

Herbal Medicine is the Way of Potential Therapeutic Option for the Treatment of Novel Corona Virus (COVID-19): Recent Updates

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ABSTRACT

COVID-19 is an acute, progressive, respiratory illness, which is highly contagious. In 2020, COVID-19 has become a major health issue; its prevalence has been increasing at an alarming rate across the world. Less availability of COVID-19 drugs, high treatment cost and side effects affect the quality of life of a person infected with COVID-19 in countries with a poorly developed health system. Through infection patient can die due to Acute Respiratory Distress Syndrome (ARDS) initiated by systemic inflammatory reactions due to the undue emancipation of chemokines and pro-inflammatory cytokines by the immune effector cells. The aim of this review to summarize and evaluate the evidence of traditional medicine, which can facilitate the treatment options according to the clinical manifestations of COVID-19 patients and has proven effectiveness in prevention and control of disease. The systemic search for meditational plants for the therapeutics of COVID-19 was performed considering the articles published through the different scientific databases. The traditional medicines against COVID-19, currently under clinical trials and clinical application of traditional Indian and Chinese medicine for the treatment of COVID-19 are also found. This review highlights the major goal of herbal remedies and their significant role to cure antiviral diseases like COVID-19. It is suggested that promising polyherbal formulations and traditional plants must be investigated on the priority basis to solve current crisis.

Keywords: COVID-19; Medicinal plants; Traditional medicine; Phytotherapy

INTRODUCTION

Present decade witnessed the outbreak of life-threatening viral disease caused by Coronavirus (COVID-19). The World Health Organization (WHO) has issued a caution that, although the COVID-19 is a pandemic disease, it should be contained to prevent the global spread. It spread rapidly and to date has 3 million deaths with more than 140 million cases of infection in all over the world (wordometers.info/coronavirus). The Severe Acute Respiratory Syndrome-Related Coronavirus 2 (SARS-CoV-2), a novel and pathogenic coronavirus causing respiratory illness. The new variant of Severe Acute Respiratory Syndrome-Related Coronavirus (SARS-CoV-2) in UK found which is up to 70% more transmissible than the previously circulating form of virus, which is why every country is worried, and needs urgent follow-up and investigation [1,2]. Extensive treatment to reduce

the infection of COVID-19 is a use of allopathic medicine but we should also implement the herbal medicine to control the current outbreak because prescribe drugs used for the treatment of COVID-19, has too much cost along with their side effects due to their toxicity. These antiviral drugs show allergic reactions or hypersensitivity, with symptoms such as fever, nausea, bleeding, bone loss, heart disease, high blood sugar and kidney, liver or pancreas damage.

For public health assessment, we urgently need to develop antiviral therapy. Additionally, social, and economic problems generated by the COVID-19 pandemic also called for rapid intrusions. Therefore, at this moment herbal medicine needs special attention and efforts to protect or reduce the infection [3]. The herbal (traditional) medicines get hold of a significant proportion of >83 billion dollars annual production growing

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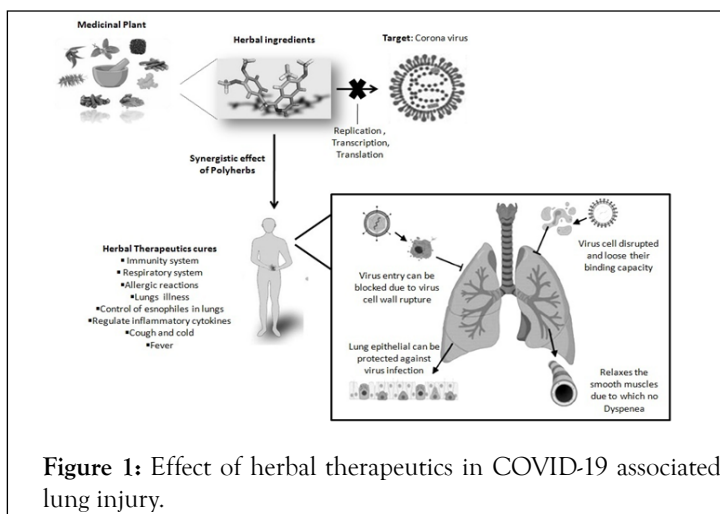
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exponentially. In developing countries like 70%-95% of inhabitants rely on herbal medicines for primary care since they are cost-effective or unavailability of conventional drugs. WHO estimated that about 80% of the world population still uses herbs and traditional medicines for fulfilling their primary health care needs [4]. In India, more than 80% of the population reliant upon herbal drugs and it shares about 2.5% of the global market. More than 60% of market share is being controlled by North America and European Union. At present herbal formulations are used more as therapeutic agents for arthritis, liver disease, diabetes, cough remedies, adaptogens and memory enhancers [5]. Despite such extensive acceptability, the number of standardized herbal drugs is less due to being short of regulatory standards and implementation protocols. Standardization requires a natural plant product to be certified at the origin itself by borrowing of good agricultural practices. There is a need for collection techniques from wild and good manufacturing practices for extraction modes and related parameters [6].

