

## A Comprehensive Overview: Use and the Role of Herbal Medicine in Treatment and Management of Covid-19.

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### ABSTRACT:

A novel coronavirus infection (SARS-CoV-2) is the cause of the present serious respiratory syndrome (COVID-19) outbreak. The World Health Organization (WHO) designated this infectious illness as a pandemic because harms global public health and human life. when there was no vaccine, herbal medicine plays important role in treatment and management of

Covid -19. The goal of this review article is to provide a comprehensive view of the potential herbs and plants that can be used in conjunction with western medicine to treat or prevent COVID-19 in humans. Traditional Chinese, Indian, and Iranian medicine recommends certain herbs for the avoidance, treatment, and recovery from diseases like COVID-19. The positive outcomes of these conventional medicines and their clinical studies, however, are still unknown. Here, we examined the most recent information on conventional medications recommended for the treatment of COVID-19.

**Keywords:** COVID19, medicinal plants, nature herbal medicine, plants extract, traditional Chinese medicine, treatment methods

### I. INTRODUCTION

In late 2019, a pneumonia sickness of an unknown source has started in Wuhan city/ China and spread rapidly to the rest of the world.<sup>1</sup> Coronaviruses are enveloped single-stranded RNA positive sense viruses with an average size between 60 nm and 140 nm in diameter with a crown-like shape under electron microscopy.<sup>2</sup> An unidentified beta coronavirus was found in samples taken from patients in a set of studies done in China. SARS-CoV-2, the coronavirus that was found, caused an outbreak illness, also known as COVID-19, was deemed a pandemic by the WHO and was described as a human-to-human transmission of infection<sup>3</sup> More than 178,700 confirmed cases were reported in more than 140 nations by the middle of March

2020, with the majority occurring in China, the virus's origin country, followed by Spain, Iran, Italy, and South Korea.<sup>4</sup> The diagnosis and treatment of COVID-19 was included in the list of epidemic illnesses treated by Traditional Chinese Medicine by the National Health Commission of China. (TCM). The TCM treatment regimen was advocated from many areas based on the sickness variation, even though the disease's manifestations, symptoms, and severity could vary depending on a number of factors, including the environment, the patient's immunity, their bodily health, and the virus itself. The sudden rise in COVID-19 cases stoked the fear of an epidemic and accelerated efforts to find a quick fix. Due to this, it was essential to investigate the effectiveness of Chinese herbal remedies against the coronavirus.

The use of Indian medicinal plants to cure various diseases is a promising area<sup>5</sup>. The Siddha and Ayurvedic traditions have their roots in India and are still extensively practiced there. Identification of the phyto-components in therapeutic plants may also be useful for reducing infection. As a result, using Indian medicinal herbs could be a novel way to stop the spread of viruses. Natural products and their derivatives have potential activities in the treatment of viral infections.

In the current study, we reviewed and summarized the published data about traditional herbal medicine for possible treatment and management of COVID-19.

### General virology and epidemiological characteristics of COVID-19:

Coronaviruses cause a lot of disorders, including respiratory, enteric, hepatic and neurologic disease.<sup>6</sup> SARS-CoV-2 is an enveloped, single-stranded, positive-sense RNA beta coronavirus. The S protein on the surface of SARS-CoV-2 induces the attachment and invasion of SARS-CoV-2 to the host cells by recognizing the ACE2 receptor.<sup>7</sup>

The invading virus then takes over the host cell's genetic replication machinery to produce new virus RNA with RdRp, synthesises glycoproteins by the host ribosome, which are then cleaved into nonstructural proteins and structural proteins (S proteins) by virus proteinases (3CLpro and PLpro), and assembles new viral particles to be released to infect additional host cells.

Therefore, the ACE2 receptor, RdRp, spike protein, 3CLpro, and PL pro are essential in the invasion and replication of SARS-CoV-2, and could be potential targets for the treatment of COVID-19 by Chinese herbal medicine.

The aetiology of COVID-19 is that SARS-CoV-2 spreads through the respiratory tract, infects the lungs, causes pneumonia, and generates inflammatory factors. The virus also replicates and releases in host cells, circulates in the blood, binds to ACE2 on the surface of numerous body organs, upsets the balance of the RAS signal pathway, and damages numerous organs throughout the body. A body's overactive immune reaction brought on by the virus can also spark an inflammatory storm that worsens the illness. Lung inflammation results in a profusion of secretions that obstruct the airflow and aggravate hypoxia in the body.

Generally, there are three routes for transmission of COVID-19: 1) aerosol transmission, 2) droplets transmission, and 3) contact transmission<sup>8</sup>. Study of a large number infected patients found out that the main transmission route of SARS-CoV-2 is person-person contact<sup>9</sup>. Moreover, it appears that the fomites can be as second suspected source of infection<sup>10</sup>. Recently, Chinese researchers reported that COVID-19 can be detected in the patient's feces, showing a possible fecal-oral transmission<sup>11</sup>.

