Exploring the synergistic potential of natural plants as antiviral agents against COVID-19

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Abstract

The proposal of novel drugs and approaches for effective treatment of the novel coronavirus is necessary after the quick outbreak of the disease. Since the commencement of the coronavirus spread, enormous efforts have been made to protect, alleviate, and cure the disease, though no specific treatment has been approved. Medicinal plant species can provide a solution as a source of natural antiviral compounds through the accumulation of secondary metabolites and lectins, as well as acting as a platform to express the viral immunogenic proteins. Several plant-derived anti-coronavirus compounds have been nominated that could be targeted for further research due to the similarity of the coronavirus disease in 2003 and the current coronavirus. This review considers plant species like Scutellaria baicalensis (Baikal skullcap) and Utrica dioica (stinging nettle) as viable candidates for the new coronavirus antiviral research. This paper examines the benefits and findings of earlier investigations into the novel coronavirus illness and earlier iterations of related corona viruses.

Keywords: Novel drugs, Medicinal plant, Anti-coronavirus, Scutellaria baicalensis, Utrica dioica, Corona virus

Introduction

At the end of 2019, the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) virus, which is caused by the 2019 novel coronavirus (2019-nCoV), became a significant public health concern. After SARS-CoV in 2002 and the Middle East respiratory syndrome coronavirus (MERS-CoV) in 2012, SARS-CoV-2 recorded the history of the third major coronavirus outbreak to affect the human population (Lai et al., 2020).

SARS-CoV-2 cases are still slowly increasing as a result of its quick human-to-human transmission, pushing 7426 people to their deathbeds by the 17th of March 2020. Meanwhile, 179,111 infected cases have been documented in more than 150 countries around the world. Even if there aren't many antiviral treatments available for patients, the lack of SARS-CoV-2- specific antiviral medications or vaccinations is making the situation worse (Organization, 2020).

Epidemiology

Globally, there have been more than three million COVID-19 cases that have been confirmed. On the websites of the World Health Organization and the European Centre for Disease Prevention and Control, you can find updated case counts in English. You can access an interactive map highlighting confirmed cases around the globe here (McIntosh et al., 2021). More than 80,000 COVID-19 cases have been recorded in China, the majority of them in Hubei and neighboring provinces, since the initial cases from Wuhan, a city in the Hubei Province, were reported at the end of 2019 (Steardo et al., 2020). According to a joint fact-finding expedition by the World Health Organization (WHO) and China, the pandemic in China peaked between late January and early February

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2020, and the number of new cases had significantly declined by early March.

Transmission: The risk of transmission is not fully understood. When the outbreak first started in Wuhan, an epidemiologic investigation found a preliminary link to a seafood market that sold live animals, where the majority of patients had either worked or visited, and which had since been closed for sanitization (Dhama et al., 2020). However, as the outbreak spread, person to person transmission became the predominant method of infection.

Route of person-to-person transmission is uncertain how severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) spreads from person to person. It is believed to spread mostly by respiratory droplets, much like influenza does (World Health Organization, 2020). When a person with an infection coughs, sneezes, or talks, the virus that is released into the respiratory secretions can infect another person if it comes into contact with the mucous membranes directly. Infection can also happen if a person touches an infected surface and then touches his or her eyes, nose, or mouth. Droplets normally do not linger in the air or fly farther than six feet (approximately 2m) (Stadnytskyi et al., 2021).

Whether or not SARS-CoV-2 may be spread by air travel (through particles smaller than droplets that remain in the air over time and distance) (Zimmerman et al., 2021).

Severe acute respiratory syndrome coronavirus (SARS-CoV or SARS-CoV-1), which caused the 2002–2004 outbreak of severe acute respiratory syndrome (SARS), and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which is causing the 2019–20 coronavirus disease pandemic, are two strains of the virus that have caused outbreaks of severe respiratory diseases in humans (COVID-19).