There are so many herbal formulations and scientifically validated herbal plants but to date, no single approved herbal drug is available for mass usage. It is due to a lack of standardization methodologies adopted before the development of drugs. However, some *in-silico*/docking studies have shown potential to treat the patient infected with COVID-19 [7]. Herbal medicinal therapy is a unique alternative for this pandemic disease COVID-19 (Figure 1). This review focuses on a new perspective regarding COVID-19 prevention. We summarized the most recent advances in COVID-19 prophylactics and vaccine development in brief and deeper insight on medicinal plants and herbal drugs used in the treatment and management of viral and respiratory diseases all over the world.



RECENT PROPHYLACTICS DEVELOPMENT OF COVID-19

The present scenario has emphasized the requirement for therapeutic opportunities to relive and overcome this latest pandemic. Despite the fact, the deteriorating developments of COVID-19, there are no drug certified to have considerable

effects in the medical treatment for COVID-19 patients. The COVID-19 pandemic requests for the rapid testing of new treatment approaches. Based on the evidence, hydroxychloroquine is the first medicine opted for the treatment of disease. Umifenovir, remdesivir and favipiravir are deemed the most hopeful antiviral agent; by improving the health of an infected patients [3,4]. Tocilizumab has emerged as an alternative treatment for patients with high risk of cytokine storms [8]. The anti-inflammatory dexamethasone is a first known steroid medicine that can save the lives of seriously ill patients, and it is shown in a randomized clinical trial by the United Kingdom that it reduced the death rate in COVID-19 patients. Antiviral drugs currently used to treat COVID-19 were initially developed for Ebola, influenza or SARS. Table 1, for mechanism of action of potential drugs used for COVID-19 treatment. Convalescent plasma might be a potential therapy for critically ill COVID-19 patients [7]. But the latest study revealed that remdesivir, hydroxychloroquine, lopinavir and interferon regimen had little or no effect on hospitalized patients [9].

Drug	Mechanism of action
Chloroquine, Hydroxychloroquine	Inhibition of endosome acidification
Remdesivir, Favipiravir, Ribavirin	Inhibition of the RNA dependent RNA Polymerase
Lopinavir/ritonavir	Inhibition of protease enzyme
Umifenovir	Inhibition to critical membrane fusion
Interferons	Inhibition of viral exocytosis
Dexamethasone	Regulate cytokines formation
Tetracyclines	Inhibition of bacterial translation
Tocilizumab	Regulate cytokines formation
Meplazumab	Inhibition of CD147
Itolizumab	CD6 inhibitor
Teicoplanin	Inhibition of cathepsin L
Nitazoxanide	Inhibition of neuraminidase enzyme
Ivermectin	Inhibition of replication
AMY101	Inhibition of C3 complement protein
Eculizumab	Inhibition of C5 complement protein
SDRV-003	Regulate cytokines formation
LCB1	Neutralizing protein

Nafamostat	Serine protease inhibitor
Famotidine	Histamine H2 receptor antagonist
Dipyridamole	Nucleoside transport inhibitor
Chlorpromazine	Antagonist of D2 dopamine receptor

Table 1: List of traditional medicine clinical trials done for COVID-19.

Vaccine is the most important therapeutic option to cure the COVID-19 infection. Vaccine is a very urgent need to prevent COVID-19 super spreading. A COVID-19 vaccine is a vaccine intended to provide acquired immunity against COVID-19. Several companies are developing DNA, RNA, protein, and vectored vaccines [3,10]. Nucleic acid-based vaccines can be produced quickly based on viral sequences, which permit a rapid path to the Clinic. Vaccines authorized for emergency use or approved for full use in USA, UK, India and other countries are Tozinameran from Pfizer, mRNA-1273 from Moderna, AZD1222 from AstraZeneca, and BBV152 from Bharat Biotech. However, medication options and standard treatment for COVID-19 are restricted.

