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## Therapeutic potential of medicinal plants and their bioactive compounds in the prevention, treatment and management of COVID-19: A comprehensive review on traditional and pharmacological interventions

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### Abstract

The COVID-19 pandemic has intensified the search for effective treatment options, including the use of medicinal plants and their bioactive compounds. Traditional medicine has long relied on herbal remedies for managing respiratory infections, and recent research suggests that certain plant-derived compounds exhibit antiviral, anti-inflammatory, and immunomodulatory properties relevant to COVID-19. This review explores the therapeutic potential of medicinal plants in the prevention, treatment, and management of COVID-19, highlighting both traditional and pharmacological interventions. Key bioactive compounds, such as flavonoids, alkaloids, polyphenols, and terpenoids, have demonstrated antiviral activity against SARS-CoV-2 through mechanisms including inhibition of viral entry, replication, and modulation of the immune response. Despite promising preclinical studies, challenges such as standardization, quality control, and the need for rigorous clinical trials remain significant barriers to widespread adoption. Regulatory considerations also impact the integration of herbal medicine into mainstream healthcare. Future research should focus on validating the efficacy and safety of medicinal plants through well-designed clinical studies while promoting collaboration between traditional medicine practitioners and modern healthcare professionals. By bridging traditional knowledge with scientific advancements, medicinal plants could serve as complementary therapeutic options for COVID-19, contributing to more holistic and accessible healthcare solutions.

### 1. Introduction

The COVID-19 pandemic, caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), emerged as a significant global health crisis. First identified in December 2019 in Wuhan, China, the virus rapidly spread worldwide, leading the World Health Organization (WHO) to declare it a pandemic on March 11, 2020. This crisis had far-reaching effects on health, economics, and societies, reshaping governance and daily life. The virus primarily spreads through respiratory droplets, causing symptoms ranging from mild flu-like conditions to severe pneumonia, respiratory failure, and death (Huang *et al.*, 2020). High-risk populations include older adults and individuals with pre-existing conditions such as diabetes and cardiovascular diseases (Zhou *et al.*, 2020). In response, governments implemented measures such as lockdowns, social distancing, and mask mandates to curb transmission (Anderson *et al.*, 2020).

Healthcare systems faced immense pressure, struggling with shortages of medical supplies, intensive care unit (ICU) beds, and healthcare personnel (Ranney *et al.*, 2020). Efforts were made to expand healthcare capacity, enhance personal protective equipment (PPE) production, and scale up testing and contact tracing (Rasmussen *et al.*, 2021). The crisis underscored the importance of a robust public health infrastructure and emergency preparedness (Gates, 2020). Economically, the pandemic led to widespread business closures, rising unemployment, and disrupted supply chains (Baldwin and Weder di Mauro, 2020). Governments introduced financial relief programs, while global organizations like the International Monetary Fund (IMF) and World Bank provided economic assistance (Ozili and Arun, 2020). The education sector also experienced significant disruptions, with many institutions transitioning to online learning, exacerbating educational disparities (Dhawan, 2020). Mental health concerns rose due to lockdowns and uncertainty, increasing cases of anxiety and depression (Xiong *et al.*, 2020). Healthcare workers faced extreme stress and burnout, prompting initiatives to enhance mental health support (Shaukat *et al.*, 2020). A major turning point in the pandemic response was the rapid development of vaccines, such as those by Pfizer-BioNTech and Moderna (Polack *et al.*, 2020). However, challenges such as vaccine distribution inequities and

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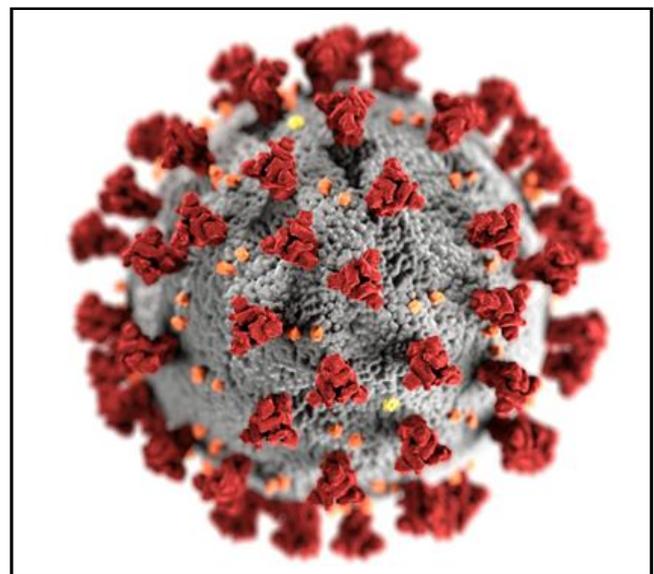
emerging variants like Delta and Omicron necessitated ongoing adjustments, including booster doses and continued monitoring (Karim and Karim, 2021). The pandemic highlighted the need for global cooperation, with organizations like the WHO and Centers for Disease Control and Prevention (CDC) playing key roles, despite challenges posed by misinformation and geopolitical tensions (Mheidly *et al.*, 2020). Lessons from COVID-19 emphasize the necessity of stronger healthcare systems and preparedness for future pandemics (Fineberg, 2020).

In addition to conventional treatments and vaccines, alternative and complementary therapies gained attention for their potential role in symptom management, immune enhancement, and overall well-being. While these therapies do not replace standard medical care, they offer supportive benefits, particularly for those seeking holistic approaches (Ang *et al.*, 2020). Herbal medicine became an area of interest, as certain medicinal plants exhibit antiviral and immune-boosting properties. For example, turmeric (*Curcuma longa*) contains curcumin, known for its anti-inflammatory and antiviral effects, potentially inhibiting viral replication and modulating immune responses (Hewlings and Kalman, 2017). Ginger (*Zingiber officinale*) is another widely used medicinal plant with immune-stimulating and anti-inflammatory properties that may help alleviate symptoms associated with COVID-19 (Rahman *et al.*, 2021). Echinacea, a traditional remedy, has been studied for its potential to enhance immune function and mitigate respiratory infections due to its bioactive compounds with antiviral activity (Ogal *et al.*, 2021). Licorice root (*Glycyrrhiza glabra*) contains glycyrrhizin, which has demonstrated antiviral properties by inhibiting viral entry and replication, making it a candidate for complementary COVID-19 management (Cinat *et al.*, 2003). Traditional Chinese Medicine (TCM) formulations, such as Lianhua Qingwen, have been utilized to alleviate symptoms like fever, cough, and respiratory distress (Hu *et al.*, 2021). These formulations include a blend of medicinal plants with antiviral and anti-inflammatory properties, supporting their potential role in symptom relief and recovery (Yang *et al.*, 2020).

