

Review Article

COVID-19 OUTBREAK: IS THERE A PLACE FOR NATURAL REMEDIES AND HERBAL MEDICINES ?

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Abstract

The outbreak of coronavirus disease 2019 (COVID-19), caused by the Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), has appeared as a severe danger for community health and the worldwide economy. The most common COVID-19 symptoms include fatigue, coughing and difficulty breathing. Pneumonia can occur in severe cases, and can ultimately lead to respiratory failure and sometimes even death. There are presently no validated medications for the dangerous respiratory infections due to the new coronavirus, although existing and experimental drugs are undergoing trials in some countries. Given the outbreak, different therapeutic practices have been considered, including herbal medicines, which were commonly used in previous contagious infections, such as SARS and influenza Hemagglutinin type 1 and Neuraminidase type 1 (H1N1). Traditional herbal preparations and natural therapies provided a variety of care choices for human diseases. The huge metabolic potential of aromatic herbs and medicinal plants has permitted the development of bioactive substances that have worked to cure or alleviate the symptoms of several illnesses, many of which are still prevalent these days. However, the World Health Organization (WHO) advised against using traditional herbs in COVID-19 therapy as developing countries are trying to handle the coronavirus contagion. There are no rigorous experimental or clinical studies to prove the efficacy of traditional herbal medicines.

Keywords: COVID-19; SARS-CoV-2; Medicinal Plants; Herbal Therapies; Chinese Traditional Medicines.

PHARMACOPÉE TRADITIONNELLE ET COVID-19 : FAUT-IL COMPTER SUR LES HERBES AROMATIQUES ET LES PLANTES MÉDICINALES ?

Résumé

L'infection virale due à la nouvelle souche du coronavirus (COVID-19), causant un syndrome respiratoire aigu sévère, s'est émergée comme une réelle et grave menace pour la santé humaine et l'économie internationale. Les symptômes cliniques de la COVID-19 les plus couramment rencontrés sont la fatigue, la toux et des difficultés respiratoires. La pneumonie peut survenir dans les cas graves et entraîner inévitablement une insuffisance respiratoire pouvant causer la mort. Il n'existe actuellement aucun médicament validé pour traiter les infections respiratoires dangereuses dues à la nouvelle souche de SRAS-CoV-2, bien que des médicaments existants et expérimentaux soient testés par certains pays. Différentes pratiques et approches thérapeutiques ont été envisagées, y compris la phytothérapie qui était couramment utilisée dans les infections contagieuses antérieures, comme le SARS et la grippe aviaire H1N1. Les préparations traditionnelles à base de plantes médicinales pourraient offrir une option de choix pour la prise en charge de ce type d'infections respiratoires virales. L'énorme potentiel préventif-thérapeutique des herbes aromatiques et des plantes médicinales a permis le développement de prometteuses molécules bioactives ayant montré une certaine efficacité dans le traitement symptomatique de certaines pathologies infectieuses. Cependant, l'Organisation Mondiale de la Santé (OMS) a déconseillé, aux pays sous-développés, d'intégrer les préparations traditionnelles d'herbes médicinales dans la stratégie thérapeutique de la COVID-19. A ce jour, aucune étude expérimentale rigoureuse ou encore un essai clinique randomisé n'ont prouvé le bien-fondé du recours à la phytothérapie pour le traitement-prévention de la COVID-19. Seul l'avenir nous dira si l'intérêt qu'elle suscite est cliniquement justifié.

Mots-clés: COVID-19; SRAS-CoV-2; Plantes Aromatiques et Médicinales; Phytothérapie; Médecine Traditionnelle Chinoise.

