



"HERBAL MMEDICINE USAGE FOR THE TREATMENT OF COVID-19 PANDEMIC"

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Abstract

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is the cause pandemic of coronavirus disease 2019 (COVID-19). For many thousands of years, herbal products and dietary plants have been prescribed for various diseases by traditional healers. Thus, this paper aimed to present main herbal products, their source, characteristics, and potential antiviral actions concerning COVID-19. Publications on herbal products related to antiviral effects were searched from different databases, such as Web of Science, Google Scholar, Medline, Scopus, and PubMed, until August 2021, using English key terms. According to different studies, there are so many important medicinal plants with antiviral activity, which can be used for viral infections or can be prescribed as supportive treatment. lack of information on the safety profile and amount of dose for different diseases is some of the limitations of medicinal plants. herbal medicine can interfere with COVID-19 patho genesis by inhibiting SARS-CoV-2 replication and entry to host cells. Some of the antiviral medicinal plant species are citrus Spp., orange (C. Sinensis), Allium sativum, Allium cepa, mentha piperita, and nigella sativa are the most desirable herbal drink or fruit that can introduce effective adjuvant components in COVID-19 management. In addition to many herbs or plants that can help relieve the symptoms of Covid 19, such as: curcumin, thyme, cloves, garlic, onions, and more.

Keywords: Herbal medicine, COVID-19 Pandemic.

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I. introduction

The COVID-19 pandemic originated in Wuhan, China, the cause for this virus is a novel coronavirus, called severe acute respiratory syndrome coronavirus, which is one of the known viruses of the Coronaviridae family capable of infecting humans. According to World Health Organization, there are over (193) million confirmed cases and over 4 million deaths. The disease is mainly transmitted through close contact with infected individuals via respiratory droplets from either sneezing or coughing. The virus shows various unspecific symptoms, ranging from mild to severe. Fever (98%) is the most frequent manifestation that is reported by patients, followed by cough (76%), myalgia or fatigue (44%), sputum production (28%), and headache (8%). Even though there are vaccines produced for COVID 19 by different manufacturing industries, people in the community and researchers are trying to find the best way to cure the disease, including herbal medicine (Lin, & Myeong, 2022).

Structure of SARS-Cove-. SARS-Cove, is one of the viruses that belong to coronaviruses, +e common coronavirus is a positive single-strand RNA virus (+ssRNA) that belongs to the order Nidovirales, family Coronaviridae, and subfamily Orthocoronavirinae. is specific coronavirus is divided into four genera: α , β , γ , and δ , each genus is further divided based on the characteristics of its subtype, genome, and phylogenetic clustering. At present, six types of coronavirus infect humans. +us, SARS-CoV-2 has become the seventh of coronavirus that can infect humans (Aucoin, 2021).

SARS-Cove and the Middle East respiratory syndrome coronavirus (MERS-Cove) are coronaviruses that infect humans. Both SARS-Cove and MERS-Cove belong to the β genus that is a predecessor for the SARS-Cove-2. +e other types of human coronavirus are 229E and NL63 that belong to the α genus and also OC43 and HKU1 that belong to the β genus is novel SARS-CoV-2 has a ~30 kb long RNA, which is the same length found in SARS-Cove and MERS-Cove that caused problem several years ago. +is novel virus has a genome-sequence similarity of 96% and 79.5%, respectively, with a known bat coronavirus and SARS-Cove (Chilot, & Alem, 2021)

Another study indicated that this virus had a genome-sequence similarity of about 45%–90% with SARS-Cove and a lower similarity of about 20%–60% for MERS-Cove, taken together, this SARS-Cove-2 has a less distant genomic sequence with a known bat coronavirus and SARS-Cove, but it has more distance with MERS-Cove.

Coronavirus is a type of virus that has an envelope, which is round or oval and is often pleomorphic. +e diameter of this virus is about 50–200 nm. SARS-CoV2 has a unique, club-shaped spike projection on the surface of the virus, which makes this virus look like a solar corona, +ere are four major structural proteins encoded by this novel coronavirus are the spike (S), membrane (M), envelope (E), and nucleocapsid (N) proteins. +e S protein is the most important structure that can bind with the receptor. +is glycoprotein is located on the surface of the virus and mediates the attachment to the host cell's receptor (Aucoin, 2021).