Acupuncture, a traditional Chinese practice, was explored for its potential to support respiratory function, reduce inflammation, and enhance overall health (Liu *et al.*, 2021). Some patients reported symptomatic relief and improved well-being with its use, although further scientific validation is required (Zhang *et al.*, 2020). Aromatherapy and essential oils, such as eucalyptus and peppermint, were also used to aid respiratory health and provide relief from congestion and cough (Ben-Arye *et al.*, 2021). These natural remedies were often incorporated into holistic care approaches to complement mainstream treatments. Despite the promising benefits of alternative and complementary therapies, their integration into COVID-19 management requires rigorous scientific validation through clinical trials (Ang *et al.*, 2020). Standardized dosages, safety profiles, and potential interactions with conventional treatments must be carefully assessed (Teschke *et al.*, 2020). Collaborative research efforts are essential to identify the most effective plant-based therapies and optimize their application in infectious disease management (Patwardhan *et al.*, 2020). As the world continues to combat COVID-19 and prepare for future health crises, exploring diverse therapeutic options may contribute to a more comprehensive and resilient healthcare system.

## 2. Pathophysiology of COVID-19 and potential targets for herbal intervention

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is an enveloped, single-stranded RNA virus belonging to the Coronaviridae family (Zhou *et al.*, 2020). Structurally, the virus has a spherical shape with spike (S) proteins protruding from its surface, giving it a crown-like appearance under an electron microscope (Walls *et al.*, 2020). The genome of SARS-CoV-2 is approximately 30 kilobases in length, encoding several structural and non-structural proteins that facilitate infection and replication (Wu *et al.*, 2020). The viral structure consists of four main proteins: spike (S), envelope (E), membrane (M), and nucleocapsid (N) (Masters and Perlman, 2020). The spike protein is crucial for host cell entry, as it binds to the angiotensin-converting enzyme 2 (ACE2) receptor found on human cells (Hoffmann *et al.*, 2020). The membrane protein plays a role in virus assembly, while the envelope protein contributes to viral budding and pathogenesis (Schoeman and Fielding, 2019). The nucleocapsid protein is responsible for packaging the viral RNA and is involved in regulating replication and transcription (Kim *et al.*, 2020). The infection process begins when the spike protein of SARS-CoV-2 binds to the ACE2 receptor on the surface of host cells, primarily in the respiratory tract (Yan *et al.*, 2020). This interaction is facilitated by the receptor-binding domain (RBD) located on the S1 subunit of the spike protein (Wrapp *et al.*, 2020). After binding, the virus undergoes conformational changes, leading to the cleavage of the spike protein by host proteases such as transmembrane protease serine 2 (TMPRSS2) or cathepsin L (Bestle *et al.*, 2020). This cleavage activates the S2 subunit, which enables the fusion of the viral envelope with the host cell membrane, allowing viral RNA to enter the cytoplasm (Matsuyama *et al.*, 2020).



**Figure 1: Schematic representation of SARS-CoV-2 virus particle. (Photo credit: <https://unsplash.com/s/photos/covid-19>.)**

Once inside the host cell, SARS-CoV-2 releases its positive-sense RNA genome, which is immediately translated by the host ribosomes to produce non-structural proteins (NSPs) (Kovski *et al.*, 2021). These NSPs form the replication-transcription complex (RTC) within double-membrane vesicles derived from the endoplasmic reticulum.

(Snijder *et al.*, 2020). The RTC facilitates the synthesis of viral RNA through a process called discontinuous transcription, generating subgenomic RNAs that encode structural proteins (Thiel *et al.*, 2003). The newly synthesized viral RNA and proteins assemble into new virions within the host cell. The structural proteins S, M and E integrate into the endoplasmic reticulum-Golgi intermediate compartment (ERGIC), where they interact with the nucleocapsid to form complete viral particles (Fehr and Perlman, 2015). These virions are then transported to the cell membrane and released through exocytosis, allowing them to infect neighbouring cells and spread throughout the body (Astuti and Ysrafil, 2020).

The immune response to SARS-CoV-2 involves both innate and adaptive mechanisms (Blanco-Melo *et al.*, 2020). The virus can evade initial immune detection by suppressing interferon responses, allowing it to establish infection (Lei *et al.*, 2020). As the infection progresses, the immune system activates T cells and B cells to eliminate the virus (Sekine *et al.*, 2020). However, in severe cases, an excessive immune response known as a cytokine storm can occur, leading to widespread inflammation and tissue damage, particularly in the lungs (Mehta *et al.*, 2020). Understanding the structure and mechanism of infection of SARS-CoV-2 is crucial for developing effective treatments and vaccines (Krammer, 2020). Targeting key viral proteins, such as the spike protein, has been the focus of vaccine development, leading to the production of mRNA vaccines that stimulate the immune system to recognize and neutralize the virus before it causes severe illness (Polack *et al.*, 2020).

## 2.1 Molecular targets in viral pathogenesis and inflammation

Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) interacts with several molecular targets in the human body to facilitate infection and pathogenesis. Understanding these key targets, including angiotensin-converting enzyme 2 (ACE2), transmembrane protease serine 2 (TMPRSS2), the cytokine storm, and oxidative stress, is essential for developing effective therapeutic strategies (Hoffmann *et al.*, 2020; Shang *et al.*, 2020).

### 2.1.1 ACE2 (Angiotensin-converting enzyme 2)

ACE2 is a crucial receptor that mediates SARS-CoV-2 entry into human cells (Li *et al.*, 2003). It is widely expressed in the respiratory tract, particularly in the alveolar epithelial cells of the lungs, as well as in the heart, kidneys, and intestines (Zou *et al.*, 2020). The spike (S) protein of SARS-CoV-2 binds to the extracellular domain of ACE2, enabling viral attachment (Walls *et al.*, 2020). This interaction triggers conformational changes that facilitate viral entry through membrane fusion or endocytosis (Yan *et al.*, 2020). ACE2 normally plays a protective role in regulating blood pressure and inflammation by converting angiotensin II into angiotensin-(1-7), a molecule with anti-inflammatory and vasodilatory properties (Imai *et al.*, 2005). However, SARS-CoV-2 binding reduces ACE2 expression, leading to an imbalance in the renin-angiotensin system (RAS), increased inflammation, and tissue damage (Vaduganathan *et al.*, 2020). This loss of ACE2 function is associated with severe lung injury and complications in COVID-19 patients (Kuba *et al.*, 2005).

### 2.1.2 TMPRSS2 (Transmembrane protease serine 2)

TMPRSS2 is a protease that plays a critical role in SARS-CoV-2 entry by cleaving and activating the spike protein (Hoffmann *et al.*, 2020). This activation is necessary for viral fusion with the host cell membrane, facilitating the direct release of viral RNA into the

cytoplasm (Shen *et al.*, 2021). TMPRSS2 is highly expressed in the respiratory epithelium and is co-expressed with ACE2 in lung and airway cells (Bertram *et al.*, 2012). Inhibiting TMPRSS2 with protease inhibitors, such as camusat mesylate, has been explored as a potential therapeutic approach to block viral entry and reduce disease severity (Hoffmann *et al.*, 2020; Zhou *et al.*, 2015). Since TMPRSS2 is not essential for normal physiological functions, targeting this protease offers a promising antiviral strategy with minimal adverse effects (Stopsack *et al.*, 2020).