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LIST OF ABBREVIATIONS

COVID-19 = Coronavirus Disease 2019
 H1N1 = Hemagglutinin type 1 and Neuraminidase type 1
 MERS-CoV = Middle East Respiratory Syndrome Coronavirus
 NIH = National Institutes of Health
 OMS = Organisation Mondiale de la Santé
 SARS-3CLpro = Severe Acute Respiratory Syndrome 3C-Like protease
 SARS-CoV-2 = Severe Acute Respiratory Syndrome Coronavirus 2
 TCM = Traditional Chinese Medicine
 WHO = World Health Organization

1. INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2), formerly known as 2019-nCoV is a newly identified strain of coronavirus that causes disease extending from effects comparable to the common cold to serious diseases in people across the world [1, 2]. The outbreak of coronavirus disease 2019 (COVID-19), caused by the coronavirus SARS-CoV-2, has appeared as a severe danger for community health and the economy worldwide [3]. This respiratory infection was first identified in early December 2019, and by the middle of March 2020, the World Health Organization (WHO) considered COVID-19 as a pandemic [4]. As of 4 June 2020, there have been more than 6,662,064 confirmed cases in at least 213 countries and territories around the world and 2 international conveyances. The majority of cases were reported in mainland USA, followed by Brazil, Russia and Spain [5]. Currently, SARS-CoV-2 has rapidly spread across China and around the world [6]. Epidemic diseases are not a new phenomenon, but easy access to transport in the modern world has accelerated their spread. Tens of thousands of people, comprising many health workers, have been infected, and thousands have died. Patients may develop multiple fections due to an incubation time of 14 days or longer before signs are detectable. It has yet to find a successful treatment [7]. The most common COVID-19 symptoms include fatigue, coughing and difficulty breathing. Pneumonia can occur in severe cases, and may ultimately lead to respiratory failure and sometimes even death [4, 8].

The suggested safety precautions against COVID-19 usually involve effective hand cleaning with an alcohol-based hand sanitizer, regular soap and water washing of hands for 20 seconds, trying to cover your mouth and nose with a face mask or reusable tissue, trying to cough or sneeze into the flex of your elbow, wearing gloves, social distancing by seeking to avoid contact with individuals who are ill and staying at home and self-isolate from others if you are unwell [9-11]. Proposing new medications and methods for successful management of the new coronavirus is a must since the epidemic has rapidly broken out. Since the advent of the spread of coronavirus, massive attempts have been made to prevent, reduce and cure the disease, but no particular therapy has been accepted. Although the use of chemical medicines and interferon therapy has shown compelling outcomes, these clinical methods have multiple pitfalls and lack the consistency needed for the therapy of the new COVID-19 [12-14]. There are presently no validated medications for the dangerous respiratory infections due to new coronavirus, although existing and experimental drugs are being undergoing trials in many nations. Since then, in controlled clinical studies, just one, the antiviral Remdesivir (Fig. 1), has been found to have some ability to improve recovery [15]. Our goal is to point out the possible benefits of phytotherapy testing in discovering new evidenced-based alternative therapies against human coronaviruses, and to include some important suggestions for scientists to use in preparing additional research.

2. EFFICACY OF HERBAL MEDICINES

Aromatic herbs and medicinal plants have provided a variety of care options for human diseases. The huge metabolic potential of aromatic herbs and medicinal plants has permitted the development of bioactive substances that have worked to cure or alleviate the symptoms of several illnesses, many of which are still prevalent today. The tradition of using medicinal plants for the treatment of humans, such as healing wounds and burns, antifungal, antiviral, and antimicrobial treatments against skin infections, has a long tradition and continues even now in the new century for primary health care [17-26].

Scientists initially discover a therapeutic agent with potent pharmacological activity against a particular target in commonly performed drug discovery. Then optimization of its structure and verification its function using *in vitro* studies followed by *in vivo* animal and clinical studies. By contrast, numerous herbal medicines have been used in health centers for hundreds of years, and therefore their quality and influences have been evaluated repetitively [27]; the quinine (Fig. 2) analogue, chloroquine phosphate, was used for malaria treatment for over 70 years [28]. Timeliness is a further benefit, especially in emergency situations. If an herbal infusion or ingredient has been shown to be successful it can be used instantly to treat patients, its protection has already been developed. Aromatic herbs and medicinal plants are not only useful as foods but also for pharmaceuticals. Identifying the phylogeny, biodiversity and herbal conservation as well as the processes of secondary metabolism and production of bioactive compounds is crucial for the success of drug products. It would be important to engage the efforts in ethnopharmacology, phytochemistry, and plant physiology to safeguard the global community from existing and potential epidemics.

