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Review Article

Plant Biodiversity and its Role in Treating COVID-19

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Abstract

After the emergence of novel corona virus infection, in Wuhan, the city of China, this deadly pandemic in no time has affected the whole world including 216 countries [1]. Till now, no specific medicine or vaccine has been identified as its ultimate treatment. According to our analysis, it is found that traditional Chinese and Moroccan medicines, Indian traditional herbal medicines, and a wide variety of plants are effective in boosting our immunity which ultimately helps to fight against this virus.

We have summarized 164 phytochemicals from these 80 plants that includes Yupingfeng San, *Astragalus, Fangfeng, Yinqiao san, Maxinshigan tang, Baihegujin tang, Radix scutellaria, Ginseng, Crocus sativus*, etc. All the phytochemicals were found to have different roles in inhibiting and suppressing the virus mechanisms and in relieving the symptoms against COVID-19. Further in-vitro and in-vivo experiments and research on these phyto-chemicals are needed to find the best possible treatment against COVID-19.

Keywords: Plant biodiversity; COVID-19

1. Introduction

The first person who was observed to be contracted with COVID-19 was most probably a 55-year-old individual from the province of Hubei in China [1]. The upsurge of the COVID-19 is creating chaos globally due to deficient danger calculation concerning the seriousness of the stich [2]. COVID-19 is positive sense RNA virus [3], having altogether

39 species beneath the inclusive monarchy of Riboviria, which belongs to the family Coronaviridae, suborder Cornidovirineae and order Nidovirales [4]. Nearly all the species under this monarchy are enzootic and only a few of them can cause human infections. Presently, seven human coronaviruses have been confirmed [5]. The very first article associated with 2019-nCoV was published on January 21st, which affirmed that 2019-CoV resides with the group β-CoV, sharing heritage with bat coronavirus HKU9-1 [6]. Latest researches revealed that SARS-CoV-2 has a genomic organization analogous to β-coronaviruses [7], which consists of a viral capsid proteins (N) gene, a spike protein (S) gene, 5′-UTR, 3′-UTR, a replicase compound (orf1ab) programming non-operational protein (nsps), a sheath protein (M) gene, wrapping protein (E) gene, and several unidentified non-structural open reading frames [8]. By Dec 2021, this pandemic has caused 5,595,610 deaths worldwide, as per the reports presented by World Health Organization.

As there is no actual treatment of this disease, natural compounds with high bioavailability and little cytotoxicity appear to be the most effective runners in this regard.

2. Mode of Transmission

Pigs, camels and bats generally establish a common host system for the coronaviruses. These coronaviruses are somehow transmitted from these animals to humans [9]. And are transferred from human to other human by means of cough, sneezing, or hand shaking; and thus, settle themselves in the respiratory tracts [10]. Coronaviruses have an incubation period of about 2 to 14 days [11].

3. Symptoms

The symptoms may vary person to person but the common symptoms of this disease include high fever, sore throat, fatigue, breathlessness, cough, loss of taste or smell, tiredness and diarrhea etc. In severe cases, loss of movement and multi-organ failure and severe pneumonia has been observed.

4. Traditional Chinese Medicine

TCM believes that Qi is the structure that maintains basic functions of the body. This can be helpful in maintaining the body functions but can also harm our health by damaging our lungs. Therefore, the purpose of TCM is to guard lungs. The lungs are not only essential for oxygenating our body but can also play a role in immune system of the body. When your immune system is strong, you can prevent coronavirus. There are some medicines that help to keep our immune system strong.

Yupingfeng San, a prehistoric herbal drug used to prevent lung diseases. There are three herbs used in this medicine: Astragalus reduces phlegm, Fangfeng removes dampness, Atractylodes improves Qi of spleen, which can disturb our ingestion. Thus, regulating body's immune function.

Coronavirus mild infected individuals repeatedly have perspiration, thirst, fever, sore throat and floating pulse etc. These patients can be treated with Yinqiao san, a medicinal herb that has antiviral functions and can be used to boost invulnerable functions of upper respiratory tract [12].

If pathogenic Qi is too strong, the healthy Qi will be damaged and lungs will not work. Therefore, extra saliva will be produced and patients to respire any longer. Maxinshigan tang (decoction) and Baihegujin tang are the Chinese medicinal herbs which can be used to expel pathogenic Qi and benefit the lung to eject saliva [13]. Another Chinese herb, Baicalin is a flavonoid from *Radix scutellaria* was originated to be an inhibitor of SARS-CoV in vitro [14]. Ginseng stem-leaf saponins actively stimulates the exact antibodies response against infectious bronchitis virus [15].