### 2.1.3 Cytokine storm

A cytokine storm is an excessive immune response characterized by the uncontrolled release of pro-inflammatory cytokines, such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- $\alpha$ ), and interleukin-1 beta (IL-1 $\beta$ ) (Mehta *et al.*, 2020). In severe COVID-19 cases, hyperactivation of the immune system leads to widespread inflammation, organ dysfunction, and acute respiratory distress syndrome (ARDS) (Moore and June, 2020). The excessive cytokine production damages lung tissues, resulting in severe respiratory failure (Huang *et al.*, 2020). Treatments targeting cytokine storms, such as IL-6 inhibitors (tocilizumab) and corticosteroids (dexamethasone), have been used to modulate the immune response and reduce inflammation in critically ill patients (Stone *et al.*, 2020).

### 2.1.4 Oxidative stress

Oxidative stress occurs when there is an imbalance between reactive oxygen species (ROS) production and the body's antioxidant defence (Delgado-Roche and Mesta, 2020). In COVID-19, oxidative stress contributes to inflammation, endothelial dysfunction, and tissue damage (Chernyak *et al.*, 2020). Increased ROS levels promote cytokine release, worsening the inflammatory response and lung injury (Suhail *et al.*, 2020). Antioxidants, such as vitamin C, N-acetylcysteine (NAC), and glutathione, have been investigated for their potential to mitigate oxidative stress and improve patient outcomes (Silvagnoet *et al.*, 2020; Horowitz *et al.*, 2021). Reducing oxidative stress may help alleviate inflammation and support recovery in COVID-19 patients (Cecchini and Cecchini, 2020).

## 3. Ethnopharmacology in COVID-19 management

Ethnopharmacology, which explores traditional medicinal practices and their biologically active compounds, has garnered significant attention in the context of COVID-19 management. Many traditional healing systems, including Ayurveda, Traditional Chinese Medicine (TCM), and Unani medicine, have been investigated for their potential in boosting immunity, alleviating symptoms, and supporting post-infection recovery (Ang *et al.*, 2020; Patwardhan *et al.*, 2020). Herbal remedies with immunomodulatory, antiviral, and anti-inflammatory properties have been particularly studied for their role in mitigating the effects of COVID-19 (Tillu *et al.*, 2020; Rastogi *et al.*, 2020). Notable medicinal plants such as *Withania somnifera* (Ashwagandha), *Tinospora cordifolia* (Giloy), *Curcuma longa* (Turmeric), and *Glycyrrhiza glabra* (Licorice) have been explored for their therapeutic properties in reducing inflammation and modulating immune responses (Balkrishna *et al.*, 2020; Yang *et al.*, 2020). Additionally, ethnopharmacological approaches integrate lifestyle modifications, dietary interventions, and mind-body practices like yoga and meditation to promote overall well-being and manage stress, which is crucial for immune resilience (Nambi *et al.*, 2021). While many traditional medicines have demonstrated therapeutic potential, further

scientific validation, standardization, and large-scale clinical trials are necessary to establish their efficacy and safety in the management of COVID-19 and other emerging infectious diseases (Patwardhan *et al.*, 2020; Zhang and Liu, 2020).

### 3.1 Ayurveda in COVID-19 management

Ayurveda, an ancient Indian medical science, is based on the principles of balancing bodily energies (Doshas: Vata, Pitta, and Kapha) and emphasizes natural healing through herbs, diet, and lifestyle modifications. During the COVID-19 pandemic, Ayurvedic formulations were explored for their potential to enhance immunity, alleviate symptoms, and mitigate post-viral complications (Tillu *et al.*, 2020). Various herbs, such as Ashwagandha (*Withania somnifera*), Giloy (*Tinospora cordifolia*), Turmeric (*Curcuma longa*), and Tulsi (*Ocimum sanctum*), have been extensively studied for their immunomodulatory, antiviral, and anti-inflammatory properties (Balkrishna *et al.*, 2020; Rastogi *et al.*, 2020). Ashwagandha, known for its adaptogenic properties, has shown promise in reducing stress-related immunosuppression and enhancing overall immune response (Chandrasekhar *et al.*, 2012). Giloy, revered in Ayurveda as Amrita (nectar of immortality), has been recognized for its role in modulating cytokine storms and reducing inflammation (Vikaspedia, 2020). Curcumin, the active component in turmeric, possesses potent antiviral and anti-inflammatory activities, which have been suggested to aid in controlling respiratory distress and oxidative stress in COVID-19 patients (Di Matteo *et al.*, 2020). Tulsi, a widely used medicinal plant, has demonstrated antiviral properties against respiratory pathogens and supports lung health by reducing congestion and inflammation (Pattanayak *et al.*, 2010). Additionally, Ayurvedic formulations like Chyawanprash, a polyherbal preparation rich in Vitamin C and antioxidants, have been traditionally consumed to enhance immunity and resistance against infections (Tiwari *et al.*, 2021). Herbal decoctions (Kadha), a blend of medicinal spices and herbs, were widely recommended during the pandemic for their expectorant and immune-boosting properties (Tillu *et al.*, 2020). Furthermore, Ayurveda integrates yoga and pranayama (breathing exercises) to improve lung function, reduce stress, and enhance overall vitality, which proved beneficial in managing long-COVID symptoms and respiratory complications (Nambi *et al.*, 2021). Clinical studies and pharmacological investigations have provided scientific validation of many Ayurvedic interventions, supporting their role as adjunct therapies in COVID-19 management (Ang *et al.*, 2020). Despite the promising outcomes, challenges such as standardization of herbal formulations, quality control, and large-scale clinical trials remain key areas for further research (Patwardhan *et al.*, 2020). The integration of Ayurveda with modern medicine through interdisciplinary research can potentially provide a complementary approach to tackling emerging infectious diseases, including COVID-19. The pandemic has underscored the relevance of traditional knowledge systems, highlighting Ayurveda's potential in preventive healthcare and holistic well-being. Moving forward, a concerted effort towards evidence-based validation and regulatory frameworks can further establish Ayurveda as a credible and globally accepted medical system in managing viral diseases and strengthening public health resilience (Tillu *et al.*, 2020).

