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Research Article

Contribution of Plants in Fighting Viral Pandemics

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Abstract:

Viral pandemics, such as the COVID-19 crisis caused by the SARS-CoV-2 virus, have underscored the pressing need for innovative approaches to combat infectious diseases. Nature, in the form of plants and their diverse array of bioactive compounds, has emerged as a valuable resource in the battle against viral pandemics. This study explores the multifaceted contributions of plants in fighting viral pandemics, highlighting the potential of plant-based solutions in preventing, managing, and mitigating the impact of viral infections. Over centuries, plants have synthesized a rich reservoir of natural compounds with potent antiviral properties. Alkaloids, flavonoids, terpenoids, and polyphenols are among the many bioactive molecules that have demonstrated efficacy against a wide range of viruses. This research delves into the mechanisms of action of these compounds and their potential applications as antiviral agents. The contribution of plants in fighting viral pandemics is multifaceted and holds immense promise. As we navigate the challenges posed by emerging infectious diseases, harnessing the potential of plants represents a sustainable and holistic approach to pandemic preparedness and response. The study advocates for interdisciplinary research, bridging traditional knowledge with modern science, and responsible stewardship of plant resources to advance our capacity to combat viral pandemics effectively.
Keywords: Viral, Pandemic, Infectious, Antiviral, Agent

Introduction

Viral pandemics have, throughout history, posed significant threats to human health and global stability. The emergence of novel viral pathogens, such as the SARS-CoV-2 virus responsible for the COVID-19 pandemic, underscores the need for innovative strategies to combat infectious diseases. In this context, the role of plants in fighting viral pandemics has gained increasing recognition and significance.

Plants have been an essential source of human medicine and remedies for millennia. Their remarkable ability to synthesize a vast array of bioactive compounds has provided humanity with a pharmacopeia of natural antiviral agents. Traditional systems of medicine, including Traditional Chinese Medicine (TCM), Ayurveda, and Indigenous healing practices, have relied on plant-based remedies to treat viral infections effectively.

This exploration into the contributions of plants in the fight against viral pandemics encompasses various dimensions. Firstly, it delves into the diverse arsenal of antiviral compounds that plants produce, including alkaloids, flavonoids, terpenoids, and polyphenols. These compounds have demonstrated potent antiviral properties and

serve as potential sources for the development of novel antiviral drugs.

Furthermore, traditional herbal medicine offers a wealth of knowledge and wisdom in the use of plant-based remedies to manage and prevent viral infections. Bridging the gap between traditional practices and modern science is essential for a comprehensive understanding of the potential of plant-derived therapeutics.

Plant-based vaccine development represents another innovative avenue in pandemic control. Plant expression systems, such as those involving Nicotiana benthamiana, have demonstrated promise as platforms for scalable and cost-effective production of viral antigens and vaccines.

Moreover, plants play a pivotal role in supporting immune function and overall health during viral outbreaks. Herbal supplements and botanicals have gained popularity for their immune-modulating effects, and the scientific basis of these interventions is explored.

However, the sustainable use and conservation of plant resources are critical considerations. As the demand for plant-based remedies grows, overharvesting, habitat destruction, and threats to plant biodiversity become increasingly relevant. Ethical sourcing and conservation efforts are essential to ensure a continuous and responsible supply of plant-based solutions.

In this evolving landscape of viral pandemics, the multifaceted contributions of plants offer a holistic and sustainable approach to pandemic preparedness and response. They represent not only a link to ancient healing traditions but also a source of innovative solutions for the complex challenges posed by emerging infectious diseases. As we embark on this exploration of the role of plants in combating viral pandemics, we aim to shed light on the potential, challenges, and ethical imperatives of harnessing nature's pharmacopeia in the service of global health.