APPLICATION OF TRADITIONAL MEDICINE TO PREVENT AND TREAT COVID-19

Traditional medicine has therapeutic effects on all clinical stages of COVID-19. Traditional medicines are effective in preventing COVID-19, In China and India medical staff averts an iatrogenic infection by using a decoction made centered on the principal of clinical trial. As of March 2020, latest cases of COVID-19 in China have reduced to single digits. Traditional Chinese Medicines (TCM) therapeutic outcome was outstanding, with a national participation rate of over 90% [11]. For primary stages, traditional medicines can relieve fever, cough, and shortness of breath and can improve the cure rate by preventing the infection from becoming severe. For sever and critical cases, traditional medicines combined with supportive therapy such as modern medicine and oxygen therapy, can enhance pulmonary ventilation function and an excessive immune response. Taking traditional medicine compound decoctions can help to reduce pulmonary interstitial fibrosis and pulmonary inflammation, as well as restore physical strength [12].

The development of new agents against COVID-19 is not realistic to pass toxicity tests and safety measures in short time. Consequently, active compounds affecting viruses or host targets in existing herbal medicines were screened by many scientists. Currently various natural products have been found to potentially possess anti-SARS-CoV-2 activity [13]. There are some compounds with anti-coronavirus activity. Clinical findings have revealed that integrated medicine tends to reduce the mortality rate of SARS and help in improving the clinical symptoms of COVID-19 patients. The effective experience of

fighting COVID-19 has shown that traditional medicine has a distinctive advantage in infectious diseases.

LITERATURE REVIEW

Medicinal plant with antiviral effect

There are many herbal remedies suggested for viral and respiratory disease complications. To cure these diseases, there have been many plants reported during the last 20 years.

Withania somnifera

Withania somnifera belongs to Solanaceae family, is commonly known as “Ashwagandha” in Indian tradition, has been studied to some point as an antioxidant, but it has powers to boost the immune system [10]. The application of the biologically active new compounds derived from the *Withania somnifera* makes it the potential to treat various immunological diseases [14]. Ayurveda uses the root of this plant as a general health tonic, adaptogenic, nootropic, immunomodulatory, etc. With its extensive and expanding use, it becomes judicious to systematically evaluate and document both the efficacy and safety of this plant in humans [15]. It is also used for the treatment of arthritis, tuberculosis, cancer [16]. A recent study highlights the significance of natural origin phytochemicals in controlling COVID-19 entry into host cells and presents a desirable and eccentric means for managing of COVID-19 infection. Withering A, an active constituent of *Withania somnifera*, has been revealed to have a broad range of medicinal properties including its anti-viral activity [7]. This study provides shreds of evidence for the reasonable inhibitory potential of Withering A. The results demonstrate a strong binding affinity of Withering A toward neuraminidase, the key enzyme in the life cycle of the influenza virus [16]. Another active Constituent of *Withania somnifera* is Methadone revealed to interact with the main protease of SARS-CoV-2 and inhibit its activity [8]. *W. somnifera* could well be the first choice of medicinal herbs in these directions, to control the COVID-19 infectivity.

Asparagus racemosus

Asparagus racemosus is a well-known medicinal plant, grown in the tropical and subtropical regions of India. Its therapeutic importance is well recognized in the Indian and British Pharmacopoeia along with several traditional systems of medicines such as Ayurveda, Siddha and Unani [17]. Traditionally, this plant is popularly known as ‘Shatavari’, and designated in Ayurveda as a potential Ramayana which prevents aging, provides immunity, increases longevity, improves mental function and also helps in the treatment of diseases related to the female reproductive system, inflammation, dysentery, biliousness, tumor and diseases of the blood and eyes [18]. The pharmacological studies carried out on this plant has revealed the potential adaptogenic, immunostimulant, anti-inflammatory, anti-microbial, antioxidant, anti-ulcer, galactagogue, phytoestrogenic, neuroprotective, aphrodisiac, anti-dyspepsia, anti-tussive and anti-cancerous activities [19]. Shatavari has been reported for its anti-bacterial, anti-candidal,

anti-viral activities. There is a study in 2020 shows that *in-silico* investigation of phytochemicals from *A. racemosus* as the credible antiviral agent to treat COVID-19 [15].

