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Herbal medicine use for the management of COVID-19: A review article

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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, the aim of this review is 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 pathogenesis 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.

1. Introduction

The occurrence of coronavirus disease (COVID-19) has been stated as a pandemic by the World Health Organization (WHO) on March 12, 2020 [1]. It is a new viral disease caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which had not formerly affected humans. As of September 2021, more than 230,953,959 patients are infected and about 4,734,427 deaths were reported due to COVID-19 worldwide; the total number of cases and mortality in Ethiopia were 336,762 and 5,254, respectively [2].

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. currently, various type 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 [3].

Different findings suggested that herbal medicine can reduce the severity and prevent COVID-19 [3,4]. China and India use herbal

medicine with modern medicine parallelly to enhance the immunity of patients [5,6]. Traditional Chinese medicine showed appreciable results in improving clinical symptoms, reduce mortality, and recurrence rates of the virus [7]. Previous studies revealed that Echinacea supplementation may be related to a reduced level of pro-inflammatory cytokines TNF, IL-6, IL-8, and increase the anti-inflammatory cytokine IL-10 [8]. 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 [9]. 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 [10].

Herbal medicines have also helped to alleviate the effects of infectious diseases such as SARS-CoV-2. Evidence supports that herbal medicine may be effective in reducing and managing the risk of COVID-19. The use of herbal medicine as an alternative remedy for COVID-19 in

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combination with modern medicine, and has released several recommendations on herbal therapy [11]. 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-CoV-2, since conventional treatments are still not well succeeded [12].

In children, rhinorrhea, abdominal pain, and diarrhea are faced while the common symptoms are similar with adults [4]. Cases with comorbidities or older patients having (immunodeficiency, digestive, and endocrine disease cardiovascular, hypertension, HIV, respiratory (TB), cerebrovascular, etc...) are more predisposed to severe forms of viral cases [13,14]. In Ethiopia, the number of COVID-19 case are increasing rapidly. Health care facilities are more fragile and have poor infrastructure. To treat those comorbid conditions, in addition to the supportive treatment they use plant material. The elder people living in rural areas have more knowledgeable about herbal plants to treat COVID-19 [15].

The Ethiopian government had also used medicinal plants as an immunity inducer. But there is a piece of false information, regarding which type of medicinal plants are used for the disease. people are randomly using it to combat COVID-19 which may lead to adverse reactions. Thus, the aim of this review is to present main herbal products, their source, characteristics, and potential antiviral actions concerning COVID-19.

2. Current prevention of COVID-19

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 [7]. Similarly, traditional medicines are used for the management of COVID-19 parallel with modern medicine and vaccinations in India.

Based on the sign and symptoms of COVID-19 infection can be classified as "wet, heat, congestion", in the respiratory system. According to Chinese traditional medicine, lung function is the first affected part of the body. "Wet" refers to the factor with sticky and high turbidity that can lead to prolong the disease severity and damage the body function. "Hot" refers to the factor with hot, dry, and rising turbidness that can lead to the virus. "Congestion" is a contributing factor that can affect blood circulation and cause symptoms such as pain [16]. China to protect respiratory function. a kind of prevention value is chosen because of the nature of viral condition by using Yupingfeng San. it is an ancient herbal medicine in China that contains three types of plants: Astragalus can (improve lung function), Fangfeng (to relieve the pathogen), and Atractylodes (enhance the spleen function and digestion and absorption of our body function). studies have shown that Yupingfeng San could optimally regulate the body's immune function [15].

In this background, home preparations, like the use of medicinal plants supported by the relevant establishments can serve as an alternative option to combat COVID-19 in Ethiopia. Some medicinal products such as garlic, ginger, turmeric, chili, lemon, hot water with salt would be used for viral suppression.

2.1. Treatment of mild infection of COVID-19

COVID-19 Patients with mild infection often have a fever, headache, sweat, thirst, dry cough, sore throat, red tongue tip, and floating pulse. Based on the management it is different from a severe case of the disease. According to theories of Traditional Chinese Medicine, they used the method of two types of prescriptions, "clearing lung heat and dampness" to treat the lung. In China classified into two Sangju yin and Yinqiao san, which are commonly used in clinical management. The main purpose is to clear lung heat, expel, relieve cough, regulate the patient's lungs and restore normal respiratory function. Clinically, in China patients who had a high fever used Yinqiao san, and patients who had a severe cough used Sangju yin [16]. A study done on different herbal supplements showed that ginger, lemon/orange, vitamin C, honey, black seed, costus have a significant impact on COVID-19 management [17].

2.2. Treatment of severe infection of COVID-19

In the early course of COVID-19 management, if the infection cannot be easily controlled, respiratory failure, multiple organ failure, and death will be worsened, then serious infection should be considered. These infectious patients have the following main manifestations: highgrade fever, dry cough, breathing difficulty, sweating, chest stiffness, fatigue, nausea, bloating, red or dark red tongue, yellow coating, and oily. Some of the preventive and supportive management of COVID-19 through tempering the immune system *G. glabra, Thymus vulgaris, Allium sativum, Althea officinalis, and ginseng* may become effective [15].