HERBAL REMEDIES, NUTRACEUTICALS, AND DIETARY SUPPLEMENTS FOR COVID-19 MANAGEMENT

The coronavirus epidemic has reached pandemic proportions and spread to other countries. Fever, dry cough, and breathing difficulty are all symptoms of COVID-19, which can cause serious respiratory consequences. Herbal medications and nutritional supplements have shown promise as potential therapeutic agents in the treatment of COVID-19. Treatment and supportive therapy for this viral infection often involve the use of herbal plants and the phytochemicals they contain. Adjuvant therapy using botanical medications (such as Boozari) has been proposed for the treatment of COVID-19. Different natural extracts and TCM have been recognized as useful based on their mechanism of action, but clinical investigations have not been undertaken or proven. In-silico screening approaches employing targeted COVID targets, such as angiotensin-converting enzyme 2 (ACE-2) and SARS-COV-2 3Cl, led to the discovery of TCM's potential applicability. Molecular docking analysis revealed that a variety of naturally occurring antiviral compounds, including baicalin, bilirubin, corosolic acid, glycyrrhizin, hesperidin, mulberroside A, rutin, saikosoponin A, and verbascoside, are effective against the covid virus. Several herbal medications, both patented and unpatented, have been shown to alleviate the cough, fever, and exhaustion associated with severe acute respiratory syndrome Coronavirus 2 (SARS-CoV-2). Some of the herbal medications used in COVID-19 have been discovered to have a small number of adverse effects, despite the fact that natural therapies have been shown to have less of

these occurrences overall. In the case of COVID, the usage of Xiyanping, a herbal medication formulation, was limited after reports of side effects including sleepiness, lightheadedness, vomiting, and in rare cases, liver damage. Traditional Indian herbal medicines are among the world's oldest pharmaceuticals, dating back to the dawn of humankind. Minister of AYUSH (Ayurvedic, Yoga, and Naturopathy, Unani, Siddha, and Homeopathy) in India recommended consuming 'Kadha' during the COVID-19 epidemic. Kadha is an extract produced from several herbal medications, and its advantages are proved to promote immunity. Complications from COVID-19 have been shown to respond favorably to many herbal medicines that originate in India, including Curcuma longa, Ocimum sanctum, Phyllanthus emblica, and Withaniasomnifera. Nutritional supplements like vitamins D and C, together with herbal treatments, have been shown to have an immune-boosting effect, and therefore are being advised by health professionals throughout the epidemic. Vitamin D insufficiency is a common health problem that affects people of both sexes. This shortcoming can increase the likelihood of severe COVID-19 disease and perhaps death. Vitamin D supplementation has been shown to reduce the likelihood of contracting a covid infection.

CURRENT GLOBAL SCENARIO OF COVID-19

As 2019 comes to a close, the globe is still reeling from the devastation wreaked by the COVID-19 epidemic that began at the end of the year. The CDC provides a comprehensive taxonomy of Coronavirus subtypes, and ongoing research on the virus's capacity for mutation. Any alteration to the genetic code is referred to as a mutation. Mutations in nucleotides occur naturally in the building blocks of complex compounds like RNA and DNA. Changes to the amino acid sequences contained in a virus's genome can trigger more viral replication. Deleterious mutations are rare, although harmful substitution mutations are more common. Constant mutations of SARS-CoV-2 have been generally cited as a cause of the increase in Coronavirus infections. About 230 million confirmed cases were reported in 24 hours, according to WHO estimates. More than 8 billion doses of vaccination have been distributed worldwide as of January 31, 2022. In order to battle the pandemic, several medications are repurposed and vaccines are licensed under an emergency use approval procedure. Vaccination rates vary from country to country, but every effort is being made to control and prevent this disease. How contagious it will be and how long it will take to lift the lockdown are the two biggest mysteries. People will be unable to stop its spread if it is far more infectious, therefore social distance limits may be essential in the future. Even in individuals who have been immunized, an exponential rise in the infection rate might lead to widespread illness, a rise in hospitalizations, and a huge pressure on the national health system.

POTENTIAL MECHANISM OF HERBAL MEDICINE FOR CORONA VIRUSES

Frequent clinical signs of the SARS-CoV-2-caused 2019 coronavirus disease pandemic (COVID-19) include fever, dry cough, and exhaustion. Patients with advanced illness and elevated levels of cytokines and chemokines are at risk of developing cytokine storm, which can lead to life-threatening complications and even death. There have been 237,383,711 confirmed instances of COVID-19 and 4,842,716 fatalities as of 11 October 2021 [. Clearly, COVID-19 has become the worst public health emergency on a worldwide scale since the 1918 influenza epidemic. At the same time, people of various ages, races,

sexes, and health backgrounds are vulnerable to COVID-19, and further research is needed to determine the vaccine's efficacy and when it should be administered. Cases of SARS-CoV-2 infection throughout the world continue to rise. The worldwide public health problems and financial burden of disease are being made worse by COVID-19. However, there is still major cause for concern because the disease mechanism of COVID-19 has not been elucidated, and because there are no currently available effective vaccines or specialized antiviral medications for SARS-CoV-2. The worldwide response to the COVID-19 threat is hampered by the fact that no individual country's medications can rush through the necessary safety and toxicity testing.