Some molecular assays, including Real-Time Polymerase Chain Reaction (RT-PCR) and next-generation sequencing, were recommended for individuals with suspected infections for viral detection and characterization. Swabs from the pharynx, lower respiratory tract secretions, and sputum are the three clinical samples most frequently used to test for SARS-CoV-2. Additionally, CT imaging can be helpful for detecting SARS-CoV-2, and studies have shown that it frequently returns good results in those SARS-CoV-2 patients who have coughs, fevers, and fatigue. Bilateral pulmonary parenchymal ground-glass shadow and nodules are seen in individuals with severe illness.

## Prevention and treatment options

### Traditional herbal medicine:

For several years, medicinal plants have been used in different indigenous health schemes and traditional medicines for treating diseases.<sup>12</sup> Naturally occurring herbal medicine provides a wide variety of natural products, which can be used as an ancillary guide to unlocking many mysteries behind human illnesses.<sup>13-14</sup> In developing nations, 80% of people depend on conventional plants for their health needs, according to a WHO report.<sup>15-16</sup> Alternative therapies are being re-examined at an increasing rate, especially from herbal sources, as a result of the increased resistance of microorganisms (bacteria, viruses, and parasites) to conventional anti-microbial therapy. Understanding the natural products with antiviral properties is crucial for offering an alternative COVID-19 management option as worries about the COVID19 outbreak spread across the globe.

Today, many people turn to natural products and phytomedicine in various national healthcare systems for the treatment of a variety of health issues. The use of these products and phytomedicine is continuing to expand quickly throughout the globe. In cases where they were the only treatments available prior to the introduction of antibiotics, herbal phytoconstituents successfully reduced infectious conditions. The development of novel antivirals is especially well served by the use of herbal medicinal goods. Since the dawn of society, people have used these plants. Traditional Chinese medicine includes treatments of herbal and acupuncture, where those aim to prevent and treat diseases by enhancing the immunity of the body. Chinese medicine needs experience and knowledge; here, no adverse reactions could be identified if Chinese herbs are properly used,<sup>15-16</sup> Three of the seven coronaviruses that have been found to have the potential to spread among people are dangerous: SARS (severe acute respiratory syndrome, China, 2002), MERS (middle east respiratory syndrome, Saudi Arabia, 2012), and SARS-CoV-2. (COVID-19, 2019). These viruses are part of the coronavirus species' coronaviridae family. SARS-CoV-2 was determined by the genome sequence study to be a member of the beta type genus, which is also home to SARS, MERS, and the Bat SARS-like coronavirus. Additionally, COVID-19 is a betacoronavirus because of similarities in the nucleic acid structure.

. With regard to SARS and Covid-19, this review piece seeks to survey and introduce significant medicinal plants and herbs.

#### **ANDROGRAPHOLIDE:**

An extract of the perennial plant *Andrographis paniculata* (green chiretta) contains the labdane diterpenoid andrographolide. Due to this component's remarkable biological activity, which includes immune system regulation, anti-hyperglycemia, anti-bacteria, anti-virus, anti-parasite, and anti-tumor properties, it has been used in a variety of medicinal applications.

Being a potent immunomodulator, andrographolide can also be tried in combination therapies to treat infectious diseases.

Andrographolide looks to be successful against a variety of viral infections, and in the future, it can be used in drug development, either alone or in combination, for the inhibition of viral infection and treatment of infectious diseases.

Andrographolide is a drug that has antiviral<sup>17</sup>, antimicrobial<sup>18,19</sup> and anti-parasitic effects<sup>20,21</sup>. It is a labdane diterpenoid, that can be purified from the aerial parts of different plants that belong to the genus *Andrographis* (family Acanthaceae) and that flourish at varying altitudes.

The *Andrographis paniculata* plant is known as the "King of Bitter" because of its bioactive ingredient's bitter flavour. *A. paniculata* can be found at altitudes of up to 1000 m in Japan, China, Malaysia, Sri Lanka, Thailand, and India<sup>22</sup>. It is an annual herb that grows between 30 and 110 centi-metres long. The flowers are white with purple spots on the petals. *A. paniculata*, *A. alata*, and *A. lineata* can all be used to separate andrographolide, which is soluble in organic solvents like ethanol, chloroform, ether, acetone, and dimethyl sulfoxide

Previous reports showed that andrographolide could treat multiple viruses such as influenza A virus (IAV), human immunodeficiency virus (HIV),<sup>23</sup> Enterovirus D68 (EV-D68),<sup>24</sup> dengue virus (DENV),<sup>25,26</sup> and Chikungunya virus (CHIKV)<sup>27</sup> due to its wide range of antiviral properties. Recently, Enmozhi et al. found that andrographolide could be a good inhibitor for SARS-CoV-2 through in silico studies by influencing the viral 3-chymotrypsinlike cysteine protease (3CL<sup>pro</sup>).<sup>28</sup>

Andrographolide is generally very abundant, inexpensive, and cytotoxic; however, more research is required to fully understand its potent antiviral action against various viruses.

