



## UTILIZING HERBAL MEDICINES IN THE MANAGEMENT AND PREVENTION OF CORONAVIRUS DISEASE (COVID- 19): PROS AND CONS

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### Abstract

A recently detected coronavirus that was found in Wuhan, China, is the source of the 2019 coronavirus disease (COVID-19). Worldwide competition is underway to provide COVID-19 clinically validated medications as soon as possible and to create a vaccination that is both safe and effective. Severe acute respiratory syndrome Coronavirus-2 (SARS-COV.2), a virulent member of the large coronavirus family, is the source of the COVID-19 infection. These viruses have caused many recent infection outbreaks, including the deadliest COVID-19 outbreak, SARS (2003) and Middle East Respiratory Syndrome, (MERS) 2012 outbreaks. The COVID-19 virus has been shown to have a relatively high mortality rate in older patients, children, individuals with underlying medical conditions, and immunocompromised individuals. Natural products have been used for a very long time and have been shown to be effective; so medicinal plants may be used as potential healing agents. By strengthening the immune system or having a viricidal effect, these agents may help people fight off infection and lower the death rate associated with SARS-CoV-2 infections. Unfortunately, there haven't been any particular preclinical or clinical studies to assess the effectiveness of herbal immunoregulators. Certain natural substances, based on basic principles from earlier investigations, may be useful for treating COVID-19. This review discussed some herbal remedies derived from plants, such as *Echinacea*, *Cinchona*, *Curcuma longa*, and *Curcuma xanthorrhiza*, among others, that are used to treat COVID-19. Furthermore, the advantages and disadvantages of using herbal medicine during the epidemic were investigated, some conclusions reached, and recommendations made.

**Keywords:** Herbal medicines, COVID-19, SARS-COV-2, Immunoregulators, MERS-2012.

### 1.0 Introduction

The infectious agents that cause respiratory tract infections are coronaviruses, which can also impact the digestive system and infect humans and animals systemically (Malik *et al.*, 2020). Single-stranded RNA viruses, or

coronaviruses, were originally identified in 1960 and are incredibly varied. The majority of coronavirus strains are found in bats and wild birds, and they have the ability to infect other organisms through contaminated wild animal meat and seafood sold in Chinese

marketplaces, historically. On 31<sup>st</sup> December, 2019, the first case of COVID-19 was reported in Wuhan, China. Two days later, on January 13, 2020, another instance of the illness was reported outside of Mainland China (Hui *et al.*, 2020). COVID-19 affected around 210 countries and territories worldwide, with the United States, the United Kingdom, Spain, France, and Italy among the nations with the highest number of cases. Frequent signs and symptoms of COVID-19 include fever, coughing, breathing difficulties, diarrhea, and, in more serious cases, pneumonia or even death (WHO, 2020). The infection may be contacted by respiratory droplets, bodily contact, and vomits. Incubation stage may last 14 days or longer, and the illness may remain contagious until the latent period (CDC, 2020).

Severe Acute Respiratory Syndrome with Virulence Coronavirus 2 (SARS-COV-2) is the virus that causes the COVID-19 infection. SARS-CoV-2 is a positive-sense, single-stranded RNA beta coronavirus, according to Malik *et al.* (2020). Viral protein can be produced in up to 14 open reading frames (ORFS), and its genome consists of 28,852 base pairs. Nucleocapsid (N), membrane (M), envelope (E), and spikes (S) are the names of the four primary structural proteins found in viruses. These proteins help the virus encapsulate DNA in its capsid and improve the ACE-2 receptor's ability to reach human cells.

The lives of humans and other living things have been challenged by recently discovered virally transmitted infectious diseases. Viral viruses, including Ebola, SARS, human influenza, and HIV, have drawn increasing

attention and pose a danger to the modern health care and pharmaceutical industries because they are typically harder to control and have a wider public impact (De Clercq & Li, 2016). There have been numerous reports of infections and aberrant physiology brought on by various coronaviridae family viruses (Kitazato, Wang, & Kobayashi, 2007). Currently, there are only supportive and preventive strategies available for COVID-19 that aim to minimize organ damage and subsequent problems (Rodríguez-Morales, MacGregor, Kanagarajah, Patel, & Schlagenhauf, 2020). New medications must, however, specifically target the virus' RNA-dependent RNA polymerase (RdRP), the spike protein (S-protein), and the SARS-CoV-2 cell membrane receptors (ACE-2). Depending on the structure and mode of virus replication, different plant extracts have different antiviral properties. Certain plants, known as immunomodulators, help strengthen the body's defenses against viruses. (Webster, Taschereau, Lee, & Jurgens, 2006).