II. Available Therapy for COVID-19

A definitive therapeutic agent for managing COVID-19 has not been recommended for humans until now. Current preventive and treatment efforts for COVID-19 have focused on developing vaccines and specific therapeutic agents targeting SARS-Cove-2 +e preventive method that could potentially hamper the spread of diseases is vaccination. A vaccine for COVID19 involves the active immunization of the vaccine components to induce the production of neutralizing antibodies specific to the SARS-CoV-2 antigen. +e target antigen of the antibody is the S protein found on the surface of the virus. Some experimental studies have shown that giving the full-length S protein may induce the release of a protective antibody by blocking the binding of the virus with the ACE2 receptor [19]. Clinical testing of this vaccine is being conducted by some investigators from the National Institute of Allergy and Infectious Diseases-Vaccine Research Center (Belachew & Tsegaye, 2021).

There are some potential therapeutic agents for COVID19 management, such as antiviral agents, chloroquine/ hydroxychloroquine, dexamethasone, and convalescent plasma transfusion, but most of them still show inconsistent results. Several antiviral agents are under investigation as a treatment for COVID-19. Remdesivir is one of the antiviral agents that used for COVID-19 and known as an adenosine analogue that can be merged into viral RNA chains resulting in their early termination. Davies et al. studied about the systematic benefit-risk assessment of remdesivir in the treatment of COVID-19, but is study showed that there might be a favourable benefit-risk profile for remdesivir compared with placebo in severe cases of COVID-19 infection. +ere is still a need for benefit and safety data for remdesivir to provide further studies. Wang et al. reported that remdesivir exhibited a promising effect in vitro. However, a randomised, double

blind, placebo-controlled, multicenter clinical trial of remdesivir was stopped early because of serious adverse events among the treatment and control groups. They also reported that the results were not associated with a difference in time to clinical improvement. Moreover, the further investigation suggested that remdesivir did not significantly reduce the mortality risk of the patients (8%) compared with the placebo group (11.6%), and NIAID ended the trial because of the insufficient benefit results and unethical issues (Getnet & Edmund, 2021).

III. Herbal medicine usage for COVID-19

The world was relying on self-care practices that include the use of traditional medicine, traditional medicine is gaining attention for the design and development of novel anti-infective that might have been used in the prevention and treatment of infectious agents. Complementary and Alternative Medicine (CAM) is a set of practices that are not fully integrated into the modern healthcare system and include herbal products, animal products, spiritual healers, yoga, and relaxation techniques, the practice has been used throughout the world for centuries to prevent and treat chronic and acute illnesses including, respiratory tract infections. The immunity of patients plays an essential role in COVID-19. Therefore, Herbal and traditional medicines having immunomodulatory effects could be potential candidate for preventive and treatment of COVID-19 patients. (Shujie & Zhangfeng, 2021).

During the early stage of the disease, the community was consuming herbal medicines containing certain active substances, which have antimicrobial or antiviral, anti-inflammatory and immunostimulatory activities, such as Echinacea, Quinine, and Curcumin. These herbal compounds are assumed to modulate the immune system of patients, and they might have beneficial effects on preventing or treating COVID-19 there are limited clinical trials on the effectiveness of traditional medicines in the prevention and treatment of COVID-19. However, collecting patient's views and experiences of using traditional medicine in COVID-19 is essential for future practice. Collecting data on common information queries received in community pharmacies, other medical institutions, and Internet forums will help develop evidencebased information. These interns support effective consultation and communication practices for patients, There are theoretical approaches suggesting ACE2 (Angiotensin Converting Enzyme 2) could be one target for managing the COVID-19 infection.¹⁰ Plant extracts showed an inhibitory effect on ACE.

Cerasus avium (L.) Moench, *Alcea digitata* (Boiss.) Alef, and *Rubia tinctorum* L, inhibit ACE up to 100%. *Citrus aurantium* L.; *Berberis integerrima* Bge *Peganum harmala* L. and *Allium sativum* L inhibit the enzyme up to 70% or more (Shujie & Zhangfeng, 2021).

