



Functional Food Plants and their Potential Antiviral and Immunomodulatory Properties: the Covid-19 Perspective

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Abstract: The pandemic of coronavirus disease (Covid-19) which is caused by the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2), is continuously hitting the world and millions of individuals have been affected so far. Limited therapeutic options are available for the treatment of Covid-19 while scientists around the globe are working hard to make the vaccines clinically available to the maximum human population. Alarmingly, SARS-CoV-2 variants are emerging in different regions of the world, hence threatening the efficacy of the clinically available vaccines. In such a scenario, the utilization of medicinal plants or traditional medicine could be the most preferred choice along with the precautionary measure to be adopted against the Covid-19. The current article has summarized few important food plants that have previously exhibited promising immunomodulatory or antiviral activities. These medicinal plants could be suggested for boosting the immune system and could be utilized against their utilization against SARS-CoV-2. It could be concluded that medicinal plants especially *Allium sativum*, *Curcuma longa*, and *Allium cepa* along with other plants/herbs/spices could not only be used against SARS-CoV-2 but also other viral, bacterial, or other parasitic diseases other prevalent diseases prevalent in the region.

Keywords: Medicinal plants, Antivirals, Immunity boosters, Covid-19.

1. INTRODUCTION

The second wave of coronavirus disease-19 (Covid-19) pandemic has been experienced around the globe continued to affect millions of individuals across the globe [1] the situation is further proceeding towards 3rd and 4th wave. The Covid-19 which is caused by severe acute respiratory syndrome coronavirus-2 SRAS-CoV-2 was initially originated from Wuhan city of China in late December of 2019. Coronaviruses belonging to the *Coronaviridae* family are positive sense, enveloped single-stranded RNA viruses, and have a genome that ranges from 26 to 32 kb in length [2]. Coronaviruses have been reported both in avian hosts and numerous mammals, which include bats, masked palm civets, dogs, and camels, and were initially considered to be pathogens causing

moderate to severe diseases in immunocompetent individuals until coronavirus emerged in 2002 inducing SARS-CoV outbreak [3-6]. There are seven species of coronaviruses currently known to infect humans and can cause common or/and serious diseases. For more than 30 years, HCoV-229E, OC43, NL63, and HKU1 have been the only existent human coronaviruses, causing only mild symptoms of common cold, respiratory tract illness, and pneumonia [7, 8]. The remaining three coronaviruses, named SARS-CoV (emerged in 2002-2003, led to the spread of SARS and cause serious illness) and the MERS-CoV appeared in Saudi Arabia in 2012, caused infection in humans and camels [9]; SARS-CoV-2 which emerged in 2019 in Wuhan, China, spread throughout the world (and serious efforts are being made to control its outspread) [10, 11].

For the treatment of Covid-19, several therapeutic approaches have been suggested such as anti-inflammatory drugs, Lopinavir/Ritonavir, nucleoside analogs, etc. These drugs could be clinically effective against other infections however, their clinical usefulness in Covid-19 still needs to be explored [12, 13]. The food and drugs regulatory administration (FDA) approves a drug and its treatment mechanism after ensuring its safety from injection to ejaculation from the body. Consequently, instead of scratching a completely new drug and investing time and lives, plant-based antiviral treatments against the viruses like SARS-CoV-2 have been suggested. Considering the structure and infection strategies the virus adopts, various phenomenon can be used as targets for treatment including receptor binding and membrane fusion inhibition, viral RNA synthesis inhibition, virus-specific enzyme inhibition, exocytosis inhibition of new viruses from the host cell, and so on. With the help of therapeutic anti-inflammatory drugs, post-viral respiratory symptoms are tried to be diminished [13].

For centuries, in almost all cultures around the world, medicinal plants have been used for the treatment of several diseases including viral, bacterial, fungal, and other infections [14, 15]. Medicinal plants have been extensively reported to have high antioxidant, antiviral, antibacterial, antifungal, and other biological activities. We have summarized some medicinal plants and their bioactive compounds reported against respiratory viruses in Table 1. Bioactive compounds such as alkaloids, tannins, flavonoids, phenolic diterpenes, and other phenolic compounds have been isolated from plants [15-19]. Similarly, functional and nutraceutical foods have been studied and attempts have been made to scientifically validate their health improving potential [19, 20].

The current article was aimed to document medicinal plants and indigenous resources to fight viral infections, particularly accessible food plants that have been reported to be biologically active against respiratory tract infections. Developing countries like Pakistan are continuously affected by several diseases particularly viral infections such as dengue, HCV, polio, HIV, along with bacterial, fungal, and parasitic infections [21-28]. The less-developed infrastructure and limited health facilities

could make the situation worsen especially in conditions like the current pandemic of Covid-19. Therefore, several important medicinal plants with promising antiviral and immunomodulatory properties need to be utilized. The current review could also help the public/researchers to increase the uses of medicinal food plants hence utilizing both the therapeutic effects as well as potential preventive effects, especially boosting the immune responses to infections.

