

Review Article

Herbal Remedies with potential COVID-19 Activities

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Abstract

The novel coronavirus disease 2019 (COVID-19) was generally viewed as presenting a major danger to mankind owing to its uncertain, impending pandemic. This latest virus has high infectivity, death and latency. The virus's genetic (antigenic) structures are constantly changing, which makes developing a vaccine difficult. Many conventional drugs are being repositioned (i.e. repurposing) and used for prophylactic and therapeutic purposes, while several vaccine trials are underway. The results, on the other hand, were not very encouraging, and they frequently resulted in serious negative consequences. Safe alternative remedies are therefore required to reduce the severity and duration of acute disease and its complications. Traditional and complementary medicine combined with allopathic drugs, and Moroccan medicinal plant extract showed significant benefit in symptomatic SARS-COV-2 patients. Traditional medicine derived from Indian herbal plants has been used to treat

human diseases in India since ancient times. It is widely available, inexpensive, and free of side effects. Antiinflammatory, immunomodulatory, and antiviral bioactivities have been demonstrated for phytonutrients, flavonoids, phytomelatonin, and other compounds found in Indian herbal plants. We discuss some of the potential antiviral herbal plants in this review based on their history of use in treating COVID-19 or other viral infections. Given the advantages of these preparations, government agencies should be more interested in them and provide more funding. More experimental (basic, translational, and clinical) studies are needed to determine the efficacy and safety of these ingredients, either alone or in combination.

Key words

Herbal, Remedy, Covid – 19.

Introduction

The world faces a new coronavirus pandemic (COVID-19) from Coronavirus 2 Severe Acute Respiratory Syndrome (SARS-CoV-2). A report dated 8 April 2020 reported that approximately 1.43 million people were infected, and 82,100 were killed. The number of infected people and deaths increased daily despite the lack of therapeutic medicine, all of which were taken preventively in the entire infected country. The infection with Coronavirus is now caused by the deadly pandemic worldwide. Whilst COVID-19 therapies are not yet officially licensed pharmacologic agents, and several international health agencies are actively interested in clinical trials of various compounds [1-16].

The pandemic persists, and finding innovative prevention and medicines or vaccinations is vital and necessary as early as possible. Moreover, efficient interventions must be introduced to identify, exclude and diagnose individual patients, as well as to reduce visibility and distribution through social contacts and activities. CoV disease therapies are ineffective or approved, and protective vaccines are still being examined. Powerful antivirals must therefore be discovered to protect and manage CoV infection in humans [17-23].

This review highlights the outbreak of the pandemic of Coronavirus, the infection mechanism and the most appropriate medicinal plants. Since ancient times, medicinal plants

have been used for various diseases, including viral infection. The latest pharmacology industry also depends mainly on herbal medicinal formulations for most of the developed diseases worldwide. Prevention actions, such as hand sanitizing, hand washing, social distance, etc., to deal with this pandemic are, therefore now the time to develop therapeutic medicines. The cognition of antiviral medicinal plants can apply to the new formulations of the drug or can be consumed at the social level to strengthen the human immune system.

Ayurveda, an old Indian medicine method, has been practiced in India for almost 5000 years and relies heavily on plants for its formulation. Ayurvedic herbal supplements and immunity boosters show the way to a large-scale, hour-needed antiviral drug. There have been reports for plants such as Glycyrrhizaglabra, Andrographispaniculata, Phyllanthus spp., Zingiberofficinale, Withaniasomnifera and longa Curcuma antiviral. Others, like Tinosporacordifolia and Emblicaofficinalis[24-25]. Therefore, Ayurveda has a considerable role to play in alleviating the pandemic, but the studies should be significantly carried out, simplifying learning, proving and providing a way forward [26].