A review by the British organization Cochrane that examined the results of alternative therapies used during the SARS epidemic suggested that in general combinations of herbal medicines complementary to conventional therapy do not lower mortality, but may improve quality of life; reduce the chances of deep lung infiltration, and the application of low doses of drugs such as corticosteroids. Different findings suggested that herbal medicine can reduce the severity and prevent COVID-19.

China and India use herbal. Chinese medicine showed appreciable results in improving clinical symptoms, reduce mortality, and recurrence rates in improving clinical symptoms, reduce mortality, and recurrence rates of the virus, previous studies revealed that Echinacea supplementation may be related to a reduced level of pro-inflammatory cytokines, and increase the anti-inflammatory cytokine, interestingly, curcumin has been revealed in-silico studies to prevent the entry of the SARS-CoV-2 into cells, and viral replication, while a recent experimental finding has shown that bromelain may also inhibit viral entry into cells (Silveira, 2020).

According to a saudian study published in the American Journal of Public Health Research, a group of researchers at Taibah University in Saudi Arabia confirmed the success of a treatment protocol for coronavirus patients that rely on herbs in accelerating the recovery process for patients and raising their immunity to confront the virus when infected. The researchers also made herbal sprays for the topical treatment of pneumonia or bronchial pneumonia that affects severe cases of corona, and they confirmed that this spray helps protect pulmonary tissue and has antiviral effects, especially for patients with bad breath, and they indicated that *Nigella sativa* works to enhance immunity. Chamomile exerts tissue protection effects and inhibits viral replication to the greatest extent (Silveira, 2020).

With the publication of this study, some doctors have used it to support the immunity of coronavirus patients, while following other treatment protocols. Dr. Amr Al-Rashidi, director of the Sohag Fever Hospital, announced on his Facebook page the success of this herbal recipe in accelerating the recovery of 3 cases of Corona patients after supporting their immune system in parallel with their intake of the treatment protocol

followed in the Ministry of Health hospitals with Corona patients.

Furthermore, potential specific antiviral agents such as the decoy mini protein CTC, 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 such as SARS-Cove-evidence supports that herbal medicine may be effective in reducing and managing the risk of COVID 19 (Ni, 2020).

The usage of herbal medicine as an alternative remedy for Corvid 19. combination with modern medicine, and has released several recon emendations on herbal therapy Since many botanical drugs show antiviral efficacy, the use of herbal medicine for therapeutic purposes should not be underestimated. Currently, well-known herbal medicines with antiviral activities are being used as an additional treatment to suppress SARS-Cove, since conventional treatments are still not well succeeded (Jebiril, 2019).

Traditional Chinese medicine seems to have revealed encouraging results in reducing the rate of mild, severe, overall mortality, and shortening total disease duration. When combined with

modern biomedicine, herbal medicines could exert antiviral; relieve chronic obstructive pulmonary disease and hypoxemia, immunoregulatory, and anti-inflammatory, activities, similarly, traditional medicines are used for the management of COVID-19 parallel with modern medicine and vaccinations in India (Shankar, 2020).

Some herbal medicine used in COVID-19 IV.

In the researches of herbal medicine single plant species have much medicinal value. It is now well understood that a single plant may contain a wide range of biochemical, making that study the pharmacologic value of plants is challenged, generally classified as antiviral, anti-inflammatory, immunomodulatory, and mixed-effects having more than one purpose based on valuable evidence for efficacy. On top of exhibiting direct antiviral effects, herbal drugs with reported 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, most likely related to cytokine storm, some examples of herbal medicine used in the management of COVID-19 are summarized in Table 1.

Table 1: Possible medicinal plants used for prevention and treatment of COVID-19.

Scientific name	Family name	Constituents	Mechanism/outcome
<i>Malva sylvestris</i> L.	Malvaceae	Polysaccharides	Tetrastigma hemsleyanum Diels & Gilg/Vitaceae Tetrastigma hemsleyanum Diels & Gilg/Vitaceae Emollient/potent antitussive activity
<i>Aloe barbadensis</i> Mill.	Asphodelaceae	HF1Z (polysaccharide)	Emollient/potent antitussive activity
<i>Salvia officinalis</i> L.	Lamiaceae	Polysaccharide	Emollient/potent antitussive activity
<i>Cynara scolymus</i> L.	Compositae	Cynaroside	ACE inhibition/IC50 = 49.7%
<i>Erigeron abajoensis</i> Cronquist	Compositae	Flavone (Scutellari)	ACE inhibition
<i>Hibiscus sabdariffa</i> L.	Malvaceae	Anthocyanins	ACE inhibition/decrease serum angiotensin- converting enzyme, decrease plasma aldosterone
<i>Hancornia speciosa</i> Gomes	Apocynaceae	Chlorogenic acid	ACE inhibition
<i>Isatis indigotica</i>	Brassicaceae	Phenol (indigo, sinigrin, aloe emodin, hesperetin, Sinigrin), 2,2- indolyl)- 3-indolone, Phaitanthrin D	SARS-3CLpro inhibition/IC50 = 53.8 ± 4.2 µg/mL