2. COMMON ROUTINELY USED FUNCTIONAL FOOD PLANTS

For a long time, human are cultivating and using plants not only as a food source but also as therapeutic agents for several diseases. Plants having impressive immunomodulatory effects and therefore have grabbed the attention of researchers to explore such bioactive compounds in plants. Several compounds with incredible immunomodulatory properties have been reported including polysaccharides, flavonoids, terpenoids, and alkaloids. Importantly, these compounds possess comparatively fewer adverse effects than allopathic medicines [29]. The routinely used food plants with immunomodulatory effects and/or antiviral effects include the following plants.

2.1 *Allium cepa* L. (Onion)

Allium cepa L. which is commonly known as the onion is famous for its taste in flavors mostly used in salad. Onions contain compounds such as quercetin which could help reduce blood pressure, increase superoxide production, and hence increase the bioavailability of nitric oxide [30]. Potential antioxidant activities of onion have also been reported as onion contains flavonoids and sulfur compounds. Antiviral activities of compounds present in onions have also been reported [31, 32]. Flavonoids have been known to be very effective against viruses as they either inhibit or kill the viruses [33-36]. Flavonoids inhibit viral growth by inhibiting the synthesis of viral nucleic acids and proteins [37-39]. Phytochemicals such as kaempferol and quercetin found in onion play a vital role in inhibiting viral growth while also exhibit virucidal activities [40]. The virucidal activities have been reported against herpes simplex type I virus, rabies virus, polio virus, mengo virus,

pseudorabies virus, sindbis virus, and parainfluenza type 3 virus [41, 42]. It has also been reported that quercetin could inhibit the replication of several respiratory viruses hence reducing viral load [31, 32]. We suggest that *Allium cepa* L. can be further investigated for its anti-SARS-CoV-2 properties.

2.2 *Allium sativum* L. (Garlic)

Garlic has been extensively studied for its tremendous biological activities and has been a popular herbal remedy for centuries. Studies have reported the beneficial effect of garlic on immune systems along with its antiviral properties as it is a source for Sulphur containing compounds and polyphenols [43-45]. It has been reported that proteins in garlic improve the activities of human peripheral blood lymphocytes and natural killer cells; resulting in increased immunity against viral infections. Mitogenic activities of garlic compounds on lymphocytes, basophils, and mast cells have also been observed [46, 47]. Garlic has tremendous immunostimulatory effects and could be used for boosting immunity and enhancing host resistance [15]. Because of such biological activities, garlic is recommended to be used in the current pandemic crises.

2.3 *Curcuma longa* L. (Turmeric)

Turmeric is a spice that has been used in traditional medicine and is an integrated part of Asian cooking and culture. In turmeric, curcumin is present which possesses antimicrobial, anti-inflammatory, wound-healing, antioxidant, hypo-glycaemic, chemo-preventive and several other properties [48, 49]. Turmeric has been widely used as a household remedy for treating sore throat, respiratory illness, and cough as in Asia. Antiviral properties of curcumin derivatives have been reported against infections of influenza viruses [50, 51]. The beneficial effects of curcumin against other viruses particularly against human immunodeficiency viruses have been reported. Antiviral activities of turmeric against chikungunya, dengue, hepatitis B virus, and hepatitis C virus had also been observed. With a good safety profile, turmeric has been used for centuries and its promising activities against the influenza virus could support its uses against other respiratory viruses particularly SARS-CoV-2, however, well-defined randomized studies for its

way along with the value of usage are needed.

2.4 *Camellia sinensis* (L.) Kuntze (Tea plant)

Camellia sinensis (L.) Kuntze is very important plant, and black/green tea is being made from its leaves for thousands of years. Interestingly, after water, tea is the second most consumed beverage in the world [52]. Its consumption has been associated with beneficial effects against inflammation, diabetes, vomiting, cardiac ailments, and cancer. Black tea has been investigated to have increased lympho-proliferative action when applied to cultured human peripheral mononuclear cells [53]. The immunomodulatory properties of green tea have been observed due to the presence of quercetin, gallic acid, and epigallocatechin [54]. Other compounds such as tannic acid, catechins, isothaflavin-3-gallate have been observed to have 3CL protease activities which suggest the potential use of tea plants against the infection of SARS-CoV-2 and other respiratory viruses which are a major threat to the human population globally [55]. Locally, black tea (containing sugar particularly black/brown sugar) is routinely used against different types of respiratory illnesses. However, there is no evidence of this remedy to be effective against SARS-CoV-2.