Huangdi's Internal Classic (Huang Di Nei Jing) records the preventative benefits of herbal remedies used in ancient China for the treatment of viral infections. In particular, its usage in 2003 showed considerable promise in halting the spread of the SARS-coronavirus (SARS-CoV) and decreasing fatalities. Given the lack of a viable treatment or vaccine, the Chinese government has turned to traditional Chinese medicine in an effort to stem the spread of the COVID-19 epidemic. The Chinese government's COVID-19 Guidelines not only suggest using conventional and TCM approaches to treating SARS and MERS, but also show that these approaches are effective in preventing and treating SARS-CoV-2 infections in children, adults, and the elderly. Furthermore, it is likely safe to assume there will be no unintended consequences. Here, we compiled and analyzed the most up-to-date reports on the use of traditional herbal medicine for the prevention and treatment of COVID-19, taking into account both the guidelines' suggested treatments and any alternatives, as well as any developments in the field of herbal medicine's molecular mechanism for treating COVID-19. The study's goal is to get a basic sketch of how traditional herbal medicine is being used to combat COVID-19 so that existing licensed antiviral medications and herbal medicine may be used to treat SARS-CoV-2.

USAGE OF HERBAL MEDICINE AGAINST COVID-19 IN MAINLAND CHINA

Chinese herbal medicines recommend by Chinese guidelines of COVID-19 treatment

Rapid onset of severe asthma the coronavirus 2 (SARS-CoV-2) strain is responsible for the chronic respiratory sickness known as COVID-19 (coronavirus disease 2019). Since June 2022, the international community has been paying particular attention to therising number of newly confirmed cases of pneumonia related with COVID-19. This article collects and evaluates research on the effectiveness of using TCM to treat COVID-19. TCM's advantages and efficacy in treating COVID-19 were systematically examined, and the underlying processes of this treatment were summed up. This review of the research underlines the promise of TCM for the treatment and prevention of COVID-19 thanks to the antiviral, anti-inflammatory, and immunomodulatory properties of its various constituents. Jing Si herbal drink (JSHD), Lianhuaqingwen Capsule (LHC), Taiwan ChingguanYihau (NRICM101), and Qing-Fei-Pai-Du-Tang (QFPDT) are all well-known TCM formulations.

Fever, cough, tiredness, myalgia, diarrhea, and consequences from various organ dysfunction are the most prevalent clinical signs of COVID-19. Currently, there are no small-molecule antivirals that canalleviate any of these symptoms. Controlling COVID-19 requires effective approaches for both prevention and therapy. As a "epidemic

disease" brought on by an epidemic evil associated with moisture and heat (Li-Qi in Chinese), COVID-19 is classified as such in the philosophical framework of traditional Chinese medicine (TCM). When Li-Qi invades a human body, it first settles in the lungs, where it causes a stagnation of Lung-Qi (the lung's vital essence, whichcontrols the body's respiration and qi). This, in turn, leads to trouble breathing, a buildup of phlegm-heat, and a blockage, before eventually releasing the body's dead Yin and Yang. To return the body to normal functioning, according to TCM, moisture must be removed first, then heat. Pathogenesis includes "wet, heat, poison, stasis, deficiency," and lesions appear mostly in the lung, spleen, and stomach.

Using theprinciple of "multi-component, multi-target, multi-pathway," Chinese medicine bases its general idea and therapeutic approach on the syndrome, physical condition of various people, and the living ambient factors. According to traditional Chinese medicine, COVID-19 is a syndrome of dampness, blood stasis, and insufficiency. Different Chinese medicines are advised for patients with COVID-19 at various stages of the disease in China. QingfeiPaidu Tang (QFPD), Artemisia annua, Huoxiang, Cangshu, Gancao, and other forms of Chinese traditional medicine have been formally approved for use in conjunction with conventional medication in the treatment of COVID-19 patients by the Health Commissions of 26 provinces in China.

However, regardless of illness stage or geographical status, the Chinese national diagnosis and treatment recommendations propose QFPD Tang, a herbal formula consisting of four separate herbal formulas totaling twenty-one herbs (Table 1). It's important to note that only three of these recommendations address pediatric COVID-19 therapy specifically. Most likely because of the overall prevalence of illnesses among Chinese mainland youngsters. Yin Qiao San and Xiang Su San are suggested for mild sickness, whereas Ma Xing Shi Gan Tang and San Ren Tang are appropriate for the treatment of intermediate disease, according to a closer examination of the herbal formulae indicated in these three children's guidelines. The severe disease is treated by using Buhuan Jin Zhengqi San, XuanbaiChengqi Tang, and GanluXiaodu Dan. Table 1 also suggests Liu Junzi Tang + Yu Ping Feng San for COVID-19 therapy throughout the recovery phase. The relevant literature is cited and synthesized in Table 1. Ophiopogonis radix, Poria sclerotium, and Citri reticulataepericarpium were found to be the most commonly suggested Chinese medications in our summary of TCM results in these guidelines (FIGURE 3).