5. Indian Herbal Medicines

Indian herbs have been used traditionally against various microbial diseases and are considered to be anti-inflammatory and immune boosting medicines. A variety of species can be used for the treatment of COVID-19. *Glycyrrhiza glabra* [16] and *Allium sativum* [17] prevents the viral replication of SARS-CoV and could be used against SARS-CoV-2. *Andrographis paniculata*, used in Ayurvedic medicinal system has strong effect against viral respiratory tract infections.

It was observed that *A. paniculata* suppressed the pathogenic effects of SARS-CoV [18]. *Vitex trifolia* and *Sphaeranthus indicus* reduces inflammatory cytokines in a pathway implicated in respiratory distress in SARS-CoV [19]. *Salacia oblonga* [20] another plant suppresses angiotensin II and AT1 gesture associated to lung harm. *Clerodendrum inerme Gaertn* acts as inhibitor by targeting ribosomes of SARS-CoV-2 [21].

Indian medicinal herbs have been recommended to use against covid-19. Among these *Tinospora cordifoliza* (Ayurveda) for chronic fever, *Andrographis paniculata* (Siddha) for fever and cold, , *Zizyphus jujube*, *Cydonia oblonga* and *Cordia myxa* (Unani) as anti-inflammatory, smooth muscle relaxant, anti-influenza agent, and *Arsenicum album* 30 (Homeopathy) as effective drugs, have been recommended as preventive medicinal herbs against covid-19. *Agastya haritaki* (Ayurveda) for upper respiratory tract infections, *Anuthaila* for respiratory infections, *Adathodai manapagu* (Ayurveda) against temperature, *Bryonia alba* reduce lung inflammation, *Rgus toxico dendron* for viral infections, *Atropa belladonna* for asthma and *Bignonia sempervirens* (homeopathy) for asthma, chronic lung diseases, *Eupatorium perfoliatum* for respiratory symptoms, *Vishasura kudineer* (Siddha) for fever and *Kabasura kudineer* (Siddha) for sore throat, fever, cough, shortness of breath have been recommended as treatment against various symptoms of COVID-19.

6. Ayurvedic Medicine “Kadha”

Kadha is a liquid formulated from less juicy or dry herbs and spices. The ministry of Ayush, Government of India recommends the use of Kadha for immune boosting against coronavirus. There are almost 108 phytochemicals in the herbs used in recipe of Kadha which has been mentioned in table 1 [22]. Ayurvedic medicines are used for treating many viral diseases for more than 2000 years. These medicines involve formulation of Kadha (decoction) for oral intake [23, 24].

Herbs	**Common names**	**Phytochemicals**
Ocimum sanctum	Tulsi	Beta-caryophyllene, Oleanolic acid, Ursolic acid, Rosmarinic acid, Cirsimaritin, Eugenol, Estragole, Linalool, Eugenic acid, Apigenin, Isothymusin, Isothymonin, Orientin, Carvacrol, Vicenin and Cirsilineol
Curcuma Longa	Haldi	Curcumin, Bisdemethoxycurcumin Demethoxycurcumin, Ar-turmerone, Atlantone, Alpha-turmerone, Cyclocurcumin, Beta-turmerone, Calebin A, Vanillin, Trans-Ferulic acid and Vanillic acid
Tinospora cordiofolia	Giloy	Magnoflorine, Cordioside, Choline, Tinocordioside, Tinocordifolin ,Beta-Sitosterol, Jatrorrhizine, Tinosporide, Cordifolioside A, Berberine, Tinocordifolioside and Tinosporaside
Piper nigrum	Black pepper	Piperamide, Piperamine, Pipericide, Sarmentosine, Sarmentine, Brachyamide B, Dihydropipericide, N-Formylpiperidine, Guineensine, Isochavicine, Pentadienoylpiperidine, Tricholein, Trichostachine, Piperettine, Piperolein B, Retrofractamide A, Chavicine, Piperine, Piperic acid, Isopiperine, β-caryophyllene and Nerolidol
Zingiber officinale	Ginger	10-gingerdiol, 6-gingerol, 6-shogaol, Bisabolene, 6-paradol, Zingiberene, 1 dehydrogingerdione, 6- gingerdione, 6-gingerdiol, Eucalyptol, 4-gingerdiol, Citral and 10-gingerdione
Syzgiumaromaticum	Clove	Methyl salicylate, beta-caryophyllene, Vanillin, Eugenol, Campesterol, Crategolic acid, Eugenin, Kaempferol, Rhamnetin, Gallic acid, Oleanolic acid, Stigmasterol, Eugenitin, Acetyl eugenol and Flavonol glucosides
Elletaria cardamomum	Cardamon	Linalool, Geraniol, Protocatechuic acid, Alpha-terpinyl acetate, 1,8 cineole, Linalyl acetate, Limonene, 4-terpineol and Protocatechualdehyde
Citrus limon	Lemon	Eriodictyol, Hesperetin, Phloroglucinol, Quercetin, Vitamin C, Umbelliferone
Withania somnifera	Ashwagandha	Withanolide ,Withanolide A, Withaferin A, Somniferine, Anaferine, Withanolide B, Withanone and Choline