Ocimum Sanctum

Holy basil is a culinary herb belonging to the family *Lamiaceae* that has several health benefits [20]. Essential oils obtained from basil have been reported to have strong inhibitory activity against a wide range of pathogenic microorganisms. Basil extracts, thus, provide an attractive mode of treatment strategy against many emerging pathogens that demand viable therapeutic options. The application of extracts and purified components of basil as possible antiviral agents has already been reported. The extracts and specific purified compounds have shown broad-spectrum activity against both DNA and RNA viruses. However, basil leaves have been tested directly on the Zika virus and it showed that basil leaves extract inhibits the entry of Zika virus. Basil seed oil revealed to modulate both humoral and cell-mediated immune responsiveness and these immunomodulatory effects. Based on the molecular simulation study, *Ocimum sanctum* extract can be incorporated as a preventative measure against COVID-19 due to its potential to prevent replication of COVID-19. *Ocimum sanctum* and different species of *Ocimum* have been shown to target the reverse transcriptional activity of HIV and can be studied for activity against SARS-CoV-2 as well. These findings give a clue to investigate and find the structure-based drug designing in the development of newer drug moieties against the COVID-19.

Echinacea

Echinacea is a plant genus belongs to the family *Asteraceae* and is comprised of 11 of herbaceous and flowering plants. *Echinacea* preparations are generally used for preventing and alleviating the symptoms of bacterial and viral infections. Furthermore, some *Echinacea* preparations are known to exert antioxidant and anti-inflammatory and potential immunomodulatory activities. *Echinacea*, a native plant of North America, is widely used to prevent or to provide early treatment for the common cold. Studies with *Echinacea* lend plausibility to the idea that herbs somehow stimulate the immune system and numerous clinical trials have documented the beneficial effects of *Echinacea* preparations. Kumar, et al. showed that *Echinacea* can enhance immune function by increasing immunoglobulin production [4]. Furthermore, this herb might regulate antibody production by enhancing both Th1 and Th2 cytokine production. One pharmacodynamics study showed significant bronchodilatory and anti-inflammatory effects of *Echinacea* complex that was like the effects of classic synthetic drugs. Thus, this herb in traditional medicine used as a treatment for allergic disorders of the airways, such as asthma and may improve the bronchopulmonary illness [21].

Foeniculum vulgare

Foeniculum vulgare universally known as Fennel is a medicinal plant belonging to the Umbelliferae (*Apiaceae*) family, used by humans since ancient times, due to its flavor. It was cultivated nearly in every country. A series of studies revealed that *F.*

vulgare effectively controls numerous infectious ailments of bacterial, fungal, viral, mycobacterium, and protozoal origin. It has antioxidant, antitumor, chemo preventive, cytoprotective, hepatoprotective, hypoglycemic, and oestrogenic activities. Study done in 2014 showed that has a special kind of memory-enhancing impact and can reduce stress. Limited clinical trials as well as *in-vivo* studies showed that chronic use of *F. vulgare* is not harmful. Ethanol extract and essential oil from *F. vulgare* exhibited bronchodilatory activity on contracted tracheal chains of guinea pig and contributed to its relaxant effect on guinea pig tracheal chains.

Allium sativum

Allium sativum (Garlic) has been traditionally used for both gastronomic and medicinal purposes. Garlic is alleged to have antimicrobial, antifungal, antidiabetic and antiviral properties. It has properties to lower the cholesterol and triglyceride levels, reduce blood pressure, and slow down the development of atherosclerosis and act as an anticoagulant. Garlic extract alone or as an adjunct to classical antibiotics retains the great potential for the treatment of drug-sensitive as well as drug-resistant tuberculosis. Qin, et al. study has showed anti-carcinogenic and immunomodulatory effects. The exact usage of garlic for the common cold most likely varies countrywide [9]. A cross-sectional population study conducted in Australia in 2007 found that 10.7% of participants used garlic, 29.8% for cold, flu or fever. According to Chikhale, et al. in USA in 2004, 3.76% of the population used garlic supplements [12]. Since many manufacturers of garlic supplements claim their products enhance the immune system and support in the prevention and cure of the common cold. The pervasiveness of herbal medicine use seems to be relatively reliable between Western countries.