3. CONVENTIONAL TREATMENT OF COVID-19: IS THERE A ROOM FOR HERBAL MEDICINES ?

The use of aromatic herb and medicinal plant species as natural remedies in the preparations for herbal medicine, as well as other natural products around the world, is expected to significantly increase with the COVID-19 outbreak. Here we focus into what has been learned regarding the use of natural remedies in phytomedicine in managing the COVID-19 infection to date, and what precautions should be implemented in place to insure that these and other natural compounds remain accessible in the long term to support healthcare [30-33]. Given the outbreak, different therapeutic techniques were considered, including herbal medicine, which was commonly used in previous contagious diseases, such as SARS and influenza H1N1. To date, two nations, China and South Korea, have provided directives on the management and cure of COVID-19 for treatment using medicinal herbs [34].

Evidence supporting the activity of aromatic herbs and phytochemical extracts against coronaviruses comes often from experimental studies, while other clinical research is limited and refer in particular to multi-component herbal formulations used in phytomedicine and traditional therapy [35]. Overall, two potential studies have been directed at pursuing the discovery of valuable phytotherapeutic substances to treat infections induced by coronaviruses [36]: (i) Alternative medicines with effectively protective effects, acting primarily through a general immune response boost. *Astragalus membranaceus* (Fig. 3a) or *Echinacea purpurea* represent two examples [37]. Remarkably, in herbal formulations against SARS in phytomedicine, *Astragalus* was frequently added [35]. Due to its immune-modulatory properties, *Uncaria tomentosa* and polysaccharides from medicinal mushrooms could be other choices to investigate. Testing whether there are medicinal herbs and natural compounds that can be used as adjuvants in addition to a prospective vaccination might well be helpful. (ii) Herbal treatments have a possible beneficial effect, working on viral penetration and reproduction through various mechanisms. *Cinchona* bark pharmacological analogs, such as chloroquine, are already being suggested as promising drugs [38]. Reviews of clinical investigations have recommended the efficiency of specific phytochemical extracts or isolated pure compounds from *Sambucus nigra*, *Pelargonium sidoides* (Fig. 3b), or *Cistus incanus* (Fig. 3c) for the management of respiratory infections, regardless of their etiology [39-41]. A range of 13 plant-derived substances has recently been described as a set of *in vitro* anti-SARS-Cov molecules, such as cryptotanshinone (Fig. 4a), kaempferol (Fig. 4b) and quercetin (Fig. 4c) [42].

Phytochemicals and plant-derived substances typically act at varying phases of viral permeation and reproduction, such as attaching the protein at the viral spike or preventing SARS-3CLpro activity [31]. Such results will be used to extend the scope of plant-based items that would apply for potential studies.

Testing if there are natural products or phytochemicals able to grow the time over which an infectious patient stays contagious can even be beneficial in minimizing the spread of the disease.

In fact, phytomedicines may play a significant role in the management and/or treatment of common medication side effects [31]. Several historical epidemics have used antiviral herbal medicines, such as the two preceding coronavirus infections (SARS-CoV in 2013 and Middle East Respiratory Syndrome Coronavirus (MERS-CoV) in 2012), seasonal outbreaks caused by influenza viruses and dengue virus. Extracts from *Lycoris radiata*, *Artemisia annua* (Fig. 3d), *Lindera aggregata*, *Lonicera japonica*, *Pyrrosia lingua*, *Sambucus formosana*, mulberry (*Morus alba* var. *alba*, *Morus alba* var. *rosa*, and *Morus rubra*), and the natural products isolated from *Isatis indigotica*, *Boenninghausenia sessilicarpa*, *Laurus nobilis* essential oil, *Scutellaria baicalensis*, *Torreya nucifera* and *Houttuynia cordata*, black tea, *Glycyrrhiza radix*, *Bupleurum* spp., *Heteromorpha* spp., *Scrophularia scorodonia*, *Scutellaria baicalensis*, *Glycyrrhiza uralensis* and *Griffithsia* sp. showed anti-SARS effects [30, 43, 44]. The plant flavone baicalein may prevent the transmission of dengue virus into the host and may limit replication after entry [45]. In addition, *Pelargonium sidoides* roots and dandelion (*Taraxicum* spp.) natural products have anti-influenza properties, since they suppress virus penetration and main viral enzyme production [46-47]. One of the natural medicines, licorice (*Glycyrrhiza glabra*), which has the active substances of glycyrrhizin (Fig. 5a), glycyrrhetic acid (Fig. 5b), liquiritine and isoliquiritine, could be used as an antiviral agent to deactivate COVID-19 [48].