#### **QUERCETIN:**

Quercetin is considered to be a strong antioxidant due to its ability to scavenge free radicals and bind transition metal ions<sup>29</sup>.

It is a flavonoid substance that is typically present in fruits and veggies. In addition to having nutritional benefits, quercetin also has a variety of biological properties, such as its ability to fight off diseases like cancer, allergies, cancer-causing agents, oxidants, viruses, and inflammation.<sup>30,31,32</sup>

Quercetin has been shown in prior research to have antiviral activity against a variety of viruses, including IAV,<sup>33</sup>

C Virus (HCV),<sup>34</sup> Enterovirus 71 (EV-71),<sup>35</sup> SARS-CoV, etc.<sup>36,37</sup>. Regarding the SARS viruses, quercetin showed a relatively high inhibition rate and half-maximal inhibitory concentration (IC50) values of 82% and 73  $\mu$ M, respectively, against SARS-CoV 3CL<sup>pro</sup> in *Pichia pastoris* fungus.<sup>38</sup>

#### **BAICALIN:**

In East Asia, baicalin has long been used as a conventional medicine. Baicalin has a broad range of pharmacological properties, including effects that are anti-inflammatory, anti-pruritic, and anti-cancer. According to Chen et al., baicalin has been shown to have antiviral activity against SARS-type viruses, with an effective concentration of 12.5 g/ml being able to reduce the virus-forming unit by 50% (EC50) within two days.<sup>39,40</sup>

Baicalin was discovered to be an effective in vitro inhibitor of angiotensin-converting enzyme (ACE), with an IC50 value of 2.24 mM, who also used UV spectrophotometry to detect angiotensin-converting enzyme inhibition.

Baicalin's minimal toxicity suggests that using it as a medication or treatment agent against COVID-19 could be successful.

#### **CURCUMIN:**

It is a natural antioxidant compound that is non-toxic, extremely promising, and has many biological uses. In the near future, curcumin is expected to potentially be used as a new drug. to regulate the development of different diseases, such as inflammatory conditions, cancer, and oxidative stress-induced pathogenesis.

Through computational methods, two polyphenols with a dual binding affinity, catechin and curcumin, were described in this study. With binding energies of -10.5 Kcal/mol and -8.9 Kcal/mol, respectively, catechin attaches to viral S-protein and ACE2. It therefore bonds with a stronger affinity than curcumin, which is 7.8

Kcal/mol for ACE2 and 7.9 Kcal/mol for S-protein, respectively. Catechin binds to the area around the viral S-protein's RBD sequence, whereas curcumin binds straight to the receptor-binding domain (RBD) of the protein. Curcumin directly binds with as shown by a molecular simulation analysis. In contrast, catechin binds with S-protein near the RBD site and causes fluctuation in amino acid present in the RBD and its proximity. In conclusion, this computational study predicted the possible use of the above two polyphenols for therapeutic/preventive intervention.<sup>41</sup>

#### **GLYCYRRHIZIC ACID:**

It comes from the licorice shrub, which is used in traditional Chinese medicine. (Chinese name: Gan Cao). Thymol and carvacrol, two active substances discovered in the Chinese liquorice plant *Glycyrrhiza uralensis*, have been shown to have antiviral and antibacterial effects. The active ingredient in licorice root known as glycyrrhizin, has been used in therapeutic settings to treat ulcers, allergic inflammation, and hyperlipemia. Many studies showed that licorice and its ingredients could prevent lung infections and damage, making it an excellent herbal candidate to treat SARS viruses.<sup>42</sup>

Cinatl et al. looked into how the antiviral medications ribavirin, mycophenolic acid, glycyrrhizic acid, 6-azouridine, and pyrazofurin affected the SARS-CoV virus. A decrease in viral adsorption and penetration was found to be caused by glycyrrhizic acid, which had the greatest inhibitory effect among the other compounds.<sup>43</sup> Thereby, it is rational to recommend studying this component against SARS-CoV-2 infection intensely.

#### **MYRICETIN:**

A common flavonoid produced from plants, myricetin has a variety of nutritional benefits. Additionally, it frequently appears in the ingredients of various meals and drinks.

Previous plants and herbs that contained myricetin exhibit a broad range of potential and functions as anti-inflammatory, anti-cancer, anti-diabetic, and antioxidant. More than a century has passed since the creation of this component. The first isolation was from *Myrica nagi* Thumb (Myricaceae) in the late 1800s in India and was finally obtained as pale-colored crystals.<sup>44</sup> Yu. et al. reported that myricetin in vitro inhibited SARS-CoV's helicase protein by influencing the ATPase

action, but not the unwinding activity of nonstructural protein 13 (nsP13).

Additionally, it was discovered that myricetin and scutellarein had no cytotoxicity when compared to MCF10A cells with typical breast epithelial cells. It is possible that naturally occurring flavonoids, such as myricetin, could act as a SARS-CoV 2 suppressor.