**Virus classification**

<table>
<thead>
<tr>
<th>Unranked</th>
<th>Virus</th>
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<tbody>
<tr>
<td>Realm</td>
<td>Riboviria</td>
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<tr>
<td>Kingdom</td>
<td>Orthornavirae</td>
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<tr>
<td>Phylum</td>
<td>Pisuviricota</td>
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<td>Pisoniviricetes</td>
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<td>Betacoronavirus</td>
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<tr>
<td>Subgenus</td>
<td>Sarbecovirus</td>
</tr>
<tr>
<td>Species</td>
<td>Severe acute respiratory syndrome-related coronavirus</td>
</tr>
</tbody>
</table>

**Genome**

The SARS-related coronavirus is an enclosed, positive-sense, single-stranded RNA virus, and upon entry into the host cell, the ribosomes directly translate the positive-sense RNA genome (Astuti, 2020).

**Structural proteins**

Spike, envelope, membrane, and nucleocapsid

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**Life cycle**

**Attachment**

The spike protein and the angiotensin-converting enzyme 2 (ACE2) receptor play a role in how the SARS-related coronavirus attaches to the host cell (Beyerstedt et al., 2021).

**Entry**

Following attachment, the virus can enter the host cell by two different paths first e path the SARS e coronavirus: may use endocytosis and e uptake of the e virus in an endosome to enter the host cell. The host's pH-dependent cysteine protease, cathepsin L, subsequently activates the receptor-attached spike protein. A conformational change brought on by the receptor-attached spike protein's activation leads to the fusion of the viral envelope and endosomal wall.
Second path

The host's TMPRSS2 or TMPRSS11D serine proteases can cleave the receptor-attached spike protein, allowing the virus to enter the cell directly. By causing conformational changes that are not well understood, the C-terminal activation of the spike protein in the SARS coronavirus causes the viral envelope and host cell membrane to fuse (Sakai et al., 2014).

Genome translation

The viral genome is released when the nucleocapsid enters the cytoplasm following fusion. Two-thirds of the genome is translated by the cell's ribosome, which also functions as messenger RNA. The polyproteins have built-in proteases called PLpro and 3CLpro that cleave them at several specified places. 16 nonstructural proteins are produced upon the cleavage of polyprotein pp1ab (nsP1 to nsP16). Product proteins include diverse replication enzymes such as exoribonuclease, RNA helicase, and RNA-dependent RNA polymerase (RdRp) (Malone et al., 2022).

Replication and transcription

Multi-protein replicase-transcriptase complex is formed when many of the nonstructural replication proteins come together (RTC). The RNA-dependent RNA polymerase is the primary protein involved in replicate transcription (RdRp). It participates directly in the transcription and replication of RNA from an RNA strand (Yadav et al., 2021).

Functions of the replicase-transcriptase complex is to transcribe the viral genome

The production of molecules of negative-sense subgenomic RNA from positive-sense genomic RNA. These negative-sense subgenomic RNA molecules are then translated into their equivalent positive-sense mRNAs.

The creation of negative-sense genomic RNA using positive-sense genomic RNA as a starting point. The replication of positive-sense genomic RNA from negative-sense genomic RNA occurs next.

The four structural proteins (S, E, M, and N) that make up the progeny virus particles are produced from the replicated positive-sense genomic RNA, which also serves as the genome of the offspring viruses (Schoeman and Fielding, 2019).

Assembly and release

The endoplasmic reticulum is where RNA translation takes place. The secretory route carries the viral structural proteins S, E, and M into the Golgi intermediate compartment. Following their binding to the nucleocapsid, the M proteins control the majority of protein-protein interactions necessary for the assembly of viruses there. Viral offspring are exocytosed from the host cell via secretory vesicles (Upadhyay and Gupta, 2022).

Common symptoms

Fever
Pain
Headache
Myalgia
Sore throat
Conjunctivitis

Respiratory symptoms

Dry cough
Shortness of breath

Digestive symptoms

Diarrhea
Loss of appetite

Commonly asked questions about Coronavirus What is the virus really?