Table 1: Phytochemicals in herbs used for Kadha preparation.

7. Moroccan Medicinal Plants

By molecular docking, collaboration among the particles are investigated and the receptor of COVID-19. The consequences of molecular docking displayed that amongst 67 molecules of natural basis, three molecules (Crocin, Digitoxigenin, and β-Eudesmol) are projected as inhibitors in contrast to the coronavirus constructed on the energy types of contact amongst these molecules and considered protein.

7.1 Crocin

Crocin is the carotenoid chemical compound responsible for the color of *Crocus sativus* (saffron). Crocin helps to boost the body's immune system and makes it easier for our body to compete a deadly virus such as COVID-19. It also has the capability to prevent the repetition of HSV before and after the entrance of virions in Vero compartments [25].

7.2 Digitoxigenin

This signifies 11.25% of the amount present in *Nerium Oleander*, byproducts of these molecules are castoff as anti-cancer and anti-viral inhibitors [26]. Recent studies suggest that Nerium oleander can expectedly border the spread of HTLV-1 by aiming an exceptional phase in the retroviral lifespan [27].

7.3 β–Eudesmol

In spite of its little quantity of *Lauris Nobilis L* which covers only 2.39%, this complex has a good communication with the goal, and it has important antiviral and antibacterial control [28].

8. Herbal Treatments

Herbal medicines have been used as conventional medicine for dealing with various diseases. *Anthemis hyalina*, peels of *Citrus sinensis* and *Nigella sativa* have been used against microbial diseases and are used as traditional medicines against Covid-19. There are many plant species that were used to treat SARS like *Lonicera japonica* (Japanese honeysuckle used for digestive disorders), *Astragalus membranaceus* (Chinese flowering plant used to treat cold, respiratory infections), *Glycyrrhiza uralensis* (improves spleen function and blood circulation and also reduce cough), etc. *Ocimun sanctum* (tulsi plant) is the herb of all reasons- with vitamin C, antioxidants and antiviral properties. Its extract can be helpful against CoV due to its possibility to inhibit replication of this virus by its ACE II blocking properties and immunomodulatory feature [29].

8.1 *Anthemis hyaline*

The extract of a chamomile plant called *Anthemis hyalina* was shown to inhibit virus replication [30]. Chamomile is used in tea making and is also an anti-inflammatory and anti-microbial agent that helps in decreasing the wound healing time [31]. The major components found in the extract were carvacrol and α-pinene [32].

8.2 *Citrus sinensis*

Citrus sinensis also called sweet orange, herb used for medicinal treatments. Turkish people consume *Citrus sinensis* by making jam and by taking it as raw fruit to increase vitamin C levels to help recover from flu during flu seasons. *C. sinensis* peel extract majorly consists of flavonoids like limonene and linalool [33]. These show anti-oxidant and antiviral effects.

8.3 *Nigella sativa*

Nigella sativa also recognized as black cumin or black seeds are commonly used in bakery items. Combination of *Nigella sativa* seeds and honey has been used to treat nasal and upper respiratory tract infections. The large traditional use of *Nigella sativa* as panacea in North African, Indian, Pakistani and Turkish societies came from Islamic belief and also Bible. It has been used in many researches works due to its antiviral, anti-inflammatory, immune-modulatory and antimicrobial actions. The main components of *N. sativa* that act as inhibitors for COVID-19 are Nigellidine and α-heredin. The traditional practice of using black seed formula and its steam relieves the symptoms of the COVID-19 [34-36].