Research into Vitex trifolia and Sphaeranthus has shown that the NF-kB pathway was inhibited following the reduction of inflammatory cytokines which involve SARS-CoV respiratory distress [27, 28], for coronaviral anti-mouse

activity. Clitoriaternatea has the inhibitory effect of ACE shredding metalloproteinase, primarily linked to virus replication. It is documented that the plant *Strobilanthes Cusia* blocks HCoV infection [29]. Amber et al. [30] confirmed that the traditional use in the bronchitis of the *Justicia adhatoda*, *Verbascum Thapsus* and *Hyoscyamus Niger* reduced influenza virus infections. Kambizi, et al. [31] showed that *Aconitum ferox* and *Withaniasomnifera* have anti-HSV-1 activity for aqueous extracts.

Several medicinal plants can inhibit the action of ACE [32, 33, 34], including *Cynarascolum*, *Punicagranatum*, *Coscinium fenestratum*, *Boerhaaviadiffusa*, *Cassia occidentalis*, *Embeliaribes*, and *Coriander sativum*. In one *Salacia oblonga* sample, anti-angiotensin II activity was reported [35]. *Andrographis paniculata*, commonly referred to as Kalmegh is recognised for its effectiveness against viral respiratory infections [36-41]. The antispasmodic, odontalgic, antirheumatic and ruby-acient drug has a very good background. The Chinese sassafras oil is produced by *C. Camphora*. It is made from camphor, sofrole, linalool, borneol, dipentene, terpineol and film [42]. It has also been well established that Camphors has antihistamine, antibacterial activity, anti-inflammatory activity, antioxidant bronchitis, sprain, pain with rheumatism, etc. A typical organized feature of the camphor molecule is its rigid cage-hydrocarbon structure like amantadine, rimantadine and most powerful antiviral medicines [44].

Antiviral activity of these compounds has been caused by the blockade of virally encoded protein M2, which acts as a protein channel essential for hemmagglutinin cleavage and viral envelope and host cell membranes [45]. New biologically active antiviral compounds achieve the chemical modification of natural compounds. Camphocene is a new amino-camphor derivative with high antiviral activity and low toxicity [46]. Camphocene is dependent upon hepten-2-ylidene-aminoethanol-1,7,7-trimethylbicycle

(2.2.1); amino camphor derivatives are an effective inhibitor of M2 influenza ion channels [47]. Bananins are strong antiviral compounds near classical drugs (trioxa-admantene moiety covalently linked to pyridoxal derivatives). The bananas and their derivatives have been confirmed by Tanner et al. [48] to be both strong inhibitors of SARS-Coronavirus ATPase and helicase activity, inhibiting the replication of SCV. Camphor-1 M greatly decreased COVID-19-related deaths in Iran by using homeopathic drugs. In India, the Ayurvedic, Yoga and Naturopathic, Unani, Sidha and Homoeopathy (AYUSH) Ministry recommended the use in the COVID-19 medical surveillance for prophylaxis of *Arsenicum Album 30* (Ars Alb 30C) and *Camphor 1 m* (homo-opathic formulations). These narcotics have therefore been given to many Indian states and police forces.

Tulasi (*Ocimum sanctum*) belongs to the family of plants *Lamiaceae*s, commonly used in Indian medicines; also known as Holy Basil, Mother of Natural Medicine, and the Queen of Herbs. This is contained in the Himalayas in India, up to 1800 m above sea level. *Tulasi*'s major bioactive molecules are oleanolic acid, rosemary acid, ursolic acid, carvacrol, eugenol and caryophyllene. There are hundreds of scientific studies indicating that this plant has a particular combination of antidiarrheal, antioxidant, antimicrobial, hepato-protective, antiinflammatory, antidiabetic, cardioprotective, anti-allergic, antipyretic, cardioprotective, cardiovascular, antimalarial and antiprotozoal behaviour. *Ocimum sanctum* extract has considerable potential to inhibit the free radicals in the cell formed. The phenolic compounds, namely apigenin and rosmarinic acid, isothymusin, cirsimaritin, cirsilineol, and significant quantities of eugenol from the stems and leaves, had high antioxidant activity [49].

The immunomodulatory effect of *Ocimum Sanctum* is demonstrated by raising the number of IL-'4, NK, IFN- α and T-helper cells [50]. Since the 1990s, herpes simplex virus types 1

and 2 have had increased antiviral effects in cell culture from flavonoid molecules such as 6 hydroxyflavone, apigenin (**Figure - 1**), tangeritin, wogonin, scutellarein, chrysin and luteoline [51]. Pandey, et al. [52] have identified natural flavonoids that have inhibited SARS-CoV helicase activity due to the elimination of ATPase activity.