A virus known as SARS-COV-2, a member of the Coronaviridae family, is the root cause of the current coronavirus pandemic and causes the illness COVID-19.

How does it infect?

A spike-like feature that adheres to the plasma membrane of human cells allows it to infect cells.

How long does it take for people to feel sick?

People can have the virus in their system for up to 14 days before symptoms ever appear because the virus has an incubation period of up to two weeks (however, there are many instances of asymptomatic or weakly symptomatic cases) (WHO, 2020).

What part of the body does SARS-COV-2 virus affect?

It primarily targets the respiratory system, which in the most severe cases can lead to viral pneumonia and be complicated by the acute respiratory distress syndrome (ARDS), sepsis, and septic shock, as well as multiorgan failure, including acute kidney injury and cardiac injury as well as sepsis and septic shock (Hussain et al., 2021).

Is there a cure or vaccine for coronavirus?

No. Researchers are working around the clock to try to develop a treatment, but there is no vaccine or confirmed cure. Doctors are investigating various treatment options, including plasma therapy and hydroxychloroquine (Samuels and Kelly, 2020).
If I have coronavirus, are there things I can do to get better?

Yes. If their symptoms are not severe, many people are being advised to stay at home and avoid going to the hospital. But if you need to treat yourself at home and want more advice, it's crucial to get in touch with a medical expert. This guide offers some suggestions for how you might aid in your body's healing, but treating your symptoms without the support of a qualified medical practitioner is not recommended (Samuels and Kelly, 2020).

What are doctors recommending?

Ibuprofen is currently prohibited unless expressly prescribed by a doctor for persons who have a coronavirus infection since it has been shown to aggravate the course of the infection. In addition, some medical professionals advise taking more vitamin C and D, eating a balanced diet, exercising frequently, adhering to a regular sleep pattern, and reducing stress (Meng et al., 2020).

What else can I do to get better?

More gentle herbal treatments, together with rest, a healthy diet, and stress reduction, may be able to control many coronavirus symptoms (Nawrot, Gornowicz-Porowska et al., 2022).

The plant play role synergistic effect with antiviral in treatment Covid 19

The plant play role

Because there is presently no specific coronavirus medication or vaccine available. Clinical studies have demonstrated the usefulness of various anti-viral medications, including chloroquine phosphate, lopinavir/ritonavir, interferon, ribavirin, and favipiravir in treating coronavirus patients. We thus use some plants that are effective at inhibiting entrance viruses, genome translation, and transcription in order to boost the efficacy of these treatments. In addition to these, plants help the body's defenses against illness by supplying vitamins and minerals vital for boosting defenses against coronavirus. It also serves as a form of viral defense. At this time, it is crucial to use plants to boost the effect of antivirus on improving the condition of people with the coronavirus so that they can recover. These plants either use fresh food or blend with other components to improve their taste.

Classified of plant according to the effect on replaction cycle

Inhibition attachment of virus stage 1 by

Lectin

A complex protein or glycoprotein with the capacity to bind to cells or cell membranes and trigger biochemical events as a result of its ability to bind to particular carbohydrate structures. These proteins have the ability to start a variety of reactions, but they do not engage in any enzymatic activity.
Mechanism of lectin against COVID 19

Prevents the virus attachment by inhibition of the SARS-CoV spike (S) glycoprotein

Examples on the food that contain high lectin Beans, Wheat, Peanuts, Tomatoes, Potatoes.

Rout of prepared plants to administration either fresh food or by one of the methods dependent on the plant’s preparation, prepared from plants.

Teas - 2 types

For leaves, flowers, and roots with a higher water content, infusion is used. Steep the herbs or tea in boiling water for 7 to 10 minutes.

Decoction- For tougher herbs and roots. Bring the water to a boil, add the selected herb, lower the heat, and let simmer for 30 to 60 minutes.

