

Traditional Indian medicines and Corona virus: A Fight against global pandemic

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ABSTRACT

Coronavirus disease 2019 (CoViD-19) newly recognized single-stranded (ss)RNA genome that rapidly spread across China and around the world, a respiratory infection caused by a group of viruses infecting respiratory tract, lungs and which is found variously in humans and animals. There are no specific anti-virus drugs or vaccines are available for the treatment of this sudden and fatal disease. Various medical researchers and clinical workers have made great efforts to understand the pathogenesis and clinical characteristics to develop effective drugs for the treatment. Traditional Indian medicines have acquired abundant experience in the treatment of infectious diseases for thousands of years and it is a class of medicines of nature origin and considered to be devoid of adverse events. In this review, we suggest traditional medicinal plants as possible novel therapeutic approaches, exclusively targeting SARS-CoV-2 and its pathway based on ancient knowledge of Indian medicinal plants. Although inhibition of viral replication is often considered a general mechanism for the antiviral activity in most natural products, studies have shown that certain natural products can interact with key viral proteins associated with virulence.

Keywords: Coronavirus disease 2019, SARS-CoV-2, India Medicinal Plants, Global pandemic

INTRODUCTION

The coronavirus disease 2019 (CoViD-19) has received great attention for its worldwide prevalence, caused by Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) [1]. On February 11th, 2020, the Director General of the World Health Organization (WHO), Dr. Tedros Adhanom Ghebreyesus, named the disease caused by the SARS-CoV-2 as “CoViD-19”, and on March 11th, 2020, WHO declared CoViD-19 a pandemic [2]. According to statistics from Ministry of health and family welfare (MoHFW) of the India, by March 02, 2020, a total of 26535 active cases and 1223 fatal cases of CoViD-19 have been confirmed in India. The common symptoms of CoViD-19 include fever, cough, and difficulty in breath. In severe cases, pneumonia may occur and eventually lead to multiple organ failure and even death. Currently, there are no specific vaccines or available medicines for the treatment of CoViD-19 [1]. Human Coronaviruses (CoVs), including Severe Acute Respiratory Syndrome Coronavirus (SARS-CoV), Middle East Respiratory Syndrome Coronavirus (MERS-CoV) and 2019 novel Coronavirus (SARS-CoV-2) have caused three recent major global epidemics with significant morbidity and mortality. In addition, SARS and MERS were associated mainly with nosocomial spread, whereas SARS-CoV-2 is much more extensively transmitted in the community [3].

Table I provides a comparison of the epidemiological characteristics of MERS-CoV, SARS-CoV, and SARS-CoV-2.

Features	SARS-CoV-2 [4]	SARS-CoV [5]	MERS-CoV [5]
Phylogenetic origin	Clade I, cluster IIa	Clade I, cluster IIb	Clade II
Receptor	Angiotensin Converting Enzyme 2 (ACE2)	Angiotensin Converting Enzyme 2 (ACE2)	Dipeptidyl peptidase-4 (DPP4)
Animal reservoir	Most probably bats	bats	bats
Intermediate host	Unknown	Civets and raccoon dogs	Camels
Main form of transmission	Human-to-human, animal-to-human	Human-to-human, animal-to-human	Animal-to-human, human-to-human

Route of transmission	Droplets, contact	Droplet, contact, fecal-oral, aerosol, transplacental	Droplets, contact, airborne
Incubation period	Typically between 2 to 14 days	Typically between 2 to 10 days, and upto 14 days	Current estimates between 2 to 10 days, and upto 14 days
Number of cases	Over 34,20,000 as of 2 May, 2020	8098	2506
Number of death	Over 2,44,000 as of 2 May, 2020	774	862
Fatality rate	2.3%	9.5%	34.4%
Estimated R_0	2-3.5	1.7-1.9	0.7

Table 1: Pathogenetic, phylogenetic, and epidemiological characteristics of SARS-CoV-2, SARS-CoV and MERS-CoV

CoViD-19 is a single stranded RNA virus, with a typical crown-like appearance coronavirus under an electron microscope due to the presence of spikes of glycoprotein on its envelope [6]. The SARS-CoV-2 genome sequences share a 79.5% sequence identity to severe acute respiratory syndrome-related coronaviruses (SARS-CoV) [7]. The angiotensin-converting enzyme-2 (ACE-2) receptors on host cells have been shown to be the target of spike(S) proteins [8]. It undergoes structural changes to merge with the host, which ultimately allows viral genes to enter the host cell [7]. According to the Centers for Disease Control and Prevention (CDC), transmission of SARS-CoV-2 occurs mainly from person to person via respiratory droplets in a range of 180 cm [4]. The virus can also be transmitted if a person touches a mucosal surface after touching an object with the virus [8]. The WHO said that currently there are no specific vaccines or antiviral drug available for treatment [10]. TCM in China and proposed herbs in Indian medicine interventions for treating CoViD-19