<i>Alnus japonica</i> (Thunb.) Steud.	Betulaceae	Diarylheptanoid (Hirsutenone)	PLpro inhibition/IC50 = 4.1 μM
<i>Paulownia tomentosa</i> Steud.	Paulowniaceae	Geranylated flavonoids	PLpro inhibition/IC50 = 5.0–14.4 μM
<i>Torreya nucifera</i> (L.) Siebold & Zucc.	Taxaceae	Biflavone [Amentoflavone (9)], Authentic flavones (Apigenin)	SARS-3CLpro inhibition/62% at 100 μg/mL
<i>Citrus Spp.</i>	Rutaceae	Hesperetin, hesperidin, Neohesperidin	Rhoifolin, SARS-3CLpro inhibition in dose-dependent manner
<i>Psoralea corylifolia</i> L.	Fabaceae	Bavachinin, isobavachalcone, Omethylbavachalcone, corylifol A	neobavaisoflavone, 40 psoralidin, 38.4 μM) PLpro inhibition/dose dependent - manner (IC50 between 4.2 and 38.4 μM)
<i>Artemisia capillaries</i> Thunb.	Compositae	Capillarisin (flavone)	Decrease TNF-α, IL-1β, IL-1α, and IL-6/antipyretic
<i>Angelica decursiva</i>	Apiaceae	Columbianadin	Decrease IL-1β, NO/decrease airway inflammation
<i>Glycyrrhiza glabra</i> L.	Leguminosae	Arabinogalactan protein	Spasmolytic activity, protective effects on mucous/ # citric acid-induced cough Guinea pigs

V. The following is a brief explanation of what is stated in Table 1.

. *Gymnanthemum amygdalinum* 1

Vernonia amygdalina is mostly found in Asia and high tropical Africa countries. It is under the family (*Asteraceae*); an angiosperm of species classified as genus *Vernonia* that contains around 1000 species. It has shown immune-inducing effects as an adjunct to vaccines this plant was habitually used to relieve headache, fever, diarrhea, and cough, aqueous extracts of *G. amygdalina* showed positive effects in inducing a human immune response by increasing the levels of CD4⁺ and white blood cells.

As a plant contains different biochemical with the potential to exhibit a multimodal mechanism of action, ethanol, methanol, and acetone extracts also showed that anti-inflammatory activity in lab animals based on the modulation levels of inflammatory cytokines and mediators and anti-inflammatory markers. It is the ability to increase the number of CD4⁺ counts, this extract was showed an adjuvant to antiretroviral therapy in HIV patients. Furthermore, it has antimicrobial, antidiabetic, anti-allergic, antimalarial, antibacterial, anticancer, antifungal, antileukemia, analgesic, antipyretic, anthelmintic, hypolipidemic, hepatoprotective, and antioxidant properties. Despite the described strong activity of *G. amygdalina* maintaining the immune and inflammatory responses, the toxicity nature of these plants is ascertained. even though in an acute toxicity study done on animals there is no mortality reported. Currently, there is a lack of measurable evidence on the efficacy of this plant

in COVID-19 patients, despite several studies stated to have good antiviral, anti-inflammatory, and immunomodulatory effects (Vallianou, 2021).