#### **Sea -buckthorn:**

Due to its nutritional and therapeutic benefits, sea buckthorn (*Hippophaerhamnoides*), also known as sea buckthorn, is an ancient plant with contemporary virtues. It is a deciduous species with a broad geographic distribution, including in India. It includes a variety of vitamins, carotenoids, flavonoids, polyunsaturated fatty acids, free amino acids, and other bioactive nutrients and components.

It has been demonstrated that it has a variety of medicinal properties, including antioxidant, antimicrobial, antifungal, metabolic disorders, immunostimulatory, hepatoprotective, and anticancer action. Several studies reveal the presence of various phytochemical constituents viz., flavonoids (isorhamnetin, quercetin, myricetin, kaempferol and their glycoside compounds), carotenoids ( $\beta$  and  $\delta$ -carotene, lycopene, Zeaxanthin), few essential amino acids, sitosterol, triterpene, fatty acids, tannin acid, 5-hydroxytryptamine, umbelliferone, antioxidant vitamins and minerals in various parts of this plant.

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#### **LUTEOLIN:**

Luteolin (3',4',5',7'-tetrahydroxyflavone) is one of the flavonoid group, which naturally occurs in a large number of plants. It has a variety of pharmaceutical properties, including anti-diabetic, anti-inflammatory, antibacterial, antiviral,

anti-cancerogenic, antioxidant, and heart protective properties. The herbs used in Chinese medicine, which are inexpensive and widely accessible, are used to make this component. As a result, luteolin is recommended as a possible treatment for COVID-19.<sup>46</sup>

### Traditional Chinese medicine for treatment and management of covid -19.

The Chinese herbal remedy is a combination of various herbs that a herbalist creates based on the state and conditions of each patient. Following Chinese diagnostic principles, the diagnosis (palpation, listening, smelling, inspection, and inquiry).

Antiviral activities were reported for many Chinese herbal prescriptions, such as **YinhuaPinggan granule**, **San Wu Huangqin Decoction (SWHD)**, and **LianhuaQingwen Capsule**, which might assist in preventing the spread and propagation of the virus. Moreover, they could be able to recover and heal lungs' damage that could occur by coronaviruses.

To stop the resurgence of the deadly illness SARS, it is essential to develop anti-severe acute respiratory syndrome associated coronavirus (SARS-CoV) medications. A cell-based assay that measured the SARS-CoV-induced cytopathogenic effect (CPE) in vitro on Vero E6 cells was used in this research to assess the anti-SARS-CoV activities of more than 200 extracts from Chinese medicinal herbs. Six herbal extracts, one each from **Gentianae Radix** (the dried rhizome of *Gentiana scabra*), **DioscoreaeRhizoma** (the dried tuber of *Dioscorea batatas*), **Cassiae Semen** (the dried seed of *Cassia tora*), and **Loranthi Ramus** (the dried stem, with leaf, of *Taxillus chinensis*), were found to be potent inhibitors of SARS-CoV at concentrations. It was discovered what concentrations of the six extracts were required to block 50% of Vero E6 cell proliferation and 50% of viral replication. The most efficient extracts, CBE, GSH, DBM, CTH, and TCH, had selective index values (SI = CC50/EC50) that were > 59.4, > 57.5, > 62.1, > 59.4, and > 92.9, respectively. The SARS-CoV 3CL protease activity was significantly inhibited by the preparations CBM and DBM, with IC50 values of 39 g/ml and 44 g/ml, respectively. Our research indicates that these six herbal extracts might be candidates for the creation of anti-SARS medications in the future.<sup>47</sup>

It was suggested that **Sang Ju Yin plus Yu Ping Feng San** could regulate T cells for boosting the immune system.

After receiving traditional Chinese plant medicine treatment, many patients discharged from a hospital in Beijing. After receiving treatment with traditional Chinese herbal medicine, another recovery instance was later reported, illustrating the broad application of traditional Chinese herbal medicine. to administer the COVID-19 for medical care. The People's Republic of China (PRC) National Health Commission and other organisations released "Diagnosis and Treatment of Pneumonia Caused by Novel Coronavirus Infection" on January 27th, 2020.

### Dietary therapy and herbal medicine for COVID-19 MANAGEMENT:

Foods and plants may have antiviral properties that are effective against COVID-19 and SARS-CoV-2. To avoid infection and boost immunity, foods and herbs may be used as dietary supplements, antiviral agents for masks.

Numerous foods and plants are recognised for their antiviral and immunomodulatory properties. Aloe vera, *Angelica gigas* (Korean angelica), *Astragalus membranaceus* (Mongolian milkvetch), *Ganoderma lucidum* (lingzhi fungus), *Panax ginseng*, and *Scutellaria baicalensis* (Chinese skullcap) have all been linked to immunomodulatory effects. Their actions are founded on cytokine stimulation that is targeted, lymphocyte activation, an increase in natural killer cell counts, and improved macrophage activity. Additionally, *Lawsonia alba* (hina), *Echinacea purpurea* (eastern purple coneflower), *Plumbago zeylanica* (Ceylon leadwort), and *Cissampelos pareira* Linn (velvetleaf) all have phagocytosis-stimulating properties and show immunomodulatory effects.