### 3.2 Traditional Chinese medicine in COVID-19 management

Traditional Chinese Medicine (TCM) has been widely utilized in China and other parts of the world for managing COVID-19, offering

a complementary approach to conventional treatments. Rooted in the principles of balancing Yin and Yang, regulating Qi (vital energy), and expelling pathogenic factors, TCM integrates herbal medicine, acupuncture, dietary therapy, and mind-body practices such as Tai Chi and Qigong (Wu *et al.*, 2021). Various classical and modernized herbal formulations have been extensively studied and recommended in China for their potential antiviral, anti-inflammatory, and immunomodulatory effects (Huang *et al.*, 2021). Lianhua Qingwen, a well-known TCM formulation composed of herbs such as Forsythia (Lianqiao), Honeysuckle (Jinyinhua), and Ephedra (Mahuang), has demonstrated efficacy in reducing fever, cough, and lung inflammation in COVID-19 patients (Hu *et al.*, 2021). QingfeiPaidu decoction, another widely used herbal combination, has shown promising results in clearing lung infections, improving oxygen saturation, and reducing disease severity (Zhao *et al.*, 2020). Astragalus (Huangqi) has been recognized for its immune-boosting properties, enhancing antiviral defenses by modulating cytokine activity (Yang *et al.*, 2021). Licorice (Gancao), known for its antiviral and anti-inflammatory properties, has been used to soothe respiratory symptoms and prevent excessive immune reactions, which are linked to severe COVID-19 cases (Moung *et al.*, 2021). Clinical trials and meta-analyses suggest that TCM, when integrated with conventional antiviral and supportive therapies, can reduce hospitalization duration, alleviate symptoms, and lower mortality rates in COVID-19 patients (Zhou *et al.*, 2021). Despite these promising findings, challenges such as standardization, quality control, herb-drug interactions, and large-scale clinical trials remain critical for ensuring the global acceptance of TCM in infectious disease management. Further interdisciplinary research combining TCM principles with modern pharmacology is needed to validate its safety and efficacy, making it a viable complementary strategy for addressing COVID-19 and other emerging viral diseases (Wang *et al.*, 2022).

### 3.3 Unani and Siddha medicine in COVID-19 management

Unani and Siddha medicine, two traditional healing systems with deep historical roots, have been explored for their potential role in managing COVID-19. Unani medicine, based on the principles of balancing bodily humors blood, phlegm, yellow bile, and black bile utilizes herbal formulations, mineral-based drugs, and dietary modifications to enhance immunity and combat infections (Rahman *et al.*, 2021). Several Unani preparations, such as Joshanda (herbal decoction), Qurs-e-Suhanjana (Moringa-based tablets) and Khamira Marwareed (a pearl-based tonic), have been investigated for their immunomodulatory, anti-inflammatory, and antiviral properties (Siddiqui *et al.*, 2021). Similarly, Siddha medicine, an ancient South Indian system, relies on herbs, minerals, and lifestyle interventions for disease management (Subramanian *et al.*, 2021). Siddha formulations like Kabasura Kudineer, a polyherbal decoction containing ingredients such as *Andrographis paniculata* and *Clerodendrum serratum*, were widely recommended for respiratory health and immune support during the pandemic (Narayanawamy *et al.*, 2021). Both Unani and Siddha emphasize preventive healthcare, detoxification, and holistic well-being, integrating herbal remedies, dietary practices, and breathing exercises. While preliminary studies suggest promising therapeutic potential, further scientific validation through clinical trials is necessary to establish their efficacy and safety in COVID-19 management (Mukherjee *et al.*, 2021).

### 3.4 African and Indigenous medicinal practices in COVID-19 management

African and Indigenous medicinal practices have been explored for their potential role in managing COVID-19 through the use of traditional herbal remedies, immune-boosting therapies, and holistic healing approaches. Many African traditional medicines incorporate plants with antiviral, anti-inflammatory and immunomodulatory properties, such as *Artemisia annua* (Sweet wormwood), *Zingiber officinale* (Ginger), *Allium sativum* (Garlic) and *Azadirachta indica* (Neem) (Tugume *et al.*, 2021). Some Indigenous communities have also relied on medicinal plants like *Echinacea purpurea*, *Uncaria tomentosa* (Cat's Claw) and *Lippia javanica* (Fever tea) for respiratory support and immune enhancement (Mongalo *et al.*, 2021). These practices often integrate herbal decoctions, steam inhalation, and dietary interventions to manage symptoms and promote recovery. Additionally, spiritual and ritualistic healing methods, including energy-based therapies and community support systems, play a crucial role in Indigenous health practices (Chinsebu, 2020). While traditional medicine has shown promise in alleviating symptoms and strengthening immunity, further scientific validation, standardization, and integration with modern healthcare systems are necessary to establish their efficacy and safety in COVID-19 management (Semenya *et al.*, 2021).

### 4. Medicinal plants as antiviral agents and immunomodulators

Medicinal plants have been widely studied for their antiviral and immunomodulatory properties, offering a natural and holistic approach to disease management (Table 1). The selection of medicinal plants for therapeutic use is based on several criteria, including

traditional knowledge, bioactive compound composition, pharmacological efficacy, and safety profiles (Ogbole *et al.*, 2018). Plants with a long history of medicinal use and documented antiviral activity are prioritized for research and application. Scientific validation through *in vitro*, *in vivo*, and clinical studies further supports their effectiveness (Yuan *et al.*, 2016). The presence of bioactive compounds such as alkaloids, flavonoids, terpenoids and polyphenols is another critical factor in determining their antiviral and immunomodulatory potential (Kaul *et al.*, 2021). These phytochemicals exhibit various mechanisms of action, including inhibiting viral entry and replication, modulating the immune response, and reducing inflammation (Goyal and Sharma, 2019). Numerous medicinal plants have demonstrated potent antiviral activity against a range of pathogens, including respiratory viruses like influenza, coronaviruses, and herpesviruses. *Andrographis paniculata*, commonly known as *Andrographis*, contains andrographolide, a bioactive compound that exhibits strong antiviral effects by inhibiting viral replication and modulating immune responses (Coon and Ernst, 2004). *Glycyrrhiza glabra* (Licorice) is another well-known antiviral plant, with glycyrrhizin showing inhibitory effects against SARS-CoV and other viruses by interfering with viral replication and modulating cytokine production (Cinatl *et al.*, 2003). *Artemisia annua* (Sweet wormwood) has gained attention for its antiviral properties, particularly due to artemisinin and its derivatives, which have been explored for their potential use in viral infections (Tu, 2016). *Curcuma longa* (Turmeric) contains curcumin, which exhibits antiviral activity through multiple pathways, including suppression of viral replication and inhibition of inflammatory responses (Mathew and Hsu, 2018). *Echinacea purpurea*, widely used in traditional medicine, enhances immune function and has shown effectiveness against respiratory viruses (Schapowal *et al.*, 2015).

