, not permitting it to reach an effective concentration. The modification of the GLR structures, particularly to make amino-acid conjugates and amide derivatives can rise significantly the activity against Covid-19 but it can be at the expense of elevated cytotoxicity.

***Zingiber officinalis*^{:4}**

Indications for Zingiberaceae (Rhizome) in the setting of respiratory disorders. The herb *Zingiber officinale* is used to treat colds and coughs. It has also been used as an anti-asthma (WHO, 1999) and expectorant. Composition of chemicals. Zingerone, shogaols, gingerols, paradols, wickstromol, and carinol are some of the compounds found in ginger. This herbal remedy is effective in the treatment of fever in studies. Its anti-inflammatory, antipyretic, and analgesic properties have been reported in various preclinical studies. Ginger's anti-inflammatory properties have been thoroughly proven in both in vivo and in vitro studies.

***Commiphora molmol*:⁴**

Commiphora sp. - Burseraceae (Air-Dried Oleo-Gum Resin Exudate) Indication in the context of respiratory conditions. *Commiphora molmol* is used to treat symptoms of respiratory disease, such as minor pharyngeal mucosa inflammation (WHO, 2007). Cough, anti-inflammatory and other symptoms are also associated. Chemical composition Furanoeudesma1,3-diene and lindestrene are the main components of sesquiterpenes (Marongiu et al., 2005). It is recommended to use a commercial preparation with a defined composition, such as a tincture (0.5–5 ml in 150 ml of water three times daily for rinsing or gargling) (WHO, 2007). This herbal remedy has not been scientifically shown to help with respiratory issues.

4. Conclusion and future perspectives:

*Our review article suggests that several herbal medicines have safety margins superior to those of reference drugs and enough levels of evidence to start a clinical. An antiviral drug that is primarily approved by WHO for emergency management was remdesivir. Herbal medicine and its bioactive fractions are potentially beneficial in preventive COVID-19 and as supportive measures. Different valuable herbal medicine can interfere with COVID-19 pathogenesis by inhibiting SARS-CoV-2 replication and entry to its host cells. Different components of plants biochemical are the most desirable herbal drink or fruit that can be introduced as effective adjuvant components in COVID-19 management; and also, to reduce fever and cough as the most common complication of COVID-19 via their anti-inflammatory effect. Some herbal products such as *Azadirachta indica*, and can be used. On the other hand, numerous herbal drugs such as *G. glabra*, *Thymus vulgaris*, *Allium sativum* & *Cepa*, *Althea officinalis*, *Zingiber officinalis*, *Commifra molmol* and may become effective in the preventive and supportive management of COVID-19 through boosting the immune system. The most frequently used medicinal plant was followed by ginger (*Zingiber officinale* Roscoe), garlic (*Allium sativum* L.) & *Commifra molmol*.*

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