Medicinal herbs, which have been tried and tested by many tribal clans since olden days, could be an option, although the screening process for novel therapeutic compounds will take a while (Adhikari, Marasini, Rayamajhee, Bhattarai, Lamichhane, Khadayat, & Parajuli, 2021). Nearly 85% of the world's population is thought to receive their primary medical care from medicinal plants (Pestic & Stanković, 2015), and 40% of synthetic medications sold in pharmaceutical markets are produced from natural chemicals generated from plants and microbes (Bauer & Bronstrup, 2014). Research on emulsion-based therapy (emulsion-based invitro compartmentalized IVC) for the screening of

hundreds of natural materials should be focused on in order to develop a powerful antiviral medication for COVID-19. In order to use herbal treatments for the COVID-19 pandemic, this paper summarizes medicinal herbs and/or plants that have antiviral qualities that may be helpful in drug discovery. It also makes some recommendations.

## 2.0 Current Treatment Approaches for Viral Infection

The age of antiviral medicine development formally began in June 1963 with the approval of idoxuridine, the first anti-herpes antiviral treatment that prevents synthesis of viral DNA (Clercq, 2004). Since then, over 90 medications belonging to various functional groups have been approved for the treatment of illnesses that are viral in nature, such as influenza virus infection, HBV, HCV, and HIV (De Clercq & Li, 2016). However, there is cause for concern regarding the rise of antiviral drug resistance (ADR), which includes herpes viruses. ADR can be controlled by developing new medications, optimizing compound administration, and studying the mechanisms underlying resistance patterns. Safe and innovative antiviral medications are in high demand due to the high cost and unfavorable side effects of synthetic medications, as well as the rise of ADR. Herbal extracts are now a great substitute for antiviral medications that can block specific stages of the virus replication cycle. Moreover, some clinical trials have demonstrated the impressive efficacy of plant-based antiviral substances, such as anthocyanin (Mohammadi Pour, Fakhri, Asgary, Farzaei, & Echeverría, 2019).

It has been demonstrated that extracts from medicinal herbs such as *Polygonum multiflorum*, *Salvia millitorrhiza*, *Glycyrrhiza radix*, and *Dioscorea batatas* are effective against the coronavirus (Boukhatem & Setzer, 2020). In a study published by Li *et al.* (2005), four different plants— *Lindera aggregate*, *Artemisia annua*, *Pyrrhosia lingua*, and *Lyceris radiate*- showed strong antiviral activity. Another study by Lau *et al.*, (2008) says that *Noutluynia cordata* extract is a good way to treat pneumonia caused by SARS-COV that is also safe. *Diammonium glycyrrhizinete*, an herbal remedy derived from the sweet root, has been used. It has also been used clinically to treat liver infections caused by HBV, coughs, and stomach issues.

Also, many strong antiviral compounds have been tested against human viruses. Because of this, there is a worldwide need to find and screen particles and compounds that might be antiviral and anti-infectious from therapeutic plant and herb extracts.

## 3.0 Screening of Medicinal Plants and Herbal Medicine

Therapeutic plant extracts can be screened in vitro and in vivo using a variety of methods. This review focused on a technique that is relatively unknown in the world of medicinal chemistry: the emulsion-based in vitro compartmentalization (IVC) technique (Gianella, Snapp, & Levy, 2016). Droplets are divided into compartments for ultrahigh-throughput screening (UHTS) using a water-in-oil-in-water emulsion. IVC uses a water-in-oil emulsion to produce protein from aqueous droplets containing DNA and machinery (Rothe, Surjadi, & Power, 2006). In the new method, plant extracts and RdRp can be

separated into different areas when used with viral DNA that has been labeled with a green fluorescent protein (GFP) (Bernath, Hai, Mastrobattista, Griffiths, Magdassi, & Tawfik, 2004). Furthermore, with advancements in laboratory techniques and instrumentation, the development and analysis of herbal ingredients have increased dramatically (Fitzgerald, Heinrich, & Booker, 2020). Similar reprogramming methods could be used to look into how to stop viral protease (Ogbole, Segun, & Adeniji, 2017).

Many members of the community use herbal remedies in the COVID-19 condition, where therapeutic and preventive agents have not been identified and recommended for administration to patients. The benefits and drawbacks of these herbal remedies for COVID-19 prevention and therapy were covered in this review.

*Echinacea purpurea*: Its potential to combat viral infections has made it one of the most widely used herbal remedies in North America and Europe. The common name for it is purple cone flower. Native Americans utilize the herb for respiratory illnesses, and it can be prepared in a variety of ways, including extracts, tinctures, sprays, and teas (Hudson & Vimalanathan, 2011; Sharma, Anderson, Schoop & Hudson, 2009). Numerous bioactive compounds, including polysaccharides, alkylamides, and chicoric acid, are present in it (Barnes, Anderson, Gibbons, & Phillipson, 2005).