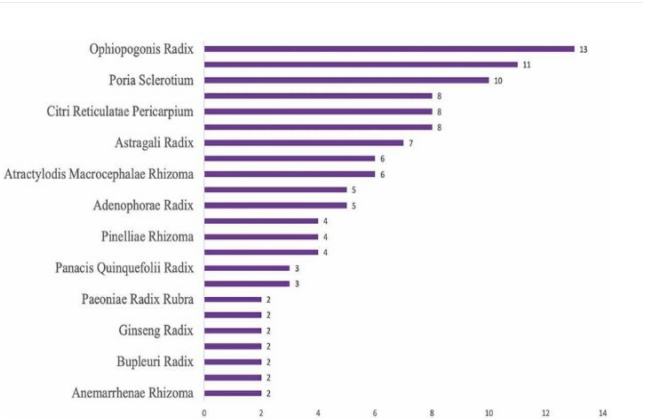

Figure 1. Frequency of commonly use herbs in herbal formulas for treating patients with COVID-19 in recovery stage.

- **Effect of herbal medicines on COVID-19 treatment**

Several small chemicals, some derived from naturally occurring substances, have been tested and proven to directly inhibit these key proteins in SARS or MERS coronavirus by in silico and biological processing. SARS-CoV-2 has a gene sequence with SARS-CoV and MERS-CoV, suggesting that these viruses are closely related. To this end, it may be useful to look for anti-SARS-Cov-2 herbal plants among the traditional Chinese herbs used to treat viral pneumonia if researchers have previously found natural chemicals effective against SARS-CoV or MERS-CoV. Yin Qiao San, Yu Ping Feng San, Sang Ju Yin, LHQW Capsule, Shuanghuanglian, Ma Xin Gan Shi Tang et etc. are only few of the Chinese herbal formulas utilized to treat SARS-CoV infection. After administration, these medications can boost immune function in the upper respiratory mucosa thanks to their antiviral, anti-inflammatory, and immuno-regulatory properties. These medicines were first used to treat SARS-CoV, and are now also being used to treat COVID-19. Patients who are currently in the medical observation phase are encouraged to consume LHQW, according the revised guidelines. Clinical data suggests that taking LHQW capsules can help reduce the severity of COVID-19 symptoms including coughing, fever, and weariness, as well as shorten the duration of a patient's fever and slow the spread of the virus. The Chinese herbal medicine Shuanghuanglian, which consists of honeysuckle and forsythia, has also been shown to be effective in blocking the spread of SARS-CoV-2. The replication of SARS-CoV-2 can also be inhibited by LHQW, which consists of 13 herbs and 733-3084 chemical components. More evidence suggests that it has something to do with calming the cytokine storm and taming the human immune response. For instance, the 3CLpro protein and host ACE2 are both targets of the Chinese medication QFPD, which is indicated for COVID-19 therapy in China. Because of its antiviral, antibacterial, anticancer, and anti-inflammatory properties, SFJD (which consists of eight medicinal herbs) is commonly utilized for COVID-19. Clinical studies and in vitro research both point to a function for Chinese medicine granules in decreasing mortality and lowering body temperature. However, these clinics are not normal randomized clinical studies, and more large-scale randomized, double-blinded, placebo-controlled clinical trials are needed to offer more reliable findings. In a Saudi Arabian open-label randomized controlled clinical study, individuals with moderate COVID-19 symptoms were treated with Nigella sativa, a popular edible spice having antiviral and immunomodulatory activity. KabasuraKudineer decreased the SARS-CoV-2 viral load in asymptomatic COVID-19 patients, according to another open-label randomized controlled clinical study conducted in India.

- **Herbs in combination with conventional therapy in COVID-19 treatment**

Furthermore, the Huashibaidu (HSBD) Formula combined with other methods showed superiority in treating COVID-19. Combining TCM with Western medication has been shown to be more beneficial to patients, namely by lowering the rate at which their condition worsens. There is also no uptick in the number of reported negative side effects. Treatment with LHQW and Arbidol was found to hasten the clearance of lung inflammation and reduce the time needed to get a negative result for SARS-CoV-2 nucleic acid detection by Liu et al. In addition to enhancing chest CT performance and clinical cure rate, another clinical investigation found that LHWQ paired with standard therapy can reduce the duration of

symptoms including fever, weariness, and cough.