Tinospora cordifolia

Tinospora cordifolia (Giloy) is a member of *Menispermaceae* family, is a large, deciduous, shrub found all over India, particularly in the tropical parts soaring to an altitude of 300 m and also in some particular parts of China. Studies on the effects of natural immunomodulators to heal various diseases associated with the immune system have been increasing interest in recent years. *Tinospora* species have been one of the widely investigated plants for their effects on the immune system to treat various diseases related to immune health. However, their ethno pharmacological uses are mainly very limited. A range of active constituents derived from the plant like alkaloids, steroids, diterpenoid, lactones and glycosides have been isolated from the different parts of the plant like root, stem, leaves and whole plant. Nowadays these plants have more importance for research to preparing several dosage forms because of its medicinal properties like anti-diabetic, anti-periodic, anti-spasmodic, anti-inflammatory, antiarthritic, antioxidant, antiallergic, anti-stress, anti-leprotic, anti-malarial, hepatoprotective, immune-modulatory and anti-neoplastic activities. *T. cordifolia* encompasses several components that might affect the body [22]. Some of these constituents have antioxidant effects while others might boost the body's immune system. It aids to eliminate toxins and purifies blood, fights against bacteria, and

helps to recover fevers. It is an anti-pyretic herb; it can reduce signs and symptoms of several life-threatening conditions like Dengue, Swine Flu and Malaria as well. It helps to improve blood platelets in fever. It has been shown to decrease in the recurrent resistance of HIV virus thus improving the therapeutic outcome thus, revealing its promising role of application in management of the disease. Study published in 2012, confirmed that an immunomodulatory protein in *T. cardiofolia* stem showed lymphoproliferative and macrophage-activating properties strengthens the rationale of the use of its preparations in several ayurvedic medicines for immunomodulation.

Panax ginseng

Panax ginseng has been described as one of the most common herbal medicines used in humans. Ginseng extracts have been reported to elevate the production of inflammatory IL-6 and IL-8 cytokines and to increase antiviral cytokine Interferon (IFN) upon influenza virus infection in mice model. Active component of ginseng ginsenoside metabolite protopanaxatriol demonstrated significant inhibition effect on IP-10 production upon H9N2/G1 infection and it could protect endothelial cells from H9N2/G1-induced apoptosis and DNA damage. Ginseng ginsenoside compounds are transformed into pharmaceutically active components by the intestinal microbes during digestion. Fermented products of ginseng exhibited antimicrobial activity [23]. Most clinical trials disclosed that ginseng, at various dosages, is a safe and effective method of prophylaxis, reducing the symptoms and lowering the risk and duration of colds and flu. So, these findings suggest ginseng as a possible therapeutic agent for respiratory infections. Nevertheless, it has been well documented whether fermented ginseng extracts have antiviral activity, conferring *in vivo* safeguard against influenza virus.

Houttuynia cordata

Houttuynia cordata belongs to the family *Saururaceae*, is a traditional Chinese medicine used for hundreds of years 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. Recently, several studies also provided scientific data to support and unveil its anti-inflammatory, anti-allergic, virucidal, anti-oxidative and anti-cancer activities. *H. cordata* extract may decrease the process of viral replication by inhibiting the key enzymes and activate negative feedback control in the immune system. Recent study published in 2018, indicated that *H. cordata* improved lung and intestine injury generated by Influenza virus infection. Site of action of *H. cordata* is associated with inhibition of inflammation, protection of intestinal barrier and regulation of mucosal immunity. *H. cordata* may have clinical potential to treat viral infection and may use as an alternative medicine for human beings.

Glycyrrhiza glabra

Glycyrrhiza glabra (licorice), also known as mulethi and sweet wood, is native to the Mediterranean and certain areas of Asia. Licorice is a perennial herb, which has extensive pharmacological effects for human beings. The most common

medical use is for treating upper respiratory diseases including coughs, hoarseness, and sore throat. Licorice is effective against Human Respiratory Syncytial Virus (HRSV) infection on airway epithelial cells. It inhibited HRSV mainly by preventing viral attachment, internalization, and by stimulating IFN secretion. Licorice extracts have been used for more than 60 years in Japan to cure chronic hepatitis, and have therapeutic benefits against other viruses, including Human Immunodeficiency Virus (HIV), Cytomegalovirus (CMV), and Herpes simplex. Deglycyrrhizinated licorice formulations are useful in treating various types of ulcers, while topical licorice formulations have been used to smooth and heal skin eruptions, such as psoriasis and herpetic lesions.