CoViD-19 is almost controlled in China. There are several reasons for disease containment in China, however, evidence of the role played by traditional Chinese medicine (TCM). The Total numbers of confirmed coronavirus cases cured by TCM are reported to be at least 60,107. Historically, when the outbreak began, traditional Chinese medicine (TCM) approaches include oral administration of preventive herbal formulas that were recommended for prevention and treatment in China [11]. For example, in 2003, Chinese medicine approaches were used to prevent and treat SARS, which was the focus of the most serious infectious disease in China before CoViD-19 pandemic [12, 13]. In 2009, during the worldwide H1N1 influenza pandemic, the National Administration of Traditional Chinese Medicine of China issued four Chinese herbal medicine (CHM) formulas for adults of different CM body constitutions and one for children [14]. The current outbreak of CoViD-19 caused many provinces in China to issue prevention and control programs for traditional Chinese medicine, among which prevention programs are mainly oral CHM formulas [13]. The consistent success of traditional Chinese medicine in managing a contagious pandemic, it is logical and essential to explore how traditional Indian medicine can help address the CoViD-19 challenge [11].

In fact, now is the time to incorporate AYUSH systems to transform Indian healthcare and demonstrate the potential of AYUSH systems to meet the challenge and restore health [15]. An understanding of the epidemiology and pathogenesis of CoViD-19 as learned through an ongoing pandemic can help us design a feasible action plan. About 80% of CoViD-19 cases have mild symptoms that require only primary medical attention. Of the rest, 20% of cases, 15% require urgent medical attention in secondary health care services. The remaining 5% are serious cases require an intensive care, and therefore need to transfer tertiary healthcare units equipped with ventilators [16]. Since ancient times, Indian medicinal plants have been used as a treatment and preventive strategy for various diseases, including respiratory viral infections. The benefit of using these herbs in viral respiratory infections is to develop immune-stimulating and inflammation-modulating effects to control the immune system [15]. For the purposes of traditional Indian drug interventions during the COVID-19 pandemic, our proposed medicinal herbs are consumed in the form of Kadha, and that are described as follows.

Pelargonium sidoides

Pelargonium sidoides is a traditional medicinal plant native to South Africa. It is used to relieve symptoms of bronchitis and also to reduce symptoms of the common cold, flu, cough, and nasal problems. It has heart-shaped leaves that have excellent medicinal properties including antibacterial and antifungal properties, influenza activity, antiviral properties, antioxidants, anti-tuberculosis effect, analgesic effects, and astringent properties [17]. The active chemical components of *Pelargonium sidoides* consists of coumarins (7-hydroxycoumarin derivatives), coumarin sulfates, phenolic, polyphenolic compounds, coumarin glycosides, gallic acid, flavonoids, hydroxycinnamic acid derivatives, and proanthocyanidins or tannins [18]. A recent study found that EPsW 7630 interferes with the replication of different respiratory viruses, including seasonal

influenza, virus strains, RSV, human coronavirus, parainfluenza virus, and coxsackie virus [19]. This extract is also given to athletes that help to strengthen the immune system, which can be compromised by extreme exercise, to protect against colds [18]. These active ingredients and medicinal properties make them very useful and powerful, as they inhibit the entry of the virus and the key activities of viral enzymes.

Glycyrrhiza glabra

Glycyrrhiza glabra, commonly known as licorice root or yashtimadhu. The natural extract of the plant can be used to deactivate the active components of this virus. As a case study, licorice was selected as a sample to neutralize the activity of viral proteins. Similar agreements are found in the literature that state “licorice root extract is effective against HIV, RSB, herpes viruses and severe acute respiratory syndrome-related corona virus, causing a serious type of pneumonia” [20]. The contents of *G. glabra* are glycyrrhizin, glycyrrhizic acid, liquiritin, and isoliquiritin that can control the spread of virus activity [21].

Sambucus nigra L.