Extract/tincture-alcohol-extracted components of herbs are frequently offered for sale at pharmacies, herbal shops, and supermarkets.

Powders-finely-herbs that have been powdered and can be used in foods, drinks, or turned into capsules or pastilles

Honey infusion/syrup-herbs cooked slowly with honey to draw out their active ingredients

Immune-supported by

- Vitamins
- Minerals

Vitamins that have antioxidant effect include

Vitamin C Sources Fruit, especially citrus fruits, and vegetables contain ascorbate. It serves as a preservative when added to other meals. Humans are not capable of synthesizing it. Vitamin C-rich foods include oranges, kiwis, kale, and broccoli (Schleicher et al., 2009).

Function

Enhance its immune-modulating properties. It is a powerful antioxidant because of its propensity to donate electrons, preventing oxidants produced by normal cellular metabolism as well as those brought on by exposure to toxins and pollutants from harming vital biomolecules (such as proteins, lipids, carbohydrates, and nucleic acids) (e.g., cigarette smoke).

At dietary intakes of less than 100 mg per day, neutrophils, which absorb vitamin C through the sodium-dependent vitamin C transporter (SVCT2), reach their peak vitamin C concentrations. It is believed that protecting neutrophils from oxidative damage involves accumulating millimolar quantities of vitamin C inside of them, especially after activating their oxidative burst.

may replenish the crucial cellular and membrane antioxidants glutathione and vitamin E as well as scavenge various harmful oxidants.

Lymphocyte B- and T-lymphocytes utilize SVCT to accumulate vitamin C in high amounts in a manner similar to phagocytes. According to in vitro research, vitamin C incubation with lymphocytes enhances antibody production by promoting proliferation and conferring tolerance to a variety of cell death stimuli. Moreover, vitamin C seems to be crucial for the differentiation and maturation of developing cells. Both mature and immature natural killer cells exhibit similar proliferation and differentiation/maturation properties.

Vitamin E

Sources

Vegetable oils are one of the main dietary sources of vitamin E. Moreover, nuts are a good source of vitamin E. Compared to other oils, soybean, sunflower, corn, walnut, cottonseed, palm, and wheat germ oils have relatively greater concentrations of vitamin E (more than about 50 mg vitamin E per 100 g oil) (Shahidi et al., 2021).

Function

Neutralizes peroxyl radicals and prevents polyunsaturated fatty acid oxidation (PUFAs). The peroxyl radical chain reaction is broken, further oxidation of PUFAs in the membrane is avoided, and peroxyl radicals react with tocopherol rather than lipid hydroperoxide. Vitamin C or glutathione can diminish tocopheroxyl radicals, which are created from tocopherol and peroxyl radicals.

By enhancing humoral reactions, on B Cells.

Vitamin E increases the activity of natural killer cells by lowering PGE2 production by inhibiting COX2 activity, which is mediated by a decrease in NO generation.

Vitamin A Sources

The carotenes, which are precursors to vitamin A, are present in the yellow and green sections of plants and are particularly prevalent in carrots. Each molecule of b-carotene can make two molecules of vitamin A, which are then hydrolyzed in the intestinal mucosa and absorbed as retinol esters and stored in the liver. This active vitamin is then created. Retinol is found in milk products and eggs as well as being delivered to tissues by the a-globulin retinol-binding protein (RBP) (Clagett-Dame and Knutson, 2011).
**Function**

**Antioxidant scavenger of free radical**

**Minerals improvement immunity system includes**

**Zinc (zn) Source**

Foods that contain zinc include lima beans, shiitake mushrooms, spinach, green peas, broccoli, okra, sweet corn, asparagus, beet greens, and lentil sprouts.

**Function**

An important micronutrient for DNA synthesis and cell growth is zinc (Fuhrman, 2020; NIH, 2020). Moreover, it controls cell signaling, the development of immune cells, and innate and adaptive immune responses.