. *Azadirachta indica* (neem)2

The main clinical symptom of COVID-19 is fever and to reduce it these plants have valuable outcomes. 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. The animal study and in-silico docking research confirmed that neem leaves extracts and their metabolic constituents such as flavonoids and polysaccharides have direct antiviral effects against different viruses including Hepatitis C Virus, specific to SARS-Cove-2, molecular docking research has demonstrated that neem-derived compounds such as nimbolin, nimocin, and cycloartenol can bind to the SARS-Cove-2 envelope (E), membrane (M), glycoproteins, and also inhibitory role. Its leaves have positive effects on immunoregulatory effects to boost immune response in animal's models. In mice vaccinated with Brucella Rev-1 vaccine, neem seed extract given subcutaneously boosted the production of IFN-γ post-vaccination (Panyod & Sheen, 2021). Neem seed extracts must be avoided in pregnant women as animal research its shown abortifacient effects. While clinical studies have reported its anti-human chorionic gonadotropin effects. Studies reported that the traditional purpose of neem for medicinal purposes mainly depends on

leaves consumption, boiled the leaves in the water, and drank. One of the main concerns is about safety, a clinical trial should be done to establishing safe doses of neem leaves specific to the formulation intended for use are required before further investigations on efficacy. Although neem leaves have been used traditionally for a long time, the toxicity profile is not well-documented. Clinical cases of acidosis and renal injury in the body system have also been reported on neem seed oil users. The main challenges of ethno pharmacological study for therapeutic claims are quality control, identification, and standardization of biomolecules on herbal products (Panyod S, & Sheen).

3. *Nigella sativa*

Based on our review, *N. Sativa* (black cumin) seed was one of the herbal products with the most published positive evidence. Ethanoic extracts of *N. Sativa* seeds established antiviral properties by reducing the viral load, alpha-fetoprotein, and enhanced liver function parameters among hepatitis C patients. In an animal study, its seed oil act as antiviral and immunomodulatory effects against cytomegalovirus, reducing viral loads to an unpredictable value. It can enhance the immune response by increasing CD3 and CD4 counts and also increase the release of interferon-gamma (IFN- γ) from Natural Killer T-cells and macrophages.

In mice studies, ethanoic extracts of *Nigella Sativa* seeds had confirmed anti-corona virus species of MHVA59 (mouse hepatitis virus-A59) replication mechanism by downregulating gene expressions of different leukocyte transient receptor proteins (TRP) like TRPA1, TRPC4, TRPM6, TRPM7, TRPM8, and TRPV4 genes. By tradition, it has a diverse range of indications including in upper respiratory diseases such as asthma by the anti-hypersensitivity and potent anti-inflammatory properties to reduce asthma symptoms. It has Positive experimental evidence of immunomodulatory and anti-inflammatory effects in separate review papers. for more safety, long-term consumption (up to three months) of *N. Sativa* seeds at 3 g/day in clinical studies reported not much significant side effect on both liver and kidney functions (Vallianou, 2021).

4. *Eurycoma longifolia*

Eurycoma longifolia is a popular plant traditionally used for improving men's health which is commonly found in Malaysian, it is one among a few natural products with established standardization and safety data available today. There are no direct antiviral effects of

standardized aqueous extract of *E. longifolia* that have been reported with clinical data but have positive effects in inducing immunity in the older population by increasing the number of CD4⁺ cells, with a safe dose of 200 mg/day. The same extract also showed low mammalian mutagenicity with no genotoxic effects.

5. *Mentha piperita*

Peppermint (*M. Pipe Rita*) is the oldest herbal remedy for different diseases 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 methane. 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 that use of peppermint during infection with COVID-19 was associated with lower odds of hospitalization (Lin & Myeong, 2022).

6. *Isatis indigotica*

Isatis indigotica. *indigotica*) comprises organic acids, lignans, alkaloids, nucleosides, flavonoids, steroids, and amino acids. Previous studies revealed that. *indigotica* possesses antibacterial, anti- inflammation, immunoregulatory, cholagogic, and antiviral effects. Prominently, it can inhibit various viruses, such as hepatitis B, influenza, herpes simplex, mumps, coxsackievirus, and cytomegalovirus. Clinically, it is often used to treat several viral diseases like parotitis, viral hepatitis, and viral influenza. Accordingly, *I. indigotica* may be helpful for the management of COVID-19. *indigotica* has the function of immune regulation, which supports its anti-virus effects in turn. Thus, *I. indigotica* may be effective for the management of COVID-though, this needs to be studied further associated with lower odds of hospitalization (Lin & Myeong, 2022).