Organum vulgare

Organum vulgare (Oregano) is a flowering plant belongs to family *Lamiaceae*, sometimes called wild marjoram known as sweet marjoram. It is native of Western and Southwestern Eurasia and the Mediterranean region. A wide range of pharmacological functions has been reported from this plant like antioxidant, antiplatelet, antifungal, antibacterial, antiprotozoal, anti-inflammatory, antiatherosclerosis, antitumor and antiulcer. Oregano oil and its active components, like carvacrol, found to have antimicrobial efficacy against numerous pathogenic bacterial species. Based on the studies, their antimicrobial efficacy is also broad-spectrum, as they are effective against MNV, a nonenveloped virus. These derived compounds appear to cause the viral capsid to lose its integrity by binding to the capsid or by preventing adsorption of the virus to host cells, thus true virus inactivation occurs. The antibacterial activity is slightly different due to the complexity of bacterial cell wall components and its structures; even so, there is some evidence that carvacrol acts directly upon bacterial membranes/cell wall components as well.

Rosmarinus officinalis

Rosmarinus officinalis (Rosemary), member of the mint family *Lamiaceae* that is widely native to in the Mediterranean region. This aromatic plant is used as a natural food preservative due to their antiseptic properties, besides their medicinal uses. Polyphenols derived from this aromatic plant have been used as natural antiviral agents, especially the flavonoids including quercetin, galangin, procyanidin and pelargonidin. The antiviral effects of these substances are higher when used before virus adsorption. While the antioxidant and antibacterial activities of this medicinal plant are variously described, its antiviral properties have been little investigated. Thus, we can presume that rosemary could be a rich source for bioactive components that can act as antibiofilm and antiviral agents against human pathogens.

Salvia

Salvia (Sage) is an important genus belongs to the family *Lamiaceae*, consisting of about 900 species. Many species of *Salvia*, including *Salvia officinalis* have been used as medicinal herbs worldwide. In traditional medicine, Sage is used for different diseases, including inflammation of the mouth and

throat. Extract of different species of salvia has been checked for their biological activities like antimicrobial, antioxidant, anti-inflammatory, antimutagenic, antiviral, spasmolytic, cancer preventive and cholinergic binding properties [21]. These mechanisms are partially described in some scientific studies. Antiviral action of the ubiquitous human pathogens was assessed against to fourteen salvia species extracts. It is also published that it works against virus disease like HSV-1, it has been also reported that extract of *S.coccinia* shows anti-HSV-1 activity. Salvia species have pharmacological activities especially targeting cardiovascular, renal, hepatic and immune systems diseases [22].

Zinger officinale

Zinger officinale (Ginger) belongs to family Zingiberales, is originated in Islands of Southeast Asia but now it is transported all over the world from Asia. This is one of the classic examples holding unique therapeutic significance and its bioactive molecules used as an immune booster and can control the extent of gastric, colorectal, liver, ovarian and skin cancers. Concealed humoral and cellular immune reactions through direct inhibition of sensitize T and B lymphocytes. An Intraperitoneal injection of ginger extract diminishes ectoxin, and IL-4, IL-5 levels along with a decrease in eosinophils to the lung. The ginger and its bioactive molecules provide protection against hepatotoxicity induced through ethanol, bromobenzene, and acetaminophen *via* modulation of enzymes [11,23]. The anti-inflammatory potential of ginger will be helpful for the management of disorders like respiratory infections. It can also protect our body from hazardous effects of chemicals; it has been highlighted in several scientific investigations [24,25].

Torreya nucifera

The Japanese torreya (*Torreya nucifera*) belongs to a family *Taxaceae*. It is a coniferous evergreen tree native to southern Japan and to South Korea's Jeju Island. Lipid metabolism studies have been done on the composition of the essential oils of the coniferous trees; some have been done on the medicinal values of *Torreya nucifera*. It has been used traditionally as a remedy for various diseases in Asian country. More than ten phytochemicals isolated from the leaves of *Torreya nucifera* were shown the anti SARS-CoV activity by inhibiting 3CLpro activity from the ethanol extracts of the leaves of *T. nucifera*. It could well be the choice of medicinal herbs in these directions, to control the COVID-19 infection [26].