3. Some herbal medicine used in COVID-19

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 wide range of biochemicals, making that study the pharmacologic value of plants is challenged [18]. 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 [19]. Some examples of herbal medicine used in the management of COVID-19 are summarized in Table 1.

3.1. Gymnanthemum amygdalinum

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 [20]. Aqueous extracts of *G. amygdalina* showed positive effects in inducing a human immune response by increasing the levels of CD4⁺ and white blood cells [21,22].

As a plant contains different biochemicals 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 [21-23]. Furthermore, it has antimicrobial, antidiabetic, anti-allergic, antimalarial, antibacterial, anticancer, antifungal, antileukemia, analgesic, antipyretic, anthelmintic, hypolipidemic, hepatoprotective, and antioxidant properties [19,23]. 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 [22,23].

Table 1

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

Scientific name	Family name	Constituents	Mechanism/outcome	References
Malva sylvestris L.	Malvaceae	Polysaccharides	Tetrastigma hemsleyanum Diels &	[54]
			Gilg/Vitaceae	
			Tetrastigma hemsleyanum Diels &	
			Gilg/Vitaceae	
			Emollient/potent antitussive activity	
Aloe barbadensis Mill.	Asphodelaceae	HF1Z (polysaccharide)	Emollient/potent antitussive activity	[54]
Salvia officinalis L.	Lamiaceae	Polysaccharide	Emollient/potent antitussive activity	[54]
Cynara scolymus L.	Compositae	Cynaroside	ACE inhibition/IC50 = 49.7%	[65,66]
Erigeron abajoensis	Compositae	Flavone (Scutellari	ACE inhibition	[67]
Cronquist				
Hibiscus sabdariffa L.	Malvaceae	Anthocyanins	ACE inhibition/decrease serum angiotensin-	[68]
			converting enzyme, decrease plasma aldosterone	
Hancornia speciosa	Apocynaceae	Chlorogenic acid	ACE inhibition	[69]
Gomes				
Isatis indigotica	Brassicaceae	Phenol (indigo, sinigrin, aloe emodin, hesperetin, Sinigrin), 2,2-	SARS-3CLpro inhibition/IC50 = 53.8 \pm 4.2 $\mu g/mL$	[70]
		Di (3-indolyl)- 3-indolone, Phaitanthrin D		
Alnus japonica (Thunb.)	Betulaceae	Diarylheptanoid (Hirsutenone)	PLpro inhibition/IC50 = 4.1 μ M	[71]
Steud.				
Paulownia tomentosa	Paulowniaceae	Geranylated flavonoids	PLpro inhibition/IC50 = $5.0-14.4 \ \mu M$	[72]
Steud.				
Torreya Nucifera (L.)	Taxaceae	Biflavone [Amentoflavone (9)], Authentic flavones (Apigenin)	SARS-3CLpro inhibition/62% at 100 µg/mL	[73]
Siebold & Zucc.				
Citrus Spp.	Rutaceae	Hesperetin, hesperidin Rhoifolin, Neohesperidin	SARS-3CLpro inhibition in dose-dependent manner	[74]
Psoralea corylifolia L.	Fabaceae	Bavachinin, neobavaisoflavone, isobavachalcone, 40	PLpro inhibition/dose dependent manner (IC50	[59]
		-Omethylbavachalcone, psoralidin, corylifol A	between 4.2 and 38.4 µM)	
Artemisia capillaries Thunb.	Compositae	Capillarisin (flavone)	Decrease TNF- α , IL-1 β , IL-1 α , and IL-6/antipyretic	[75]
Angelica decursiva.	Apiaceae	Columbianadin	Decrease IL-1β, NO/decrease airway inflammation	[76]
Glycyrrhiza glabra L.	Leguminosae	Arabinogalactan protein	Spasmolytic activity, protective effects on mucous/	[77]
	-		# citric acid-induced cough Guinea pigs	

3.2. Azadirachta indica (neem)

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 [25]. 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 [26]. Specific to SARS-CoV-2, molecular docking research has demonstrated that neem-derived compounds such as nimbolin, nimocin, and cycloartenol can bind to the SARS-CoV-2 envelope (E), membrane (M), glycoproteins, and also inhibitory role [27]. Its leaves have positive effects on immunoregulatory effects to boost immune response in animals models [28]. In mice vaccinated with Brucella Rev-1 vaccine, neem seed extract given subcutaneously boosted the production of IFN- γ post-vaccination [24]. neem seed extracts must be avoided in pregnant women as animal research its shown abortifacient effects [29]. while clinical studies have reported its anti-human chorionic gonadotropin effects [30]. Studies reported that the traditional purpose of neem for medicinal purposes mainly depends on leaves consumption, boiled the leaves in the water, and drank [31]. 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 [32]. The main challenges of ethnopharmacological study for therapeutic claims are quality control, identification, and standardization of biomolecules on herbal products.