Zingiberofficinale is one of the most widely used herbs in the Zingiberaceae family. The Rhizome is the part of the ginger that is eaten. It has been developed for a long time as a spice. It has been used as a common medicine in various medicines since the last decade [53]. Ginger comprises different compounds such as gingerol, gingerdiol and gingerdione that have anti-inflammatory, anti-diabetic, anti-cancer, chemical prevention and chemotherapeutic effects, anti-microbial and antioxidant ginger properties [54, 55, 56] ginger contains ginger.

Cordifoliatinospora is generally referred to as Giloy or Guduchi. Three major species of tinospora are found primarily in Myanmar, mostly tropical and subtropical areas in India, Sri Lanka, and in China, Tinosporacandifolia, Tinosporamalabarica and Tinosporacrispa. The active components of plants are flavonoides, glycosides, phytosterols, alkaloids, polysaccharides and others. Several chemical components were obtained from various tinosporic parts, including giloin, tinosporic acid, tinosporite, berberine, palmatin, isocolumbin, columbin, choline, tinochordifolin, etc.

This plant has also been recognised as anti-allergic, antioxidant, anti-inflammatory, antipyretic, antioxidant and anti-cancer. Giloy root extracts showed positive immune system modulation in HIV patients. Tinosporachordifolia has been confirmed to have a protective effect against swine flu. Tinospora is a powerful naturally occurring immunomodulator. It causes chemotaxis, macrophage phagocytosis and stimulates B- and other cells that regulate immune systems.

Tinosporachordifolia has a high anti-stress and antioxidant potential. Powerful against COVID-19 could be Giloy's phytochemicals, such as tinocodiside. Previously, the in-silico model tinocodisides dock was found inside the ACE2-RBD complex, suggesting that the best options for the host cell entry of COVID-19 can be rich giloy extracts from Tinocodiside. Innate immunity to COVID-19 infections will be strengthened by Giloy's immunomodulation property [58, 59].

Many in vivo and in-vitro studies have shown Licorice and glycyrrhizin to have potential as therapeutic agents against several viral diseases, including vaccine viruses, chronic hepatitis A, B and C, respiratory syncytial viruses, human immunodeficiency viruses (HIV), SARS associated coronavirus, arbovirus and VSV [60, 61, 62, 63].

Nyctanthes, also known as Harsingar or Parijatha, belong to the Oleaceae/Nyctanthaceae family. N. Arbortristis leaves contain oleanolic acid, methylated salicylate, astragaline, iridoid glycosides, amorphous resins, flavanol glycosides, nicotiflorin, carotene, β -sitosterol, benzoic acid, and nyctanthical acid. Arbortristoside A&B, oleic acid, glycerides, lignoceric acid, linoleic acid and 3-4 secotriterpene acid produce nyctanthesarbortristis seeds. Glycosides and alkaloids are found in the bark of N. Arbortristis. In vitro conditions demonstrated the bronchodilatory effect of this plant ethanol extract. Asthma treatment was shown to stabilise the mast cell and bronchodilate the activity of N. Arbortristis bark [64]. The 0.25 and 0.5 g/kg body dose administration of plant ethanol extract has shown that splenic antibody cells, leukocyte counts and the phagocytic index have increased significantly. Plant ethanol extract with Arbortristoside C and Arbortristoside A; Semliki Forest Virus (SFV) inhibitory activity and Encephalomyocarditic virus (EMCV). N. Arbortristis and the n-butanol fraction in-vivo

ethanol extract protect infected EMCV mouse from SFV [65].