**Table 1: Some of the important medicinal plants and their medicinal properties**

Common name	Scientific name	Family	Origin	Medicinal properties	Reference
Turmeric	<i>Curcuma longa</i> L.	Zingiberaceae	South Asia	Anti-inflammatory, Immunomodulatory, Antiviral	Aggarwal <i>et al.</i> , 2007
Ginger	<i>Zingiber officinale</i> Roscoe	Zingiberaceae	South Asia	Antiviral, Anti-inflammatory, Supports respiratory health	Bode and Dong, 2011
Ashwagandha	<i>Withania somnifera</i> (L.) Dunal	Solanaceae	India, Middle East	Adaptogenic, Immunomodulatory, Antistress	Mishra <i>et al.</i> , 2000
Echinacea	<i>Echinacea purpurea</i> (L.) Moench	Asteraceae	North America	Immunostimulant, Antiviral, Anti-inflammatory	Hudson, 2016
Garlic	<i>Allium sativum</i> L.	Amaryllidaceae	Central Asia	Antiviral, Antibacterial, Immune boosting	Ankri and Mirelman, 1999
Licorice	<i>Glycyrrhiza glabra</i> L.	Fabaceae	Mediterranean, Asia	Antiviral, Anti-inflammatory, Respiratory support	Fiore <i>et al.</i> , 2008
Holy Basil	<i>Ocimum sanctum</i> L.	Lamiaceae	India, SE Asia	Adaptogenic, Antiviral, Anti-inflammatory	Cohen, 2014
Andrographis	<i>Andrographis paniculata</i> (Burm.f.) Nees	Acanthaceae	India, Sri Lanka	Antiviral, Immunostimulant, Antipyretic	Coon and Ernst, 2004
Ginseng	<i>Panax ginseng</i> C.A. Mey.	Araliaceae	East Asia	Immunomodulatory, Anti-fatigue, Cognitive enhancer	Shergis <i>et al.</i> , 2013
Neem	<i>Azadirachta indica</i> A.Juss.	Meliaceae	Indian Subcontinent	Antiviral, Antibacterial, Detoxifying	Subapriya and Nagini, 2005
Aloe Vera	<i>Aloe barbadensis</i> Mill.	Asphodelaceae	North Africa	Antiviral, Skin healing, Gut health	Surjushe <i>et al.</i> , 2008

Black Cumin	<i>Nigella sativa</i> L.	Ranunculaceae	South Asia, Middle East	Antiviral, Antioxidant, Anti-inflammatory	Salem, 2005
Green Tea	<i>Camellia sinensis</i> (L.) Kuntze	Theaceae	China, India	Antiviral, Antioxidant,	Chacko <i>et al.</i> , 2010
Cat's Claw	<i>Uncaria tomentosa</i> (Willd. ex Schult.) DC.	Rubiaceae	South America	Immunomodulatory, Anti-inflammatory, Antiviral	Sandoval <i>et al.</i> , 2000
Elderberry	<i>Sambucus nigra</i> L.	Adoxaceae	Europe, North America	Antiviral, Supports respiratory health, Immune boosting	Krawitz <i>et al.</i> , 2011
Indian Gooseberry	<i>Phyllanthus emblica</i> L.	Phyllanthaceae	India, SE Asia	Immunomodulatory, Antioxidant, Liver health	Baliga and Dsouza, 2011
Guduchi	<i>Tinospora cordifolia</i> (Willd.) Miers	Menispermaceae	India	Immunomodulatory, Antipyretic, Adaptogenic	Mathew and Kuttan, 1999
Astragalus	<i>Astragalus membranaceus</i> (Fisch.) Bunge	Fabaceae	China, Mongolia	Immunostimulant, Antiviral, Supports longevity	Block and Mead, 2003
Sea Buckthorn	<i>Hippophae hamnoides</i> L.	Elaeagnaceae	Eurasia	Antioxidant, Immune Boosting, skin health	Olas, 2016
Pau d'Arco	<i>Tabebuia impetiginosa</i> (Mart. ex DC.)	Bignoniaceae	South America	Antiviral, Antifungal, Anti-inflammatory	Park <i>et al.</i> , 2005
Moringa	<i>Moringa oleifera</i> Lam.	Moringaceae	South Asia, Africa	Antiviral, Anti-inflammatory	Anwar <i>et al.</i> , 2007
Sutherlandia	<i>Lessertia frutescens</i> (L.) Goldblatt	Fabaceae	South Africa	Immunostimulant, Antiviral, Anticancer properties	Tai <i>et al.</i> , 2004
Dandelion	<i>Taraxacum officinale</i> F.H.Wigg.	Asteraceae	Europe, Asia	Antiviral, Detoxifying, Liver support	Schutz <i>et al.</i> , 2006
Olive Leaf	<i>Olea europaea</i> L.	Oleaceae	Mediterranean	Antiviral, Antioxidant, Cardio-protective	Lee-Huang <i>et al.</i> , 2003
Rosemary	<i>Rosmarinus officinalis</i> L.	Lamiaceae	Mediterranean	Antiviral, Anti-inflammatory, Cognitive enhancer	Oliveira <i>et al.</i> , 2019
Cinnamon	<i>Cinnamomum verum</i> J. Presl	Lauraceae	South Asia	Antiviral, Antibacterial, Blood sugar regulation	Sheng <i>et al.</i> , 2010
Oregano	<i>Origanum vulgare</i> L.	Lamiaceae	Mediterranean	Antiviral, Antifungal, Immune boosting	Nostro <i>et al.</i> , 2004
Baikal Skullcap	<i>Scutellaria baicalensis</i> Georgi	Lamiaceae	China, Russia	Antiviral, Anti-inflammatory, Neuroprotective	Kim <i>et al.</i> , 2002
Fenugreek	<i>Trigonella foenum-graecum</i> L.	Fabaceae	Mediterranean, Asia	Antiviral, Antidiabetic, Anti-inflammatory	Kassaian <i>et al.</i> , 2009

The immunomodulatory effects of medicinal plants play a crucial role in their therapeutic potential. Many medicinal plants enhance the body's natural defence mechanisms by stimulating the production of immune cells, modulating cytokine levels, and reducing excessive inflammation (Liu *et al.*, 2018). *Withania somnifera* (Ashwagandha) is well known for its adaptogenic and immunomodulatory properties, helping to balance immune responses and reduce stress-induced immunosuppression (Chandrasekhar *et al.*, 2012). *Tinospora cordifolia* (Giloy) has been extensively used in traditional medicine for its ability to enhance immune function by increasing macrophage activity and modulating pro-inflammatory cytokines (Saha and Ghosh, 2012). *Ocimum sanctum* (Tulsi), often referred to as Holy Basil, supports immune function through its antimicrobial, anti-inflammatory, and

adaptogenic properties (Pattanayaket *et al.*, 2010). *Zingiber officinale* (Ginger) and *Allium sativum* (Garlic) also contribute to immune enhancement by modulating inflammatory pathways and exhibiting antimicrobial effects (Sharma *et al.*, 2016). The therapeutic potential of medicinal plants in antiviral and immune-boosting applications underscores the importance of integrating traditional knowledge with modern scientific research. While many medicinal plants show promising effects, further studies are required to standardize formulations, determine optimal dosages, and assess potential interactions with conventional medicines (Ekor, 2014). As research continues to validate the efficacy of these natural remedies, medicinal plants may play a significant role in complementing existing antiviral therapies and strengthening immune resilience against emerging infectious diseases (Newman and Cragg, 2020).