**Magnesium(mg)**

**Source:** Black beans, avocados, whole grains, seeds, dark green vegetables.

**Function**

For our immune systems, a very important mineral. The natural killer cells and lymphocytes of our immune system are strengthened by magnesium, a vital mineral electrolyte. Another important source of energy for our cells is adenosine triphosphate (ATP), which is necessary for normal cell activity. Since the COVID-19 virus targets the respiratory system, magnesium supports the function of the blood protein hemoglobin, which is in charge of carrying oxygen from the lungs to every cell in the body.

**Selenium**

**Source**

Is a mineral that can be found in water, food, and soil. It is necessary for numerous bodily functions to function properly.

Food that contains selenium such as, Brazil nuts, Bread, Broccoli (Shakoor et al., 2021).

**Function**

The electrophilic center on the selenium atom or the nucleophilic center on the oxygen atom of the selenohydroperoxide group, which are both involved in the chemical pathway, operate as antioxidants.

**Classification of drugs for treatment covid 19**

**Antiviral for herpesvirus infections**

**Favipiravir:** 500 mg 3 times every 8hr for 7 days

**Mechanism of action**

Inhibition of replication and transcription by RNA-dependent RNA polymerase (RdRp) inhibitor.

**Antiviral for respiratory viral infection**

**Ribavirin**

Adults should receive 500 mg intravenously, 2-3 times per day, in addition to IFN- or lopinavir/ritonavir.

Mechanism of action: suppressing guanosine triphosphate synthesis, viral messenger RNA (mRNA) capping, and RNA dependent RNA polymerase to hinder genome translation.

**Antiviral for hepatic viral infections**

**Interferon α (IFN-α):** Adults are given IFN- by inhaling vapor at a dose of 5 million U (2 mL of sterile water for injection) twice daily.

Mechanism of action: Understanding of the antiviral mechanism is lacking. It seems to entail the activation of viral RNA-inhibiting host cell enzymes.

Translation, ultimately leading to the degradation of viral mRNA and tRNA (Malone et al., 2022).

**Protease inhibitors include**

**lopinavir/ritonavir**

The dosage is 400 mg or 100 mg twice daily for adults.

**Mechanism of action**

By cleaving the viral polyprotein into many structural proteins and several critical enzymes (RT, protease, and integrase), the viral enzyme inhibitor protease inhibits the translation of the genome. The inhibition stops the viral particles from maturing, which leads to the creation of non-infectious virions (Croxtall and Perry, 2010).

**Antimalarial drugs**

**Chloroquine phosphate:** Given twice daily at doses of 500 mg (300 mg for chloroquine).

Mechanism of action Increasing pH prevents virus entry, which prevents virus endocytosis.

**Discussion**

This review aimed to suggest potential plant species that might be implicated as anti-SARS-CoV2 drugs given the high degree of similarity between the genome and receptors of SARS-CoV and SARS-CoV2. Plant species can work in concert with
antiviral medications to treat COVID-19 disease. The host metabolism may be impacted by viral infections in a variety of ways, which could disrupt redox homeostasis. Viral infections cause oxidative stress by increasing ROS production and changing cellular ROS scavenging mechanisms. The management of oxidative stress is a crucial component of antioxidant defense; hence, plants enhance antioxidant defense by containing vitamins and minerals that scavenge ROS. Yet, a host's nutritional state can also cause viral genome alterations under oxidative stress, turning a benign or slightly pathogenic virus into a highly virulent one that could spread further in hosts with low vitamin and mineral intake. Animals, including humans, are susceptible to upper respiratory tract illnesses from coronaviruses (HCoVs). The cause of SARS has been identified as a new coronavirus. Certain plants exhibit 3C-like protease inhibition, which may be used in the future extraction of this molecule to develop it against COVID-19. The major protease is usually referred to as a 3C-like protease (3CLPro).

Conflict of Interest

The author hereby declares no conflict of interest.

Consent for publication

The author declares that the work has consent for publication.

References


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