3.3. Nigella sativa

Based on our review, N. Sativa (black cumin) seed was one of the herbal products with the most published positive evidence. Ethanolic

extracts of N. Sativa seeds established antiviral properties by reducing the viral load, alpha-fetoprotein, and enhanced liver function parameters among hepatitis C patients [33]. 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-y) from Natural Killer T-cells and macrophages [34]. In mice studies, ethanolic 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 [34–36]. 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. However, precautions should be paid for hypoglycemia and hepatic enzyme instabilities due to thymoquinone at high doses of 2-3 g/kg [37,38].

3.4. Eurycoma longifolia

Eurycoma longifolia is a popular plant traditionally used for improving men's health which is commonly found in Malaysian [39]. 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 [40]. The same extract also showed low mammalian mutagenicity with no genotoxic effects [41].

Preclinical evidence of the anti-inflammatory properties of *E. longifolia* is also available. from the strong anti-inflammatory

bioactive compounds extracted from E. longifolia include eurycomalactone, 1-4-1-5β-dihydroklaieanone, and 1-3-2-1 dehydroeurycomanone with potent NF-kB inhibitory effects [41]. Different phenolic components are obtained from the roots of E. longifolia were also reported to significantly decrease the expression of IL-6 in lipopolysaccharide-stimulated RAW macrophage [42]. The safety profile of the standardized aqueous extract of E. longifolia (acute, subacute, and 90 days sub-chronic general toxicity studies) conducted based on the standard of Organization for Economic Co-operation and Development (OECD) guidelines indicate that there are no toxic effects in animals [43]. E. longifolia has well-documented evidence about the safety profile, further investigations on the potential anti-inflammatory effects of E. longifolia may be discovered in the context of COVID-19 treatment and prevention mechanisms [44]. In conclusion, Gymnanthemum amygdalina, Azadirachta indica, Nigella sativa, and Eurycoma longifolia are the medicinal plants that may have a potentially beneficial role in COVID-19 prevention and treatment.

3.5. Mentha piperita

Peppermint (*M. Piperita*) 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 Gramnegative and Gram-positive bacteria, yeast, and fungi, mainly as a result of the presence of the abundant phytochemicals menthol and menthone [45]. 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 [17].

3.6. Allium sativum and Allium cepa

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) [46]. 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 [47]. 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 saponins [17]. 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 [17]. 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 [49].

3.7. Malva sylvestris

Malva sylvestris is used for the treatment of respiratory diseases, such

as and dry cough and pharyngeal or oral irritations [50,51]. 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 [52]; hydroxycinnamic acid and derivatives; benzoic acid and derivatives; monoterpenes [53]. 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 [54]. Another study exhibited analgesic effects and anti-inflammatory activity via in-vivo models [55]. *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.

3.8. Isatis indigotica

Isatis indigotica (I. indigotica) comprises organic acids, lignans, alkaloids, nucleosides, flavonoids, steroids, and amino acids. Previous studies revealed that I. indigotica possesses antibacterial, antiinflammation, immunoregulatory, cholagogic, and antivirus 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. I. 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-19, though, this needs to be studied further [56].

3.9. 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 [57]. This plant is also known for its antimicrobial and anti-inflammatory activities [58]. In a while, 6 aromatic constituents were isolated from seeds of Psoralea corylifolia [59]; 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, 7-methoxycryptopleurine, and Silvestro) [60]. Clinical trials of a few herbal compounds against SARS-CoV-2-3CL^{Pro} aroused hope for plant-derived *anti*-SARS-CoV-2 drugs. Very recently, 3CL protease inhibitor NLC-001, a plant product administered orally as a dietary supplement, got US FDA approval [61].

3.10. Glycyrrhiza glabra

Glycyrrhizin, also called glycyrrhizic acid (GLR), is a triterpenoid saponin mainly isolated from the roots (Glycyrrhizae Radix) of the plant Glycyrrhiza [62]. 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 [62]. 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 [62]. 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 [63]. 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 [64].

4. 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 biochemicals 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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CRediT authorship contribution statement

Chilot Abiyu Demeke: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Roles/Writing – original draft, Writing – original draft, Writing – review & editing, Software, Supervision, Validation, Visualization. Alem Endashaw Woldeyohanins: Conceptualization, Data curation, Investigation, Methodology, Project administration, Resources, Roles/Writing – original draft, Writing – original draft, Writing – review & editing, Software, Supervision, Validation, Visualization. Zemene Demelash Kifle: Roles/ Writing – original draft, Writing – review & editing, Writing – original draft.

Declaration of competing interest

The author declares that they have no competing interests.

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C.A. Demeke et al.

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