## 5. Bioactive compounds from medicinal plants and their pharmacological actions for COVID-19

Bioactive compounds derived from natural sources have been extensively studied for their potential pharmacological actions against COVID-19. Alkaloids, such as berberine, possess significant antiviral properties by inhibiting viral entry, replication, and inflammatory responses. Berberine has been found to suppress the expression of pro-inflammatory cytokines, thereby mitigating the cytokine storm associated with severe COVID-19 cases (Imenshahidi and Hosseinzadeh, 2019). Additionally, berberine interacts with viral proteins, potentially disrupting viral RNA synthesis and modulating host immune responses (Shi *et al.*, 2020). Flavonoids like quercetin exhibit broad-spectrum antiviral activity through their ability to inhibit viral enzymes, modulate immune responses, and exhibit antioxidant properties that counteract oxidative stress caused by SARS-CoV-2. Quercetin has been shown to interfere with viral replication by inhibiting key proteins like 3CL-protease and RNA-dependent RNA polymerase (RdRp) (Colunga Biancatelli *et al.*, 2020). Research also suggests that quercetin can improve cellular antiviral defences by modulating the ACE2 receptor, which SARS-CoV-2 utilizes for entry (Derosa *et al.*, 2021). Terpenoids, such as artemisinin, are known for their antimalarial effects but also exhibit antiviral and immunomodulatory properties that can be beneficial in COVID-19 management. Artemisinin and its derivatives can modulate host immune responses, suppress inflammatory cytokines, and potentially disrupt viral replication (Krishna *et al.*, 2004). Moreover, studies indicate that artemisinin derivatives can inhibit SARS-CoV-2 replication through interference with viral proteins and host metabolic pathways (Cao *et al.*, 2020). Polyphenols, including curcumin, have demonstrated strong anti-inflammatory, antiviral, and antioxidant properties. Curcumin can inhibit viral attachment, modulate immune signalling pathways, and prevent the excessive inflammatory response that leads to severe lung damage in COVID-19 patients. Additionally, its ability to regulate nuclear factor-kappa B (NF- $\kappa$ B) and downregulate cytokine production makes it a promising candidate for therapeutic applications (Jena *et al.*, 2021). The antiviral action of curcumin is also linked to its interaction with viral envelope proteins, preventing viral-host cell fusion (Zahedipour *et al.*, 2020). Saponins and other secondary metabolites also exhibit antiviral activities through immune modulation and membrane disruption. Many saponins can enhance the immune response, acting as vaccine adjuvants or direct antiviral agents by interfering with viral membrane integrity (Sun *et al.*, 2021). Additionally, certain saponins, such as glycyrrhizin from licorice, have been shown to inhibit SARS-CoV-2 replication by modulating host cell signalling pathways and reducing viral load (Fiore *et al.*, 2008). Other secondary metabolites from medicinal plants have been explored for their potential role in targeting viral proteins, modulating host immune defences, and reducing inflammation (Zhang *et al.*, 2020). Studies suggest that resveratrol, a stilbene, exhibits anti-SARS-CoV-2 activity by modulating inflammatory pathways and reducing oxidative stress (Yang *et al.*, 2020). Similarly, epigallocatechin gallate (EGCG), a major catechin in green tea, has been identified as a potential antiviral agent due to its ability to bind viral proteins and modulate immune responses (Ohgitani *et al.*, 2021). As the pandemic continues to evolve, identifying and developing bioactive compounds with potent antiviral and immunomodulatory properties remains a crucial area of investigation. By integrating these natural compounds with existing

therapeutic strategies, researchers hope to improve patient outcomes and develop effective, accessible treatments against COVID-19 and emerging viral threats (Lee-Huang *et al.*, 2023).

## 6. Mechanisms of action against SARS-CoV-2

The mechanisms by which various bioactive compounds act against SARS-CoV-2 involve multiple pathways, targeting different stages of viral infection and host immune responses. One of the primary mechanisms is the inhibition of viral entry and replication, which prevents SARS-CoV-2 from infecting host cells and multiplying. The virus enters human cells primarily through the angiotensin-converting enzyme 2 (ACE2) receptor, with the help of the transmembrane serine protease 2 (TMPRSS2), which facilitates spike (S) protein activation (Hoffmann *et al.*, 2020). Certain bioactive compounds, such as flavonoids (*e.g.*, quercetin) and polyphenols (*e.g.*, curcumin), have been found to bind to ACE2 and viral spike proteins, thereby blocking viral attachment and entry into host cells (Goswami *et al.*, 2021; Wang *et al.*, 2020). Additionally, some terpenoids, including artemisinin and its derivatives, have shown potential in inhibiting viral replication by targeting key viral enzymes like 3-chymotrypsin-like protease (3CLpro) and RNA-dependent RNA polymerase (RdRp) (Cao *et al.*, 2021). These enzymes are crucial for viral replication and transcription, and their inhibition leads to a reduction in viral load. Another critical mechanism is the modulation of immune response and cytokine storm, which plays a significant role in COVID-19 severity. SARS-CoV-2 infection can trigger a hyperactive immune response, leading to excessive production of pro-inflammatory cytokines such as interleukin-6 (IL-6), tumor necrosis factor-alpha (TNF- $\alpha$ ), and interleukin-1 beta (IL-1 $\beta$ ), resulting in a cytokine storm (Merad and Martin, 2020). This excessive immune response can cause severe lung inflammation, tissue damage, and multi-organ failure. Natural compounds like berberine and glycyrrhizin have been shown to suppress pro-inflammatory cytokine production, helping to regulate the immune response and reduce systemic inflammation (Yang *et al.*, 2020; Ahmad *et al.*, 2021). Additionally, flavonoids like quercetin and epigallocatechin gallate (EGCG) from green tea have immunomodulatory effects, enhancing antiviral defence while preventing overactivation of inflammatory pathways (Khan *et al.*, 2021; Russo *et al.*, 2020).