4. CAUTIONS AGAINST THE USE OF HERBAL MEDICINES IN THE TREATMENT OF COVID-19

Though herbal medicine and other traditional Chinese medicine (TCM) treatments for COVID-19 have been evaluated for their effectiveness [33, 50-51], some experts claim the investigations have still not been thoroughly designed and are insufficient to deliver accurate results. There are no rigorous experimental or clinical studies to support the efficacy of the traditional Chinese medicines [52]. Given that initiatives are ongoing to discover therapeutics for COVID-19.

Prudence should be taken against misleading information about the efficacy of some of these treatments (WHO), particularly on social media. For example, the herbal beverage, named “COVID Organics”, is derived from *Artemisia* which is an anti-malaria plant combined with indigenous medicinal plants. Some national leaders have supported unconfirmed “COVID Organics” therapies. Madagascar’s president has said a medicinal herb beverage can remedy COVID-19 patients. The Malagasy Institute of Applied Research, an organization that has researched Madagascar’s herbal therapies several years ago, developed the beverage. However, medical experts are critical of the drink, noting there are no scientific tests to indicate it would be effective against the novel coronavirus [53]. The WHO [54] has rejected the allegations of the president of Madagascar that the herbal cocktail manufactured inside the nation can help treat COVID-19 patients. Some African nations like Tanzania and Guinea-Bissau have arrangements to purchase the tonic containing the *Artemisia* plant. The WHO initially discouraged the use of traditional remedies to treat COVID-19. For the first months of the outbreak, they were listed on the agency’s website as “not effective against COVID-2019 and can be harmful”. The WHO advised against using traditional herbs in COVID-19 therapy as developing countries are trying to handle the coronavirus contagion. Africans need to use drugs checked against the same quality as citizens in the rest of the civilized world according to the WHO. Particularly if the treatments emerge from conventional and natural procedure, it is important to determine their effectiveness and safety by thorough clinical studies. The U.S. National Institutes of Health (NHI) also cautioned against complementary and alternative medicine, comprising certain herbal therapies and infusions, for treating or alleviating COVID-19, saying there was no confirmation they work and some may be dangerous.

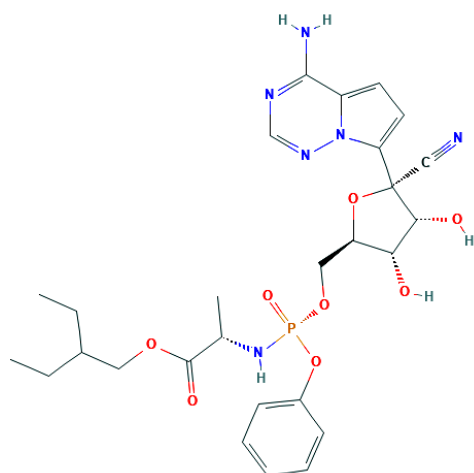


Figure 1. Chemical structure of Remdesivir [16]

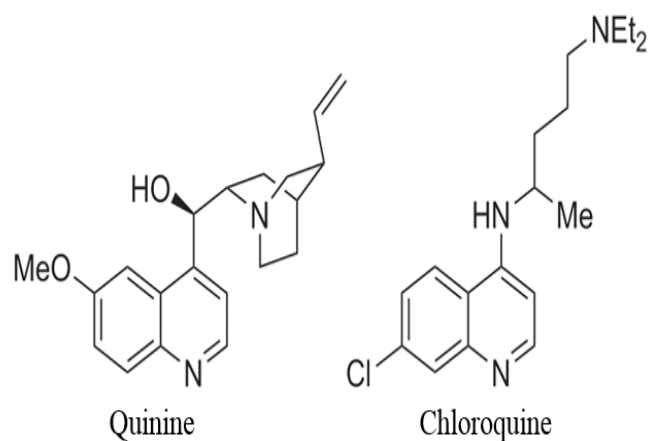


Figure 2. Chemical structures of quinine and chloroquine [29]