Tea leaves are rich in polyphenol (catechin and flavonoids) (*Camellia sinensis*) [66]. Green tea consists of six main catechin compounds such as epigallocatechin, epicatechina, catechin, galocatechin and gallate epigallocatechin (**Figure - 1**). Polyphenols range from 30% to 40% and from 3% to 10% in green tea and black tea respectively. Tea consumption's health benefits are well known and published extensively in the literature [67]. The efficacy of tea in the treatment of COVID-19 has recently become hype. Preliminary evidence has shown that tea could be a possible antiviral agent that could potentially inhibit the replication of Coronavirus (COVID-19) in the human body [68]. This led to the presumption that tea consumption could benefit from SARS Cov-2 due to its plentiful chemical components. Polyphenolic compounds like Prodelphinidine B-2 39-gallate inhibited the entry of HSV type 2, HIV-1, into target cells. ECGC has also been reporting a viral hemagglutinin binding to prevent influenza virus infection [69].

Catechins have activity of the anti-influenza virus. Epigallocatechin gallate has greater activity than viral infection after the suppression of viral DNA and RNA polymerases than epicatechingallate activity. However, the most important inhibition of these compounds with HIV reverse transcriptase was observed [70, 71]. The blocking of HIV-1 glycoprotein 120 to CD4 molecules on T-cells has been confirmed by epigallocatechin gallate [72].

Withaniasomnifera, a family Solanaceae shrub, is commonly used in folk medicine as an immunosuppressive agent. Its medicinal properties are due to its most bioactive steroidal lactones known as anolides. This is steroidal molecules oxygenated. Some 130 anti-inflammatory, anti-tumor, antioxidant, and anti-microbial properties have been well-established with *Withania* sp. isolation. The virus

replication after hydro-alcoholic extract of *W. Somnifera* was stunned [73].

The unsung floral variety of the Himalayas is known as the medicinal plants' warehouse. The ethnomedicinal properties of the available dishes were established in ancient times. Many plants found in this area have recently confirmed the properties of anti-SARSCoV-2, anti-influenza virus infection and other antiviral infections. The extract of those plants mainly inhibits the entry of the virus to the cell, inhibits viral replication, inhibits the NF-kB pathway and inhibits host cell immunomodulation [74]. *Cymbopogon* sp., which is primarily found in Asian and African countries and is commonly found in Australia, is herbal lemongrass. As an antimicrobial agent, lemongrass extracted essential oil (EO) has a strong potential. Studies have shown that the antimicrobial resistance of pathogens is affected by lemongrass EO [75, 76]. Other studies have also identified a potential antiviral extract from *Cymbopogon* sp. Bahtiar, et al. [77] confirmed that *Cymbopogon* ethanol extract attenuated the activity of herpes simplex virus serotype 1 (HSV-1), antimeasles, serotype 1, anti-hepatitis-A virus, anti-norovirus murine [78-82].

Xanthorrhizol can be used as a COVID-19 drug because it prevents proinflammatory cytokines. COVID-19 patients are vulnerable to CRS. In a patient with COVID-19 with or without CRS, xanthorrhizol can decrease the proinflammatory response. But xanthorrhizol should be administered cautiously and with consideration since no analysis of xanthorrhizol in COVID-19 has been performed. There is still an opportunity for xanthorrhizol administration to exacerbate conditions in COVID-19 patients. The use of xanthorrhizol in COVID-19 for treatment and prevention needs further evaluation, especially in the clinical trial environment. Research in hippocampal neurons and primary-culture microglia on anti-inflammatory and antioxidant effects of xanthorrhizol was in line with the previous study in patients with diabetes mellitus

and SLE. It has been shown that xanthorrhizol can suppress pro-inflammatory cytokines such as IL-6 and TNF- α generation and secretion. Its inhibition combines inhibited nitric oxide synthase (iNOS) and a decreased nitric oxide production (NO). In combination, xanthorrhizol is an immunosuppressant as an immunomodulatory substance [83].

Conclusion

In view of a large number of conventional medicinal herbs with good results, it seems fair to believe that these items contain various forms of antiviral compounds. A secondary metabolite characterization will show additional health benefits. Therefore, the widespread use of many conventional medicines for viral infection prevention is warranted. Finally, it is important for new antivirals from medicinal plants and herbs to be discovered and developed to address threats posed by specific pathogens such as the 2019 nCoV.

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