Garlic (*Allium sativum*) and onion (*Allium cepa*) are commonly used as a home remedy in Ethiopia for different disease conditions. Onion, which has been used in traditional medicine for a long time to treat various conditions and infections, was obtained to destroy the avian influenza virus (H9N2). However, the method of preparations is a crucial role, as boiled or fried onions are fairly

ineffective. Researchers reported that onion is a good candidate to manage COVID-19 patients due to its anti-inflammatory, antithrombotic, and antiviral effects, 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 alliin are the major sulfur-containing compounds, while the principal sulfur-free active compounds include flavonoids and sapiens. Garlic's ability to inhibit the SARS-Cove-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) [48]. 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 (Lin & Myeong, 2022).

7. *Malva sylvestris*

Malva sylvestris is used for the treatment of respiratory diseases, such as and dry cough and pharyngeal or oral irritations. Chemical constituents of *Malva sylvestris* include flavonoids (e.g., delphinidin, apigenin, malvidin, myricetin, genistein, and derivatives, and kaempferol); Mucilage (mainly galacturonic acids and glucuronic, glucose, galactose, fructose, trehalose, and rhamnose); tannins, hydroxycinnamic acid and derivatives; benzoic acid and derivatives; monoterpenes. Preclinical evidence revealed that *Malva sylvestris* preparations have been studied for cough. The anti-tussive activity of its isolated rhamnogalacturonan and mucilage was assessed in cats. Both substances decreased the frequency of cough and suppressed the cough reflex, particularly in the laryngopharynx area. Another study exhibited analgesic effects and anti-inflammatory activity via in-vivo models. *Malva sylvestris* has been conventionally used as cough therapy and may be valuable in the management of COVID-19 symptoms through exerting a soothing effect on the respiratory tract.

8. *Isatis indigotica*

Isatis indigotica (*indigotica*) comprises organic acids, lignans, alkaloids, nucleosides, flavonoids, steroids, and amino acids. Previous studies revealed that *indigotica* possesses antibacterial, anti-inflammation, immunoregulatory, cholagogic, and antiviral effects. Prominently, it can inhibit various viruses, such as hepatitis B, influenza, herpes simplex, mumps, coxsackievirus, and cytomegalovirus. Clinically, it is often used to treat several viral diseases like parotitis, viral hepatitis, and viral influenza. Accordingly, *indigotica* may be helpful for the management of COVID-19. *indigotica* has the function of immune regulation, which supports its anti-virus effects in turn. Thus, *indigotica* may be effective for the management of COVID-19, though, this needs to be studied further (Lin & Myeong, 2022).

9. *Psoralea corylifolia*

Psoralea corylifolia L is used in Chinese medicine and traditional Ayurveda against different types of skin diseases, such as leukoderma, psoriasis, and leprosy. This plant is also known for its antimicrobial and anti-inflammatory activities. In a while, 6 aromatic constituents were isolated from seeds of *Psoralea corylifolia*, the isolated phytoconstituents inhibited the enzyme in a dose-dependent manner with IC₅₀ ranging from 4.2 to 38.4 μ M. Likewise, numerous natural products have revealed antiviral effects at nanomolar concentration against SARS-CoV (e.g., homoharringtonine, ouabain, lycorine, tylophorine, methoxycryptopleurine, and Silvestro). Clinical trials of a few herbal compounds against SARS-CoV-2-3CL^{Pro} aroused hope for plant-derived *anti-SARS-Cove-2* drugs. Very recently, 3CL protease inhibitor NLC-a plant product administered orally as a dietary supplement, got US FDA approval (Ang, 2022).

10. *Glycyrrhiza glabra*

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 active 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 SARS-CoV-2 but it can be at the expense of elevated cytotoxicity (Shujie & Zhangfeng, 2021).

VI. Conclusion and future perspectives

The use of herbal medicine is a potential platform for answering various types of COVID-19 virus management. 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 *Gymnanthemum*, *amygdalinum*, *Azadirachta indica*, *Nigella sativa*, and *Eurycoma longifolia* can be used. On the other hand, numerous herbal drugs such as *G. glabra*, *Thymus vulgaris*, *Allium sativum*, *Althea officinalis*, and ginseng may become effective in the preventive and supportive management of COVID-19 through boosting the immune system.

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