Eucalyptus essential oil is reported to improve the innate cell-mediated immune response that can be used as an immunoregulatory agent against infectious diseases.<sup>48,49</sup>

Utilizing all of these immunostimulatory foods and plants may strengthen the immune system and shield the body from COVID19. But these findings need to be confirmed by science or medical research.

The bioactive ingredients of foods and herbs have been documented in numerous studies to be effective against the influenza virus and SARS-CoV-1, despite only being tested in vitro, in vivo, and in ovo. Not many research as the majority of clinical studies have been done on food and herb combinations or traditional Chinese formulas, research has been done on the impacts of particular

foods and herbs against the influenza virus and SAR-CoV-1 in Table 1 lists the antiviral effects of

foods and plants against the influenza virus.<sup>50</sup>

Antiviral activity of foods and herbs against influenza virus and SAR – COV -1 (table 1).

Herbs	Bioactive compound and extract	Experimental model	Mode of action	References
Allium sativum	Garlic aqueous extract (Garlic extract)	H9N2 virus infection in MDCK cells and chicken embryo H1N1 virus infection in MDCK cells	Anti-avian influenza virus H9N2 activity in both chick embryos and cell models. Inhibits H1N1 virus penetration and proliferation in cell culture	Rasool et al. (2017) <sup>51</sup>  Mehrbod et al. (2008) <sup>52</sup>
Zingiber officinalis (Ginger)	Ginger aqueous extract and Korean red ginseng powder capsule	H9N2 virus infection in MDCK cells and chicken embryo. H1N1 virus-induced respiratory tract infection in mice and MDCK cells	Anti-avian influenza virus H9N2 activity in both chick embryos and cell models Ginseng enhances immunity by increasing the levels of influenza A virus-specific antibodies and their neutralizing activities. It modulates CD69-expressing immune cells and exhibits significant enhancement of influenza virus-specific IgA antibody in mice lungs.	Rasool et al. (2017) <sup>51</sup>  Quan et al. (2006) <sup>53</sup>
Eucalyptus polybractea (Eucalyptus)	Aerosol and vapor of eucalyptus oil  Eucalyptus oil	H11N9 virus infection in MDCK cells.  H11N9 virus infection in MDCK	Inhibits avian influenza virus H11N9 in aerosol and vapor form.  Pre-coated eucalyptus oil inactivates	Usachev et al. (2013) <sup>54</sup>  Pyankov et al. (2012) <sup>55</sup>

		cells	captured H1N9 virus in fiber material	
Melaleuca alternifolia (Tea tree)	Aerosol and vapor of tea tree oil,  Tea tree oil	H1N9 virus infection in MDCK cells  H1N9 virus infection in MDCK cells	Inhibits avian influenza virus H1N9 in aerosol and vapor form,  Pre-coated tea tree oil inactivates captured H1N9 fiber material	Usachev et al. (2013) <sup>54</sup>  Pyankov et al. (2012) <sup>55</sup>
Carpesiumabrotanoides L. (Tianmingjing)	4a,5a-dihydroxyguaia-11(13)-en12,8a-lactone.	H1N9 virus infection in MDCK cells,	Inhibits H1N1 virus activity.	He et al. (2020) <sup>56</sup>
Portulaca oleracea L. (Machixian;	Water extract of P. oleracea L.	H1N9 virus infection in MDCK cell,	Inhibits H1N1 and H3N2 in the early stages of influenza A virus infection, inhibits the binding of virus to cells, and exhibits good virucidal activity	Li et al. (2019) <sup>57</sup>
Houttuynia cordata (Fish mint).	H. cordata ethanolic extract	H1N1 virus-induced acute lung injury in mice and RAW 264.7 cell model	Alleviates H1N1-induced acute lung injury in mice through antiviral and anti-inflammatory effects. Inhibition of viral neuraminidase activity and toll like receptor signaling.	Ling et al. (2020) <sup>58</sup>

Antiviral activity of herbs against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). (table2).

Herbs	Bioactive compound and extract	Experimental model	Mode of action	References
Lianhuaqingwen (Lian huaqing wen)	Lianhua-Qingwen formula (10herbs) <ul style="list-style-type: none"> <li>• Forsythia suspensa (Thunb.)</li> <li>• Ephedra sinica Stapf (Chinese ephedra;</li> <li>• Lonicera japonica Thunb</li> <li>• Isatis indigotica Fortune (Woad)</li> <li>• Mentha</li> </ul>	Vero E6 cells with SARS-CoV-2 infection model	inactivate SARS-CoV-2 replication, reduce pro-inflammatory cytokines production and affect particle morphology of virus cell.	Li et al. (2020) <sup>59</sup>

	haplocalyxBriq. (Mint) <ul style="list-style-type: none"> <li>• Dryopteris crassirhizoma Nakai (Thickstemmed wood fern)</li> <li>• Rheum palmatum L. (Chinese rhubarb)</li> <li>• Pogostemoncablin (Blanco) Benth.</li> <li>• Rhodiola rosea L. (Golden root)</li> <li>• Gypsum Fibrosum (Gypsum;</li> </ul>			
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## II. CONCLUSIONS:

There was a serious threat from COVID-19 to public health and safety globally. The need to collect information, control the pandemic outbreak, and lower the mortality rate as much as possible became critical for governments, hospitals, researchers, businesses, and even individuals. Currently, there are limited number of allopathic medicines considered effective against COVID-19. Current research supports dietary therapy, herbal medicine and traditional Chinese medicine as possible antiviral treatments against SARS-CoV-2 and as COVID-19 prevention measures. In this review article, the most effective herbal medicines from traditional Chinese medicine were used against viruses that were similar to them and exhibited high inhibitory activity. On the basis of in vitro and in vivo studies, it is expected that these plants will act as antiviral medications to treat the current SARS-CoV-2 virus. It was discovered that the medicinal histories of the ingredients in andrographolide, quercetin, baicalin, curcumin, glycyrrhizic acid, emodin, patchouli alcohol, luteolin, and myricetin were favourable. For these monomers to be able to bind to the SARS-CoV-2 virus and host targets and block the virus-host binding sites, computer simulation and molecular docking demonstrated adequate binding ability. The traditional Chinese medicine herbs are abundant, inexpensive, and low in toxicity, which promotes their use as potential COVID-19 drugs. These herbs also contain a variety of helpful ingredients.

## REFERENCE

- [1]. Lu H, Stratton CW, Tang YW. Outbreak of pneumonia of unknown etiology in Wuhan, China: The mystery and the miracle. *J Med Virol.* 2020;92(4):401–402.
- [2]. Y.-R. Guo, Q.-D. Cao, Z.-S. Hong, Y.-Y. Tan, S.-D. Chen, H.-J. Jin, K.-S. Tan, D.-Y. Wang, Y. Yan, The origin, transmission and clinical therapies on coronavirus disease 2019 (COVID-19) outbreak—an update on the status, *Mil. MedRes.*2020,7 (1) 1–10.
- [3]. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A novel coronavirus from patients with pneumonia in China, 2019. *N Engl J Med.* 2020; 38(2):727–733.
- [4]. Hadi A, Kadhom M, Hairunisa N, Yousif E, Mohammed S. A review on COVID-19: Origin, spread, symptoms, treatment, and prevention. *Biointerface Res Appl Chem.* 2020;10(6):7234–7242.
- [5]. B. Vellingiri, K. Jayaramayya, M. Iyer, A. Narayanasamy, V. Govindasamy, B. Giridharan, S. Ganesan, A. Venugopal, D. Venkatesan, H. Ganesan, COVID-19: a promising cure for the global panic, *Sci. Total Environ.*2020;13(8):277.
- [6]. T. Singhal, A review of coronavirus disease-2019 (COVID-19), *Indian J. Pediatr.* (2020) 1–6.
- [7]. F. Jiang, L. Deng, L. Zhang, Y. Cai, C.W. Cheung, Z. Xia, Review of the clinical characteristics of coronavirus disease 2019 (COVID-19), *J. Gen. Intern. Med.* (2020) 1–5.
- [8]. W.H. Organization, Modes of Transmission of Virus Causing COVID-19: Implications for IPC Precaution Recommendations: Scientific Brief, 27 March 2020, World Health Organization, 2020.
- [9]. Yuen, Kit-San, et al. "SARS-CoV-2 and COVID-19: The most important research questions." *Cell & bioscience*,2020;10(1): 1-5.