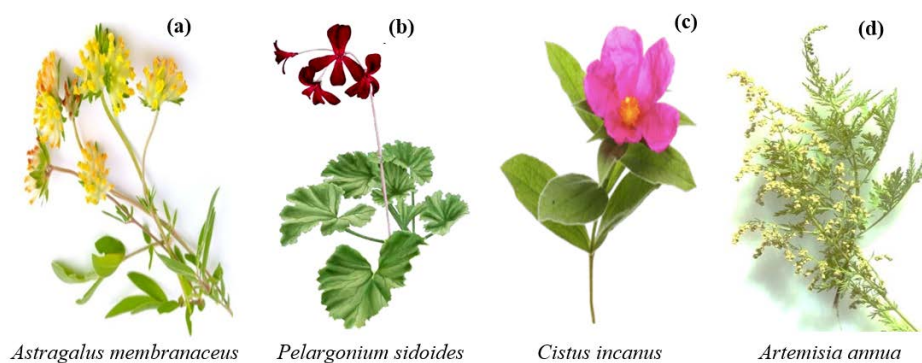


Figure 3. Impressive medicinal herbs with antiviral property

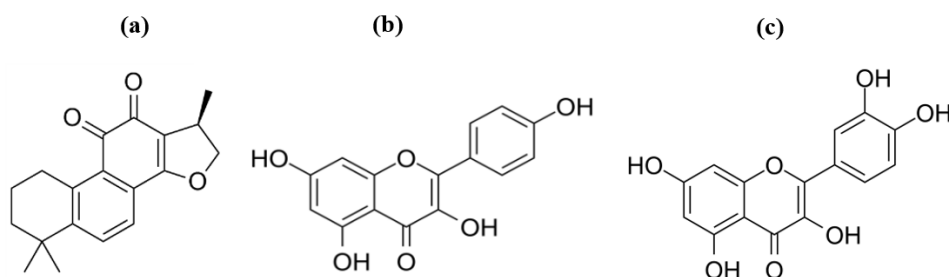


Figure 4. Chemical structure of Cryptotanshinone (a), Kaempferol (b) and Quercetin (c).

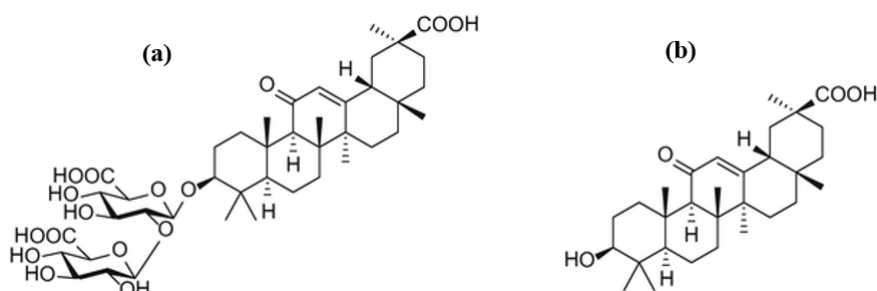


Figure 5. Chemical structure of Glycyrrhizin (a) and Glycyrrhetic acid (b) [49]

5. CONCLUSION

In conclusion, considering the current disease outbreak induced by the SARS-CoV-2 viral infection, the worldwide research community has assembled to find solutions to the COVID-19 infection as a matter of urgency. Investigation into phytotherapy and herbal medicine can effectively assess possible beneficial treatments against coronaviruses, as well as further studies are suggested to describe and evaluate all potential options. Globally, phytochemical extracts and plant-derived essential oils with some tentative indication of coronavirus antiviral activity along with phytotherapeutic treatments with immune stimulant activities emerge as excellent choices for more studies on the subject. Although these herbal medicines have been used clinically for decades, when they are applied to COVID-19, particularly in association with other antimicrobials, antivirals, and immune suppressants, the safety should be carefully assessed. Scientists and researchers say endorsing treatments that are yet to be proved safe and successful is risky.

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