Sambucus nigra, commonly known as elderflower. There is preclinical evidence that the elderflower inhibits the replication and viral binding of the human coronavirus NL63 (HCoV-NL63), a member of the coronavirus family. Elderflower appears more effective in preventing or early stage of coronavirus infections [22]. It is noteworthy that *Sambucus nigra* significantly increases inflammatory cytokines; including IL-B124, so it should be discontinued symptoms of infection (or positive test) [23]. The active components are quercetin, isoquercitrina, anthocyanins, chlorogenic acids, triterpenoids. Natural Standard Research Collaboration (NRDC) concluded that there is evidence to support the use of *Sambucus nigra* for influenza that may be applicable to the prevention of CoViD-19 [24].

Andrographis paniculata

Andrographis paniculata, commonly known as kalmegh or green chireta. It shows the antibacterial, antifungal, antiviral, antipyretic, adaptogenic, and anti-inflammatory medicinal properties. The major active constituents of *Andrographis paniculata* includes 14-Deoxy-11-dehydroandrographolide, 5-hydroxy-7,8,2',3'-tetramethoxyflavone, andrographolide, neoandrographolide, panicoline, paniculide-A, B, C [25]. Among them, the name of the drug compound andrographolide was analyzed using in silico computational coupling tools that successfully docked against the main protease inhibitor region of the SARS-CoV-2 virus with a docking score of -3.094357 Kcal/mol, the docking score showed great binding when compared to synthetic compounds when coupled against Mpro, such as disulfiram, tideglusib, and shikonin, which are -46.16 Kcal/mol, -61.79 Kcal/mol and -17.35 Kcal/mol [26]. And it also shows a great binding score compared to the recently proposed combination of three drugs, namely lopinavir, ostelmiriv, and ritonavir, whose binding scores are -4.1Kcal/mol, -4.65 Kcal/mol, and -5.11 Kcal/mol [27].

Couroupita guianensis

The *Couroupita guianensis*, (locally known as nagaling and kailashpati) possesses immunomodulatory, antibiotic, antifungal, antiseptic, anthelmintic, and analgesic qualities [28]. The trees are used to cure colds, hypertension, tumors, inflammation, malaria, and stomach aches. The whole nagaling plant contains phenols, alkaloids, flavonoids, stigmasterol, eugenol, linalool, isatin, indirubin, fernesol, nerol, quercetin, saponins, tryptanthrine, indigo, linoleic acid, α -and β amirins, carotenoids, sterols, phenolics etc [29]. These active ingredients and medicinal properties show the best herb for the treatment of coronavirus.

Tinospora Cordifolia

Tinospora cordifolia, commonly called "Guduchi", is known for its immense application in the treatment of various diseases in traditional Ayurvedic literature. It is widely used in different ailments for its antioxidant, anti-periodic, antispasmodic, antimicrobial, antiosteoporotic, anti-inflammatory, antiarthritic, antiallergic, and anti-HIV properties [30]. *T. cordifolia*, is a rich source of protein and micronutrients, such as iron, copper, calcium, zinc, copper, calcium, manganese, and phosphorus. It also contains many secondary plant metabolites, such as terpenes, alkaloids, flavonoids, steroids, and glycosides [31]. A numerous phytochemicals present in this herb that have significant docking scores and potential to inhibit different stages of SARS-CoV-2 infection, as well as other target proteins of the coronavirus [32].

Silybum marianum

Milk thistle (*Silybum marianum*) is another medicinal plant that has been used for thousands of years as a remedy for a variety of ailments [33]. The main component of the fruit extract of *S. marianum* (silymarin) is a flavonoid lignan called silybin that has been used in Indian medicines for liver and gallbladder problems [34]. An active constituent found in *Silybum marianum* displayed higher binding affinity with target proteins in SARS-CoV-2 in comparison to currently used repurposed drugs against CoViD-19 [32].

ACKNOWLEDGEMENT

The authors declare no acknowledgements

CONCLUSION

The SARS-CoV-2 pandemic is spreading worldwide at an alarming rate. It has caused more infections and deaths compared to SARS or MERS. Indian medicinal plants have enough potential and possibilities to be used for both prevention and treatment of CoViD-19. This will provide an important opportunity to learn and generate credible evidence. Traditional Indian medicinal plants have long been used for the treatment of various diseases, including antiviral therapies against various viruses. This review suggests that a medicinal herb includes *Pelargonium sidoides*, *Glycyrrhiza glabra*, *Sambucus nigra*, *Andrographis paniculata*, *Couroupita guianensis*, *Tinospora cordifolia*, and *Silybum marianum*. The proposed medicinal plants extracts or as an herbal decoction could serve as effective therapeutics for the treatment of CoViD-19.

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