- [10]. S.I. Numbers, W.R. Assessment, Coronavirus disease 2019 (COVID-19), Americas, 2020 ,10 (2) :1.
- [11]. J. Hindson, COVID-19: faecal–oral transmission? *Nat. Rev. Gastroenterol. Hepatol.* 17 (5) (2020), 259–259.
- [12]. .Kitazato K, Wang Y, Kobayashi N. Viral infectious disease and natural products with antiviral activity. *Drug DiscovTher.* 2007;1(1):14–22.
- [13]. Mahady GB. Global harmonization of herbal health claims. *J Nutr.* 2001;131(3s):1120S–1123S.
- [14]. Ganjhu RK, Mudgal PP, Maity H, Dowarha D, Devadiga S, Nag S, et al. Herbal plants and plant preparations as remedial approach for viral diseases. *Virusdisease.* 2015;26(4):225–236.
- [15]. Olayiwola A. Medicinal plants and primary health care: an agenda for action. *East Mediterr Region Drugs Digest.* 1991;8(2):11–25.
- [16]. Ekor M. The growing use of herbal medicines: issues relating to adverse reactions and challenges in monitoring safety. *Front Pharmacol.*2014;4:177.
- [17]. Liu R, Jacob JR, Tennant B United States patent, Andrographolide derivatives to treat viral infections, 2003 ;1(12):12.
- [18]. Arifullah M, Namsa ND, Mandal M, Chiruvella KK, Vikrama P, Gopal GR.Evaluation of anti-bacterial and anti-oxidant potential of andrographolide and echiodinin isolated from callus culture of *Andrographis paniculata* Nees. *Asian Pac J Trop Biomed.* 2013, 3(8):604–610.
- [19]. Hua Z, Frohlich KM, Zhang Y, Feng X, Zhang J, Shen L. Andrographolide inhibits intracellular *Chlamydia trachomatis* multiplication and reduces secretion of proinflammatory mediators produced by human epithelial cells. *Pathog Dis* .2015;73(1):1–11.
- [20]. Roy P, Das S, Bera T, Mondol S, Mukherjee A. Andrographolide nanoparticles in leishmaniasis: characterization and in vitro evaluations. *Int J Nanomed.* 2015;5(1):1113–1121.
- [21]. Zaid OI, Abd Majid R, Sabariah MN, Hasidah MS, Al-Zihiry K, Yam M.Andrographolide effect on both *Plasmodium falciparum* infected and non -infected RBCs membranes. *Asian Pac J Trop Med,* 2015;8(7):507–512.
- [22]. Alagesaboopathi C *Andrographis* spp: a source of bitter compounds for medicinal use. *Anc Sci Life,* 2000;19(3 \$4):164–168.
- [23]. Ding Y, Chen L, Wu W, Yang J, Yang Z, Liu S. Andrographolide inhibits influenza A virus-induced inflammation in a murine model through NF-kappaB and JAK-STAT signaling pathway. *Microbes Infect.*2017;19:605–615.
- [24]. Uttekar MM, Das T, Pawar RS, Bhandari B, Menon V, Nutan, et al. Anti-HIV activity of semisynthetic derivatives of andrographolide and computational study of HIV-1 gp120 protein binding. *Eur J Med Chem.*2012;5(6):368–374.
- [25]. Panraksa P, Ramphan S, Khongwichit S, Smith DR. Activity of andrographolide against dengue virus. *Antiviral Res.* 2017;13(9):69–78.
- [26]. Paemane A, Hitakarun A, Wintachai P, Roytrakul S, Smith DR. A proteomic analysis of the anti-dengue virus activity of andrographolide. *Biomed Pharmacother.* 2019;10(9):322–332.
- [27]. Wintachai P, Kaur P, Lee RCH, Ramphan S, Kuadkitkan A, Wikan N, et al. Activity of andrographolide against chikungunya virus infection. *Sci Rep.* 2015;5(1):14179.
- [28]. Enmozhi SK, Raja K, Sebastine I, Joseph J. Andrographolide as a potential inhibitor of SARS-CoV-2 main protease: an in-silico approach. *J Biomol Struct Dyn.*2020;1–7.
- [29]. de Souza, R.F.; De Giovani, W.F. Antioxidant properties of complexes of flavonoids with metal ions. *Redox Rep.,* 2004, 9, 97-104.
- [30]. D’Andrea G. Quercetin: A flavonol with multifaceted therapeutic applications? . *Fitoterapia.*2015;106:256–71.
- [31]. Li Y, Yao J, Han C, Yang J, Chaudhry M, Wang S, et al. Quercetin, inflammation and immunity. *Nutrients.* 2016;8(3):167.
- [32]. Wu W, Li R, Li X, He J, Jiang S, Liu S. Quercetin as an antiviral agent inhibits influenza A virus (IAV) entry. *Viruses.* 2015;8.
- [33]. Ángela Rojas, Campo JAD, Clement S, Lemasson M, García-Valdecasas M, GilGómez A, et al. Effect of quercetin on hepatitis C virus life cycle: From viral to host targets. *Sci Rep.* 2016;6(1):31777.