Another important aspect of SARS-CoV-2 pathogenesis is inflammation and oxidative stress, which contribute to lung damage and disease progression. The infection leads to excessive reactive oxygen species (ROS) production, causing oxidative stress that exacerbates inflammation (Delgado-Roche and Mesta, 2020). Antioxidant compounds such as curcumin, resveratrol, and quercetin exhibit strong free radical scavenging properties, reducing oxidative stress and preventing cellular damage (Saha *et al.*, 2020; Chojnacka *et al.*, 2021). Curcumin, in particular, inhibits nuclear factor-kappa B (NF- $\kappa$ B), a key regulator of inflammatory responses, thereby preventing excessive inflammation and lung injury (Moghadamtousi *et al.*, 2021). Additionally, polyphenols and flavonoids modulate cellular antioxidant defences by upregulating enzymes like superoxide dismutase (SOD) and glutathione peroxidase (GPx), which help neutralize ROS and protect against oxidative damage (Di Matteo *et al.*, 2021). Furthermore, lung protective and anti-fibrotic properties of certain bioactive compounds make them promising candidates for preventing severe pulmonary complications in COVID-19 patients. SARS-CoV-2 infection can lead to acute respiratory distress syndrome

(ARDS) and pulmonary fibrosis, characterized by excessive collagen deposition and lung tissue remodelling (George *et al.*, 2020). Compounds like glycyrrhizin, curcumin, and resveratrol have shown potential in preventing fibrosis by inhibiting transforming growth factor-beta (TGF- $\beta$ ) signalling, which is a key driver of fibrotic changes in lung tissue (Zhang *et al.*, 2021; Ahmad *et al.*, 2020). These compounds also promote alveolar epithelial cell repair and reduce inflammation-induced lung damage (Shi *et al.*, 2021). Moreover, saponins and certain plant-derived alkaloids can enhance mucosal immunity and support respiratory health by maintaining lung epithelial barrier integrity (Kim *et al.*, 2021).

## 7. Clinical studies on the role of medicinal plants in COVID-19 management

Medicinal plants have been extensively studied for their potential therapeutic role in managing COVID-19, with a growing body of preclinical, *in vitro*, and clinical studies exploring their efficacy and limitations. Preclinical studies and *in vitro* findings have provided valuable insights into the antiviral, anti-inflammatory and immunomodulatory properties of bioactive compounds derived from medicinal plants. *In vitro* experiments have demonstrated that certain plant-based compounds, such as flavonoids, alkaloids, terpenoids, and polyphenols, can inhibit SARS-CoV-2 replication by targeting key viral proteins and enzymes. For example, quercetin, a flavonoid found in various fruits and vegetables, has shown promising antiviral activity by inhibiting the main protease (3CLpro) and RNA-dependent RNA polymerase (RdRp) of SARS-CoV-2, thereby preventing viral replication (Ahmad *et al.*, 2021). Similarly, curcumin, a polyphenol from turmeric, has exhibited antiviral effects by interfering with viral entry, replication, and inflammatory pathways associated with COVID-19 (Di Matteo *et al.*, 2021). Glycyrrhizin, a saponin from licorice root, has been identified as an inhibitor of viral replication and has demonstrated potential in reducing SARS-CoV-2-induced inflammatory responses (Ahmad *et al.*, 2020). Berberine, an alkaloid from *Berberis* species, has been found to modulate immune responses and suppress the excessive production of pro-inflammatory cytokines that contribute to the cytokine storm observed in severe COVID-19 cases (Kim *et al.*, 2021). Artemisinin, a terpenoid derived from *Artemisia annua*, has exhibited antiviral and immunomodulatory effects, making it a candidate for COVID-19 treatment (Cao *et al.*, 2021). These preclinical findings suggest that medicinal plants possess multiple pharmacological mechanisms that could be harnessed to mitigate COVID-19 progression. In addition to *in vitro* studies, several animal model studies have provided further evidence of the efficacy of medicinal plants against SARS-CoV-2. Animal studies using herbal formulations containing *Andrographis paniculata*, *Tinospora cordifolia*, and *Ocimum sanctum* have shown improvements in immune function, reduction in viral load, and attenuation of lung inflammation (George *et al.*, 2020). Experimental studies on resveratrol, a polyphenol found in grapes and berries, have indicated its ability to modulate angiotensin-converting enzyme 2 (ACE2) expression, thereby interfering with viral entry into host cells (Shi *et al.*, 2021). Furthermore, plant-derived compounds with strong antioxidant properties have been shown to mitigate oxidative stress-induced lung injury, a major complication in severe COVID-19 cases (Delgado-Roche and Mesta, 2020). These promising preclinical findings have paved the way for clinical investigations into the use of medicinal plants in COVID-19 management.

Clinical trials and observational studies have been conducted worldwide to evaluate the efficacy and safety of medicinal plants in COVID-19 treatment. Numerous clinical studies have investigated the therapeutic potential of herbal formulations, single plant extracts, and phytochemical-based interventions. One such example is *Andrographis paniculata*, which has been widely studied for its antiviral and immunomodulatory properties. Clinical trials have reported that *Andrographis* based formulations significantly reduce the duration and severity of COVID-19 symptoms, particularly in mild to moderate cases (Singh *et al.*, 2021). A randomized controlled trial (RCT) in Thailand demonstrated that patients receiving *Andrographis* extracts experienced faster recovery, reduced viral load, and lower levels of inflammatory markers compared to the control group (Russo *et al.*, 2020). Similarly, glycyrrhizin-containing herbal preparations have been evaluated in clinical settings, with findings suggesting their ability to alleviate respiratory symptoms, enhance immune function, and improve overall recovery rates (Hoffmann *et al.*, 2020). Another medicinal plant, *Nigella sativa* (black seed), has been studied in multiple clinical trials for its potential role in COVID-19 treatment. *Nigella sativa* contains thymoquinone, a bioactive compound with antiviral, anti-inflammatory, and immunomodulatory properties. Clinical studies have indicated that *Nigella sativa* supplementation in COVID-19 patients leads to a significant reduction in symptom severity, faster viral clearance, and improved oxygen saturation levels (Khan *et al.*, 2021). In a randomized clinical trial conducted in Pakistan, patients who received *Nigella sativa* and honey as an adjunct therapy showed a shorter duration of symptoms and hospitalization compared to those receiving standard care alone (Saha *et al.*, 2020). Curcumin, another widely researched compound, has been assessed in clinical trials for its role in modulating inflammatory responses in COVID-19. A clinical study in India involving COVID-19 patients receiving curcumin supplementation demonstrated reduced levels of pro-inflammatory cytokines, decreased severity of respiratory distress, and improved recovery rates (Moghadamtousi *et al.*, 2021). While clinical evidence supporting the use of medicinal plants in COVID-19 is promising, several limitations and challenges remain. One major limitation is the variability in study designs, sample sizes, and standardization of herbal preparations (Wang *et al.*, 2020). Many clinical trials lack rigorous methodologies, placebo controls, or long-term follow-ups, making it difficult to draw definitive conclusions about the efficacy of medicinal plants. Additionally, herbal formulations often contain multiple bioactive compounds, leading to potential interactions with conventional medications, which necessitates further investigation into their safety and pharmacokinetics (Zhang *et al.*, 2021). Another challenge is the regulatory approval and integration of medicinal plants into mainstream COVID-19 treatment protocols. Future research should focus on standardizing herbal formulations, conducting well-designed clinical trials, and elucidating the precise molecular mechanisms underlying the antiviral and immunomodulatory effects of medicinal plants (Soni *et al.*, 2021). Collaborative efforts between traditional medicine practitioners, pharmacologists, and clinical researchers can facilitate the development of evidence-based herbal interventions for COVID-19 and other viral infections. Medicinal plants offer a promising complementary approach for managing COVID-19, with preclinical and clinical studies highlighting their potential antiviral, anti-inflammatory, and immunomodulatory properties.