Isatis indigotica

The root of *Isatis indigotica* belonging to the family Cruciferae, popularly as Ban-Lan-Gen is used as a traditional Chinese medicine for influenza, epidemic hepatitis, and inflammatory disease with redness of skin, sore throat, etc,[27]. As one of the popular herbal medicines, the root of *I. indigotica* has been documented in Chinese Pharmacopoeia since 1985 and its purified extracts have been formulated for clinical use (Ministry of Public Health, Chinese Pharmacopoeia (English Version), Part I, Chemical Industry Press, Beijing, 2000). *I. indigotica* root and phenolic Chinese herbs were frequently used for the

prevention of SARS in China, Hong Kong, and Taiwan. Some studies are there which shows antiviral activity of *I. indigotica*, so this medicinal plant can be used as antiviral treatment of COVID-19 [28].

Cannabis

Cannabinoid (CBD) is also a possible treatment for severe COVID-19 patients. Studies published in 2020 showed that cannabinoids were also used as a treatment to control the inflammatory response of COVID-19 virus. It is designed in an injectable drug form to help a serious syndrome occurs in severe cases of coronavirus "Acute Respiratory Distress Syndrome (ARDS)" [29]. This syndrome can be triggered during a cytokine storm a dangerous over-elevation of cytokines, which signal the body to produce more inflammation. It will have the advantage of impacting several pro-inflammatory signaling pathways, by enhancing the effectiveness of the drug to rapidly dampen the cytokines release and prevent the acute outcomes like ARDS. Which can be linked to drowning as the lungs fill with fluid [14]? Now, cannabinoid is designed as synthetic injectable drug named, ARDS-003, has been approved for the phase I clinical trial by FDA, it will proceed by Tetra Biopharma. Initially FDA asserted that the nonclinical was appropriate to support for starting study in COVID-19 infected patients.

A literature search was done to investigate medicinal plants, which can be used in treating COVID-19. These medicinal plants with antiviral and other important properties are present in the available literature with a high level of studies; but there have been very limited Randomized Clinical Trials (RCTs). Though, it can be observed that comprehensive chemical and pharmacological review of numerous bioactive constituents have anti-viral, anti-inflammatory, immune boosters, and hold other unique therapeutic significance activities [17]. Cohort studies and controlled trials should be done to warrant their pharmacological applications [30].

MULTIFUNCTIONAL, CONJUGATED THERAPY BY POLYHERBAL FORMULATION FOR COVID-19

Most of the studies in traditional medicine, executed are based on the single herbal active constituent. But polyherbal formulations more important and interesting than monotherapeutic herbal preparation that are commonly used because of the synergistic effect. Herb-herb combinations have been used in Chinese medicine practice for thousands of years. The pharmacological principles of polyherbal work together in a dynamic way to generate maximum therapeutic efficacy with minimum side effects. The increasing interest in the use of plant-based formulations is leading to a fast-growing market for Ayurvedic medicines [31]. In the Ayurvedic system of medicine mainly polyherbal compounds are used for the treatment of various infections. Many of them under clinical trials in COVID-19 patients. The Ministry of AYUSH (Government of India) and TCM has listed out some formulations and recommended their use as prophylactic measure. The future goal in the successful treatment of COVID-19 must be given

herbs to make polyherbal preparations that must maintain a normal respiratory function with minimal risk of severing hypoxemic respiratory episodes. Drugs prescribed for the treatment of COVID-19 reduces fever, cough and fatigue either by increasing immunity, reducing toxins in the body, or preventing the virus from fusing to the cell by blocking a receptor to facilitate the binding of virus to the cell. The systematic advancement carries with it the progress in Ayurvedic polyherbal formulation, through the study of various phytoconstituents and finding of useful herbs combinations, which can work synergistically to treat COVID-19.

CONCLUSION

The COVID-19 pandemic all over the world has led to the high-priority search for herbal therapies that work effectively. Herbal medicine is intended to exhibit therapeutic outcomes by attacking multiple diseases causing a module simultaneously. However, it is still a challenge for researchers to untangle the complex biological mechanisms and underlying material basis of herbal medicine. Along with this, there is no magic bullet available among herbs that can decrease the high level of COVID-19 infection in a short period time, so there is a need for awareness regarding the use of raw material, crude extract, or isolated compounds to promote to prevent infection. In nutshell, this review is exploring to build a systems-biology platform to investigate the molecular active compounds, with a typical example applied to an herbal formula in the treatment of COVID-19.

CONFLICT OF INTEREST

Authors declare no conflict of interest regarding authorship and publication of this review.

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