After some research revealed that *E. purpurea* extract had antiviral properties, its use in treating viral infections spread throughout society. Several studies on commercial products with Echinacea have shown that

these interleukins interact with and control the immune system to release cytokines. These cytokines can stop a number of infections (Kumar, Abbas, Fausto, & Aster, 2014; Tisoncik, Korth, Simmons, Farrar, Martin, & Katze, 2012) by causing the release or increase of pro-inflammatory cytokines, which leads to hypercytokinaemia. So, we can say that when Echinacea is injected into a group of cells that are virus-infected; it stops the production of cytokines (Sharma *et al.*, 2009).

To provide information on the safety and effectiveness profiles of giving Echinacea to COVID-19 patients, there isn't a single clinical trial available. An *in vitro* investigation demonstrated the viricidal properties of Echinacea. It must be further studied in a clinical setting to determine if it has any negative effects.

*Curcumin longa*: *Curcuma longa* is the botanical name for the rhizomatous plant that is used to make turmeric. This plant has sparked a lot of interest in both the scientific and medical domains. According to Hewlings and Kalman (2017), turmeric is a member of the genus *Curcuma* and the family Zingiberaceae. Turmeric has three main applications: flavoring, natural food coloring, and significant spice. The herb is well known for its ability to treat a wide range of illnesses and ailments. In Asia and perhaps Africa, *C. longa* serves as a supplement or medication. In addition to treating many additional conditions like diabetes mellitus, cardiovascular disease, obesity, allergies or asthma, and psoriasis, it has anti-inflammatory, antioxidant, and anti-cancer properties as a medication (Hewlings &

Kalman, 2017). Water (13.1%), minerals (3.5%), fat (5.1%), protein (6.3%), and carbs (96.4%) make up the majority of *C. longa*. Curcumin (77%), demethoxycurcumin (DMC), and bisdemethoxycurcumin (BDMC) are among the curcuminoids included in the extracts. An immunomodulator that has the ability to increase and decrease proinflammatory cytokines, are not always uniform. When COVID-19 patients are undergoing a cytokine storm, the administration of curcumin may increase the production of proinflammatory cytokines, potentially aggravating their disease. This is because certain COVID-19 patients have hypercytokinemia and inflammation. The formation and role of curcumin in COVID-19 prevention as well as its cure must be established through research that has to be conducted immediately.

*Cinchona* sp. *Cinchona* trees (*Cinchona* L, *ralatea*): These trees are very beneficial because a specific part of them contains bioactive compounds that can treat fever. Jesuit missionaries were the ones who initially identified the positive impact, which over time spread around the globe (Maldonado, Barnes, Cornett, Holmfred, Hansen, Persson, & Rønsted, 2017). Quinine alkaloids, which are produced by plant bark, have long been used as an effective malaria treatment. Quinine is regarded as a chloroquine analogue because of its comparable mode of action to that of the synthetic antimalarial drug chloroquine (Abolghasemi *et al.*, 2012). However, due to the fatality rate of COVID-19 and high prevalence worldwide, improper statements made by state and health officials prompted public panic and competitive

demand or search for quinine-containing medications, triggering spontaneous reactions.

According to D'Alessandro, Scaccabarozzi, Signorini, Perego, Ilboudo, Ferrante, and Delbue (2020), there is evidence indicating that many antimalarial drugs have been studied, and it was concluded that some of them provide benefits against viral infection. Chloroquine, for instance, has shown antiviral activity against the SARS-CoV infection. A clinical trial demonstrated that when azithromycin and hydroxyl-chloroquine are used together, the SARS-CoV-2 virus load in COVID-19 patients improves. Based on these data, it is possible to anticipate that quinine, a counterpart of chloroquine, can help eradicate COVID-19 (Gautret, Lagier, Parola, Meddeb, Mailhe, Doudier, & Raoult, 2020).

The first investigation into quinine's anti-influenza virus infection effect was conducted in 1946 by Seeler, Graessle, and Ott. Furthermore, it was reported by Baroni, Paoletti, Ruocco, Ayala, Corrado, Wolf, and Donnarumma (2007) that quinine's antiviral effect reduces viral infection by indirect means, such as inducing the protein heat shock response, blocking several pathways involved in virus replication, and inhibiting gene expression. Quinine can result in a variety of general unfavorable effects, such as immune-mediated reactions and toxic reactions, according to Liles, Page, Liles, Vesely, Raskob, and George (2015). There is also reported evidence of organ system damage, including thrombocytopenia and hemolytic anemia, dermatitis, systemic responses, hypotension, allergy, and cardiac symptoms such as pericarditis and chest discomfort.