- **Potential mechanism of herbal medicines in COVID-19 treatment**

(A) Disturb SARS-CoV-2 replication and proliferation

Many therapeutic advances aim to interrupt the virus's life cycle by targeting specific chemicals or processes that occur at each step. The S protein is essential for SARS-CoV-2 to replicate inside of a host cell. Coronavirus host tropism and tissue phagocytosis are both heavily influenced by this component. N479L and T487S mutations in the SARS-CoVS protein have been shown to greatly improve the virus's affinity for human ACE2, and alterations in the MERS-CoV S protein may contribute to the virus's zoonotic potential. This highlights the significance of the S protein and the host in coronavirus transmission between people during sexual contact. Two-thirds of the viral genome is taken up by the ORF1ab protein, which can be split into at least 16 different nsps. Among them are 3CLpro and Rdrp, which control RNA replication, and PLpro, which possesses protease and phosphatase activity and regulates the viral replication process and has the role of antagonizing IFN antagonism. As a result, anti-SARS-CoV-2 medicines now primarily target the S protein and the ORF1ab protein. Contrarily, one potential mechanism for many medications used to treat COVID-19 is the prevention of viral entrance into cells, replication, and translation. It has been found that a QFPD decoction used to treat COVID-19 can directly reduce viral invasion and replication. Structure-based screening of chemical or phytochemical databases can offer insights to a wide variety of crystal targets for the investigation of anti-SARS-CoV-2 therapeutic action. Chinese medicine compounds such as quercetin, andrographolide, glycyrrhizic acid, baicalin, patchouli alcohol, and luteolin were predicted to have binding sites against SARS-CoV-2 protein, 3CLpro, ACE2, S protein, Rdrp, and PLpro using molecular modeling. Furthermore, it has been reported that these components may be able to inhibit virus infection by binding to SARS-CoV-2 protein, preventing viral entry into cells, blocking virally induced cellular pathways, and reducing viral replication and proliferation. Active Chinese herbal remedies compounds including 9,10-dimethoxypterocarpan-3-O-b-D-glucoside were found to effect on numerous genes involved in COVID-19, according to research employing the TCM Systems Pharmacology Database and Analysis Platform. SARS-CoV-2's major protease may be a direct target for rutin, forsythoside E, and hyperoside components in LHQW, as hypothesized by Ye et al. Chinese herbs that include the chemicals baicalin, scutellarin, hesperetin, glycyrrhizin, and nicotianamine may be useful in preventing viral invasion and infection, as demonstrated by the work of Chen et al.

Kaempferol, quercetin, luteolin, baicalein, oroxylinA,licochalcone B, and glyasperin C are the active chemicals in JHQG granules that have been shown to inhibit or inhibit viral replication. These compounds may also influence PTGS2, BCL2, CASP3, and similar pathways. In the framework of COVID-19, herbal medications not only promote mental health, but also reduce tension and anxiety.

Conclusion

Throughout history, the world has faced the relentless challenge of viral pandemics, which have threatened human health and global stability. In this context, the contributions of plants in the fight against viral pandemics emerge as both a source of ancient wisdom and a beacon of hope for

innovative solutions. This exploration into the multifaceted roles of plants in combating viral diseases underscores several critical points.Plants have evolved an impressive array of bioactive compounds, including alkaloids, flavonoids, terpenoids, and polyphenols, which possess potent antiviral properties. These natural molecules hold immense potential for the development of novel antiviral drugs and therapies.

Traditional systems of medicine, deeply rooted in the use of plant-based remedies, offer valuable insights into managing and preventing viral infections. The integration of traditional knowledge with rigorous scientific research can yield a comprehensive understanding of the potential of plant-derived therapeutics.Plant-based expression systems, exemplified by Nicotiana benthamiana, have emerged as innovative platforms for cost-effective and scalable production of viral antigens and vaccines. This approach holds promise for rapid response strategies during pandemics. The contributions of plants in fighting viral pandemics represent a harmonious blend of tradition and innovation. They offer a holistic and sustainable approach to pandemic preparedness and response, drawing from the deep well of nature's pharmacopeia. As we navigate the complex challenges posed by emerging infectious diseases, the role of plants continues to evolve, bridging ancient healing traditions with cutting-edge science. It is a testament to the resilience of nature and the potential for human ingenuity to address global health crises while ensuring the responsible use and conservation of our botanical allies.

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