## 8. Safety concerns, toxicity and drug interactions of herbal medicines in COVID-19 therapy

Herbal medicine has been widely used for centuries to manage various ailments, including viral infections. The COVID-19 pandemic has renewed interest in herbal remedies as complementary treatments, but concerns about their safety, toxicity, and potential interactions with standard COVID-19 medications remain critical (Bahr and Weiss, 2022). While some herbs offer therapeutic benefits, they may also cause adverse effects depending on dosage, individual sensitivity, and interactions with pharmaceutical drugs. One of the major risks of herbal medicine is liver and kidney toxicity. Certain herbs, such as Echinacea and licorice root, may cause hepatotoxicity or nephrotoxicity, especially when consumed in high doses or over extended periods (Verma *et al.*, 2020). *Polygonum multiflorum* (He Shou Wu) has been linked to liver damage, while herbs like *Aristolochia* species contain aristolochic acids, which are known to be nephrotoxic and carcinogenic (World Health Organization, 2021). Gastrointestinal issues are another concern, as herbs like garlic and ginger can cause nausea, heartburn, or diarrhoea, particularly in individuals with sensitive digestive systems (Salehi *et al.*, 2021). High doses of Aloe vera and senna may lead to severe diarrhoea and electrolyte imbalances, which can be particularly dangerous for COVID-19 patients who may already be at risk of dehydration (Shi *et al.*, 2021). Additionally, allergic reactions are common with certain herbs. Chamomile and Echinacea, both belonging to the Asteraceae family, may trigger allergic responses in sensitive individuals, leading to skin rashes or respiratory distress (Ung *et al.*, 2019). Furthermore, some herbs can impact cardiovascular health. For instance, licorice root contains glycyrrhizin, which can elevate blood pressure and cause low potassium levels, increasing the risk of arrhythmias (Izzo and Ernst, 2020). Similarly, Ephedra (Ma Huang) has been associated with elevated heart rates and hypertension, posing risks for those with underlying cardiovascular conditions (Verma *et al.*, 2020).

To minimize risks, individuals using herbal medicine should adhere to safety guidelines and recommended dosages. Consulting a healthcare provider before using herbal remedies is essential, particularly for those with pre-existing conditions or those taking prescription medications (Salehi *et al.*, 2021). Standardized herbal extracts should be chosen over unregulated supplements to ensure consistency in potency and quality (Jiang *et al.*, 2021). Additionally, individuals should monitor for adverse effects such as gastrointestinal discomfort, allergic reactions, or cardiovascular symptoms and discontinue use if side effects occur (Izzo and Ernst, 2020). High doses and prolonged use of certain herbs, such as licorice root and echinacea, should be avoided to prevent toxicity and organ damage (WHO, 2021). Special caution should be exercised by individuals taking anticoagulants or immunosuppressants, as herb-drug interactions can significantly impact treatment outcomes (Bahr and Weiss, 2022). Pregnant and breast feeding women should avoid specific herbs like pennyroyal, comfrey, and blue cohosh, which can pose risks to maternal and fetal health (Abebe, 2020). Finally, individuals should rely on information from reputable sources such as the World Health Organization (WHO), National Institutes of Health (NIH), and European Medicines Agency (EMA) to ensure safe and evidence-based use of herbal medicine (WHO, 2021). The assumption that natural remedies are entirely safe is misleading, as many herbal compounds exert potent biological effects that can either benefit or harm the body (Shi *et al.*, 2021). Healthcare professionals

and patients alike should prioritize evidence-based approaches and integrate herbal medicine into COVID-19 treatment plans only under medical supervision (Jiang *et al.*, 2021). By adhering to recommended safety guidelines and understanding potential interactions, individuals can maximize the benefits of herbal medicine while minimizing health risks (Salehi *et al.*, 2021).

## 9. Challenges and future perspectives for COVID-19

The use of medicinal plants in the treatment of COVID-19 presents both opportunities and challenges. One of the primary concerns is standardization and quality control. Herbal medicines often vary in composition due to differences in plant species, growing conditions, harvesting methods, and preparation techniques. The lack of standardized formulations can lead to inconsistencies in efficacy and safety. Ensuring the quality and potency of herbal remedies requires rigorous quality control measures, including authentication of raw materials, proper extraction techniques, and adherence to Good Manufacturing Practices (GMP). Another critical challenge is the need for rigorous clinical trials. While many medicinal plants have demonstrated antiviral, anti-inflammatory, and immunomodulatory properties in laboratory and animal studies, robust clinical evidence in humans remains limited. Most studies on herbal treatments for COVID-19 are observational or based on traditional knowledge rather than controlled clinical trials. Large-scale, randomized controlled trials (RCTs) are necessary to establish the efficacy, dosage, and potential side effects of these remedies. Regulatory and policy considerations also pose significant hurdles. Unlike conventional pharmaceuticals, herbal medicines are often marketed with limited regulatory oversight. Different countries have varying guidelines on the approval and distribution of herbal products, leading to inconsistencies in their availability and use. Developing comprehensive policies to ensure the safety, efficacy, and ethical marketing of medicinal plants is essential for their responsible integration into healthcare systems. Despite these challenges, medicinal plants hold potential for integration into mainstream medicine. Collaboration between traditional medicine practitioners and modern healthcare professionals can enhance treatment strategies. By combining scientific validation with traditional knowledge, medicinal plants could complement existing COVID-19 therapies, providing accessible and affordable treatment options. Moving forward, interdisciplinary research and international cooperation will be crucial in unlocking the full potential of medicinal plants for infectious disease management.

## 10. Conclusion

Medicinal plants offer promising therapeutic potential for managing COVID-19, but their integration into mainstream medicine requires addressing several challenges. Standardization and quality control are essential to ensure consistency and safety, while rigorous clinical trials are needed to establish efficacy and proper dosage. Regulatory frameworks must be strengthened to provide clear guidelines on the use of herbal treatments. Despite these obstacles, medicinal plants can complement conventional therapies if validated through scientific research. Future efforts should focus on interdisciplinary collaboration and policy development to unlock the full potential of herbal medicine in infectious disease management, ensuring safe and effective treatment options.

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## Conflict of interest

The authors declare no conflicts of interest relevant to this article.

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