9. Liquorice Root

Liquorice root (*Glycyrrhiza spp*.) is used as a vital component in TCM formulations. This root is used to soothe gastrointestinal problems. It also contains glycyrrhizic acid, which have anti-inflammatory and immune boosting properties [37]. There is a compound in this root called as "Liquiritin". This compound is found helpful in treating coronavirus by stopping replication of the novel disease in monkey cells. The health professionals from Peking University wrote in a preprint paper that "We recommend liquiritin as a competitive candidate for treating COVID-19". Liquiritin purposes as an antioxidant and has neuroprotective and therapeutic consequences on patients. This is usually a form of herbal compounds in licorice tablets in China, where traditional medicines have been advertised in Beijing for the treatment of coronavirus. These medicines work on immune system of the individual and help to fight coronavirus [38].

10. Herbs that Boosts Immunity

As we all know, there is no vaccine available for COVID-19, but we can prevent the virus by supporting immune systems. Good nutrition like eating variety of food, cutting back salt and eating juices and staying hydrated can also reduce the chances to get infected.

10.1 Holy basil

Its leaves are abundant in vitamins, anti-oxidants, flavanol and Eugenol which is a bioactive complex having anti-bacterial, anti-fungal and anti-microbial properties. It also functions in decreasing stress and maintaining glucose level in plasma.

10.2 Fenugreek

It's a well-known plant which acts as a natural anti-oxidant and boosts the function of our immune system. It helps to fight against COVID-19 by strengthening immune system.

10.3 Ginger

Ginger is a well-known anti-fungal, anti-inflammatory and anti-cancer agent. It serves as a remedy for colds, coughs, asthma, nausea, travel sickness, arthritis, and several gastrointestinal sicknesses.

10.4 Garlic

It has strong anti-oxidant properties, and also helps in dropping stress and high plasma compression. It also aids in improving thiamine (vitamin B1) engagement

in body and avoids beriberi.

10.5 Turmeric

It has a bioactive complex recognized as curcumin, which acts as an anti-inflammatory negotiator.

11. Phytochemicals in Drug Therapy against COVID-19

It is reported that in a therapeutic plant catalogue screening, out of 32,297 probable antiviral phytochemicals, top nine novel non-toxic phytochemicals were selected as inhibitors of SARS-CoV-2 3CL pro activity in addition to the replication of virus. Among these identified phytochemicals 5,7,3′,4′-Tetrahydroxy-2'-(3,3-dimethylallyl) isoflavone obtained from *Psorothamnus arborescens* [39] showed highest docking scores and binding energies and it was also originated in traditional Chinese medication histories. These nine phytochemicals are mentioned in the Table 2. *Psorothamnus arborescens* has been used as anti-leishmanial plant. *Myrica cerifera* has been used to treat laryngitis, sinuses and chest congestion, sore throat due to scarlatina and it also stimulates blood production [40]. *Hyptis atrorubens Poit* has antimicrobial activity and is used for treatment of unspecified medicinal disorders. *Phaseolus vulgaris* has been used for its anti-inflammatory, anti-oxidant and anti-bacterial consequences. *Phyllanthus emblica* used in Indian traditional medicine as Unani and Ayurvedic medicines has been considered as anti-oxidant and anti-inflammatory agent. *Fraxinus sieboldiana*, a plant found in northern areas of Pakistan has been traditionally used for malaria and pneumonia. *Camellia sinensis* has been used widely for nasal and throat infections. *Glycyrrhiza uralensis* has been used for reducing cough, improving respiratory system and blood circulations. *Amaranthus tricolor* has been used to treat pain and for improvement in blood circulation. All the phytochemicals of the above plants that have been screened can be used as effective compounds for covid-19 drug therapy [40, 41]

Phytochemicals	**Plants**
5,7,3′,4′-Tetrahydroxy-2'-(3,3-dimethylallyl) isoflavone	*Psorothamnus arborescens*
Myricitrin	*Myrica cerifera*
Methyl rosmarinate	*Hyptis atrorubens Poit*
3,5,7,3′,4′,5′-hexahydroxy flavanone-3-O-beta-D-glucopyranoside	*Phaseolus vulgaris*
(2S)-Eriodictyol 7-O-(6″-O-galloyl)-beta-D-glucopyranoside	*Phyllanthus emblica*
Calceolarioside B	*Fraxinus sieboldiana*
Myricetin 3-O-beta-D-glucopyranoside	*Camellia sinensis*
Licoleafol	*Glycyrrhiza uralensis*
Amaranthin	*Amaranthus tricolor*

Table 2: Phytochemicals extracted from plants for screening.