Roza, Selly, Munsirwan, and Fadhilah (2021) have determined the interaction between quinine derivative compounds and SARS-CoV-2. According to the results, quinine was among the ten compounds that were tested against SARS-CoV-2 virus cells and showed the ability to act as an antiviral. Tallei, Tumilaar, Niode, Kepel, Idroes, Effendi, and Emran (2020) investigated the effects of 13 plant bioactive compounds, including quinine, against SARS-CoV-2 Main Protease (MPro) and Spike (S) Glycoprotein Inhibitors using molecular docking. Compared with the common chemicals hydroxychloroquine (HCQ) and chloroquine (CQ), quinine binds more quickly.

In 2020, Große, Ruetalo, Businger, Rheber, Setz, Rauch, and Schubert undertook a study to assess the impact of Quercetin (QS), Chloroquine (CQ) and Hydroxychloroquine (HCQ) on the reduction of SARS-CoV-2 cell proliferation in Vero B4 cells. Western blot analysis was used to determine the viral generation from cell culture supernatants obtained three days post-infection. Based on the results, 10  $\mu$ M QS was able to almost completely prevent the production of virion progeny while decreasing the potent SARS-CoV-2 virus's replication. QS indicated a higher amount of suppression of SARS-CoV-2 virus reproduction than CQ and HCQ. At 10  $\mu$ M QS, viral replication was reduced by 90%, whereas HCQ only reduced it by 50%. In summary, QS demonstrates increased activity compared to CQ and HCQ.

Quinine has both immunostimulant and immunological suppressive properties against viral infections, making it a poor choice for classification as an immunomodulator. When

it successfully boosts the cytokine IFN- $\alpha$  production, it acts as an immunostimulator to block viruses, but when it suppresses the release of TNF- $\alpha$  (tumor necrosis factor), it has an immunosuppressive effect on COVID-19-infected individuals. The COVID-19 patient may benefit from these various activities. It is not advised for healthy individuals to regularly consume this herbal remedy to prevent COVID-19 due to the potential for negative side effects.

Xanthorrhizol, also known as Java turmeric, xanthorrhizol (XNT; C<sub>15</sub>H<sub>22</sub>O, 2-methyl-5-[(2R)-6-methylhept-5-en-2-yl]phenol) is a main component of the rhizomes of *Curcuma xanthorrhiz* Roxb., a plant that resembles ginger and belongs to the Zingiberaceae family (Oon, Nallappan, Tee, Shohaimi, Kassim, Sa'ariwijaya, & Cheah, 2015). XNT can be chemically produced utilizing basic starting materials, or it can be isolated from the *Curcuma* rhizome (Du, Zheng, Chen, & Lv, 2011; Rahmat, Lee, & Kang, 2021). Many biological actions, including anticancer, antibacterial, antioxidant, anti-inflammatory, antihypertensive, antiplatelet, nephroprotective, and hepatoprotective properties, as well as estrogenic and/or anti-estrogenic effects, have been reported (Jantan, Saputri, Qaisar, & Buang, 2012; Oon *et al.*, 2015). Because it inhibits proinflammatory cytokines, xanthorrhizol is used as an immunosuppressant in the treatment of COVID-19. However, because Xanthorrhizol has not been investigated for COVID-19 to date, both preventive and therapeutic properties of this compound require additional investigation in a clinical trial as well. Therefore, the intake of the herb should be

done under certain conditions and gradually in other conditions.

#### 4.0 Recommendations and Conclusion

Practically no nation is unaffected by the COVID-19 pandemic. It must be managed as quickly as possible because it represents one of the biggest hazards to public health to date. In medicinal plants, numerous secondary metabolites with antiviral characteristics have been identified. The most effective strategy to stop COVID-19 infections might involve identifying the substance that is modifying or interfering with any stage of the viral replication cycle. It is necessary to investigate natural products that can inhibit or change the structure of non-structural proteins (such as 3-chymotrypsin-like protease, papain-like protease, and helicases) and accessory proteins encoded by the SARS-CoV-2 genome. Natural products may be a reliable, secure, and safe way to locate the medication that contains the current pandemic. It is also necessary to investigate protease and RNA inhibitors that have been shown to be effective against MERS and SARS. For the treatment of SARS-CoV-2-infected patients, several substances (polyphenols, flavonoids, alkaloids, terpenoids, and proanthocyanidins) that are previously known to have antiviral activity need to be quickly tested. Patients would have to rely on supportive care and symptomatic therapy in the absence of a proven COVID-19 drug. As a result, a variety of natural medicines and herbal extracts may be able to help cure the symptoms of the SARS-CoV-2 infection.

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