- [34]. Yao C, Xi C, Hu K, Gao W, Cai X, Qin J, et al. Inhibition of enterovirus 71 replication and viral 3C protease by quercetin. *Virology*. 2018;15(1):116.
- [35]. Nguyen TT, Woo HJ, Kang HK, Nguyen VD, Kim YM, Kim DW. Flavonoid-mediated inhibition of SARS coronavirus 3C-like protease expressed in *Pichia pastoris*. *Biotechnol Lett*. 2012;34:831–838.
- [36]. Ryu YB, Jeong HJ, Kim JH, Kim YM, Park JY, Kim D. Biflavonoids from *Torreya nucifera* displaying SARS-CoV-2 3CL<sup>PRO</sup> activity. *Bioorg Med Chem*. 2010;18:7940–7947.
- [37]. de Groot H, Rauen U. Tissue injury by reactive oxygen species and the protective effects of flavonoids. *Fund Clin Pharmacol*. 2019;12(3):249–255.
- [38]. Grum-Tokars V, Ratia K, Begaye A, Baker SC, Mesecar AD (2008) Evaluating the 3C-like protease activity of SARS coronavirus: recommendations for standardized assays for drug discovery. *Virus Res* 133:63–73.
- [39]. Chen HS, Qi SH, Shen JG. One-compound-multi-target: Combination prospect of natural compounds with thrombolytic therapy in acute ischemic stroke. *Curr Neuropharmacol*. 2017;15:134–156.
- [40]. Ishfaq M, Chen C, Bao J, Zhang W, Wu Z, Wang J, et al. Baicalin ameliorates oxidative stress and apoptosis by restoring mitochondrial dynamics in the spleen of chickens via the opposite modulation of NF- $\kappa$ B and Nrf2/HO-1 signaling pathway during *Mycoplasma gallisepticum* infection. *Poult Sci*. 2019;98:6296–6310.
- [41]. Atala B, Jena N, Kanungo V, Nayak. Catechin and curcumin interact with S protein of SARS-CoV-2 and ACE2 of human cell membrane: insights from computational studies. *Sci Rep*. 2021;11(2043).
- [42]. Pilcher H. Liquorice may tackle SARS. *Nature*. 2003.
- [43]. Cinatl J, Morgenstern B, Bauer G, Chandra P, Rabenau H, Doerr HW. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. *Lancet*. 2003;361(9374):2045–2046.
- [44]. Yu MS, Lee J, Lee JM. Identification of myricetin and scutellarein as novel chemical inhibitors of the SARS coronavirus helicase, nsP13. *Bioorg Med Chem Lett*. 2012;22(12):4049–4054.
- [45]. Anon. Seabuckthorn Research. Accessed on. 2005. <http://www.seabuckthornresearch.com>. 2007/02/25.
- [46]. Manzoor MF, Ahmad N, Ahmed Z, Siddique R, Zeng XA, Rahaman A, et al. Novel extraction techniques and pharmaceutical activities of luteolin and its derivatives. *J Food Biochem*. 2019;43(9):12–74.
- [47]. Wen, Chih-Chun, et al. "Traditional Chinese medicine herbal extracts of *Cibotium barometz*, *Gentiana scabra*, *Dioscorea batatas*, *Cassia tora*, and *Taxillus chinensis* inhibit SARS-CoV replication." *Journal of traditional and complementary medicine*. 2011;1(1): 41–50.
- [48]. Serafino A, Vallebona PS, Andreola F, et al. Stimulatory effect of eucalyptus essential oil on innate cell-mediated immune response. *BMC Immunol*. 2008;9:1–7.
- [49]. Sadlon AE, Lamson DW. Immune-modifying and antimicrobial effects of eucalyptus oil and simple inhalation devices. *Alternative Med Rev*. 2010;15(1): 33–42.
- [50]. Luo H, Tang QL, Shang YX, et al. Can Chinese medicine be used for prevention of Corona Virus Disease 2019 (COVID-19)? a review of historical classics, research evidence and current prevention programs. *Chin J Integr Med*. 2020;26(4): 243–250.
- [51]. Rasool A, Khan MU, Ali MA, et al. Anti-avian influenza virus H9N2 activity of aqueous extracts of *Zingiber officinalis* (ginger) and *Allium sativum* (garlic) in chick embryos. *Pak J Pharm Sci*. 2017;30(4):1341–1344.
- [52]. Mehrbod P, Amini E, Tavassoti-Kheiri M. Antiviral activity of garlic extract on influenza virus. *Iran J Virol*. 2009;3(1):19–23.
- [53]. Quan FS, Compans RW, Cho YK, Kang SM. Ginseng and salviae herbs play a role as immune activators and modulate immune responses during influenza virus infection. *Vaccine*. 2007;25(2):272–282.

- [54]. Usachev EV, Pyankov OV, Usacheva OV, Agranovski IE. Antiviral activity of tea tree and eucalyptus oil aerosol and vapour. *J Aerosol Sci.*2013; 59: 22-30.
- [55]. Pyankov OV, Usachev EV, Pyankova O, Agranovski IE. Inactivation of airborne influenza virus by tea tree and eucalyptus oils. *Aerosol Sci Tech.* 2012;46(12): 1295-1302.
- [56]. He YQ, Cai L, Qian QG, et al. Anti-influenza a (H1N1) viral and cytotoxic sesquiterpenes from *carpesiumabrotanoides*. *Phytochem Lett.* 2020;35:41-45.
- [57]. Li YH, Lai CY, Su MC, Cheng JC, Chang YS. Antiviral activity of *Portulaca oleracea L.* against influenza aviruses. *J Ethnopharmacol.* 2019;24(1), 112-13.
- [58]. Ling LJ, Lu Y, Zhang YY, et al. Flavonoids from *Houttuynia cordata* attenuate H1N1-induced acute lung injury in mice via inhibition of influenza virus and toll-like receptor signalling. *Phytomedicine.* 2020;67,153-150.
- [59]. Runfeng L, Yunlong H, Jicheng H, et al. Lianhuaqingwen exerts anti-viral and anti-inflammatory activity against novel coronavirus (SARS-CoV-2). *Pharmacol Res.* 2020, 10(4),761.