12. Nutritional Interventions

12.1 Vitamin A

It is considered as an "anti-infective" and "anti-inflammation" vitamin which exhibits immune boosting effects. Vitamin A deficiency causes diseases of respiratory tract and lung diseases while Vitamin A supplementation can prevent repeated respiratory infections [42]. The body uses vitamin A to build and repair lung tissues. Therefore, vitamin A consisting plant foods like mangoes, carrots, tangerines etc. or Vitamin A supplements could be effective in improving the immune system against the complications of COVID-19 [43].

12.2 Vitamin B

A liquid-soluble vitamin can be used as a basic option in dealing with covid-19. Vitamin B2 (riboflavin) and UV light reduces the titer of MERS-CoV in human plasma substances [44]. Vitamin B3 inhibits neutrophil penetration into the lungs produces anti-inflammatory result throughout aperture-induced lung damage [45]. Furthermore, vitamin B6 has a specific role in strengthening immune system. Shortage of vitamin B may lead to weak immune responses in host bodies therefore vitamin B supplements must be provided to diseased patients as immune boosters [42].

12.3 Vitamin C

Another vitamin also known as ascorbic acid that is soluble in water plays a significant part in immune system. It has been observed in various trials that vitamin C supplements prevented the vulnerability to lower breathing tract diseases (including ARDS, pneumonia etc.) and also acted as a weak anti-histamine agent against flu and swollen sinuses [46]. As covid-19 includes various symptoms of pneumonia, lower respiratory tract infection and many other flu symptoms, therefore vitamin C intake can enhance the immune response of body against COVID-19 and can prevent the patients from getting pneumonia and likely symptoms [42, 47]. The Association of Indonesian Clinical Nutrition Specialist recommended the usage of vitamin C. 1-gram oral consumption daily for mild cases and 4 grams IV high dose, followed by 1 gram every 8 hours of vitamin C for critical cases. Vitamin C can be secured from various vegetables and fruits like lemon, orange, red guava, broccoli and kiwi fruit etc., [48].

12.4 Vitamin D and E

Vitamin D also a hormone that enhances the development of all type of cells along with immune cells. The deficiency of vitamin E and vitamin D in young bullock was reported as a cause of bovine coronavirus [49]. Therefore, both vitamins can work as beneficial compounds for treatment of coronavirus [42].

12.5 Omega-3 polyunsaturated fatty acids

Omega-6 and Omega-3 PUFAs present in flax seeds, soy beans and walnuts show anti-provocative effects [50]. Omega-3 consisting of protecting D1, an antiviral drug can be used against this novel virus [42].

12.6 Trace elements

Plant foods consisting of trace elements like selenium, zinc and iron serve as immune boosters. Alteration of viral genome changing the mild pathogenic virus to extremely virulent virus in host under oxidative stress

is caused by selenium deficiency [51]. Use of selenium along with ginseng stem/ leaves saponins induces immunity against coronavirus vaccine in chickens [52]. Hence Selenium supplements can be helpful in treatments of covid-19. Iron and zinc deficiency also lead to respiratory tract infections. Zinc intake by zinc deficient children reduces the death rate caused by respiratory tract infections. Further amalgamation of zinc and pyrithione at little concentrations causes inhibition of reproduction of SARS-CoV [53]. Hence these phytochemicals play vital roles in treatment of Covid-19 [42].

13. Conclusion

In real, the state of our body decides whether we are more likely to fall prey to a life threating disease like corona or not. Since forever, natural products and herbal ingredients have always been proved effective as antiviral agents against different viruses. In this case too, scientists are indulged to look for a natural remedy to fight against coronavirus. Meanwhile, it is very important for us to keep our mental, physical and emotional state healthy in such a pandemic. Intake of herbal ingredients is very important to boost our immune system and maintain a healthy diet, because this is the only way by which we can checkmate COVID-19. Researchers from numerous fields worldwide are working hard to come up with operative treatments to curb this pandemic.

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