2.5 *Glycine max* (L.) Merr. (Soybean)

Several important bioactive components of soybean have exhibited antiviral activities against several viruses [56, 57]. Isoflavones from soybean could be beneficial in immune response in viral challenging conditions. Isoflavones have been reported to reduce the infectivity of rotaviruses [57]. Flavonoids from soybean have also modulated the infectivity of viruses such as herpes simplex viruses while genistein has exhibited inhibitory activities against cytopathic effects which are structural changes in host cells caused by a viral infection and leads to cell death [58]. Such bioactive compounds from soybean possess several applications in the human health sector particularly the soy-derived isoflavones that have a potential immunomodulatory effect and could be helpful in the current Covid-19 pandemic.

2.6 *Mangifera indica* L. (Mango)

Mango is a fruit-producing as well as a medicinal

plant and has been known for its therapeutic uses. The mango fruits have been documented as a vital source of vitamins, micronutrients, and other phytochemicals [59]. The immunomodulatory activities of mango have been widely reported [60]. The methanolic extract of mango has been associated with an increase in humoral antibody titers and enhanced delayed-type hypersensitivity which confirms its immunomodulatory activities [61]. Further, the hexane leaves extract of mango has been reported to increase the white blood cell count along with spleen and thymus size which further confirm its immunomodulating properties via white blood cells [62]. The antiviral activities of mangiferin have also been reported and were found to act as a potent biological modifier [63]. Antiviral activities of mangiferin against herpes simplex viruses, human immunodeficiency virus, hepatitis B virus have been reported [63-65]. The immunomodulatory properties of mango could also help alleviate Covid-19.

2.7 *Abelmoschus esculentus* L. (Okra)

Okra has been distributed in various parts of the world. The fruits of okra have been reported with promising immunomodulatory activities [66-69]. The okra flowers are also expected to be a potential source of polysaccharides with immune-stimulatory properties. Besides the consumption of okra pods as foods, it has also been used as traditional medicine for the treatment of several diseases. The okra pods have been used to treat diarrhea and dysentery in acute stomach inflammation, kidney catarrhal infections, dysuria, ardor urine, and bowels. The infusion of okra roots has also been used in syphilis treatment while the juice of the roots was used for treating wounds, boils, and cuts [70]. Researchers have recently reported that polysaccharides from okra exhibited significant macrophage stimulatory activities [71]. They also reported the immunomodulatory activities, increased spleen and thymus index, and promoted cytokines production [71]. However, *Abelmoschus esculentus* needs to be further explored for its potential anti-SARS-CoV-2 properties.

3. SPICES AND HERBS AS PROMISING ANTIVIRALS

Although the previous section has discussed

a few herbs/spices along with their potential biological activities particularly antiviral and immunomodulatory activities. However, there are several other herbs and spices which exhibited promising antiviral activities. Several herbs/plants such as *Ocimum basilicum* (Tulsi), *Allium sativum* (garlic), and *Tinospora cordifolia* (Giloy) along with many others are well known for their tremendous immunity booster properties [72]. Spices such as ginger, turmeric, cinnamon, clove, and black pepper are famous for their antiviral and immunity booster properties. These herbs could be very helpful for the treatment of Covid-19.

The commonly available medicinal plant includes ginger which belongs to the Zingiberaceae family. Other famous members of this family are cardamom, galangal, and turmeric. Several bioactive compounds such as steroids, alkaloids, and phenolic compounds are well known for their medicinal properties are present in ginger. Several other sub-compounds which are well known for their antipyretic, anti-arthritic, anti-inflammatory and antiemetic activities have also been reported from ginger [73]. More importantly, the bioactive compounds from ginger have exhibited tremendous antiviral activities against several viruses particularly respiratory viruses including SARS and influenza viruses [74, 75].

Cinnamomum cassia is commonly known as cinnamon another important medicinal plant widely used as traditional Chinese, Persian, Unani, and Indian medicines. Cinnamon has been reported as a source of compounds with tremendous antiviral, antioxidant, antidiabetic, antitumor, antihypertensive, and antimicrobial activities [76].

Black pepper which is famous for its pungent smell has significant biological properties. Several compounds from black pepper are being used in the medicine and perfume industry. An important compound i.e alkaloid piperine from black pepper is known for promising pharmacological properties such as anti-inflammatory, antipyretic, antitumor, and antimicrobial activities [77, 78]. Antiviral activity of chloroform and methanolic extract of black pepper against human parainfluenza and vesicular stomatitis virus has also been reported [79]. Bioactive compounds such as piperdardiine and piperanine are suggested for the treatment of

Table 1. Reported medicinal plants having potential efficacy against respiratory viruses.

| S. No. | Medicinal Plant | Family name | Reported against viruses | References |
|--------|-----------------------------------|------------------|--|------------|
| 1. | <i>Aesculus chinensis</i> | Sapindaceae | Influenza | [86, 87] |
| 2. | <i>Allium cepa</i> L | Amaryllidaceae | Influenza | [41] |
| 3. | <i>Argimonia Pilosa</i> | Rosaceae | Influenza | [80] |
| 4. | <i>Artemisia annua</i> L. | Asteraceae | SARS-CoV | [102] |
| 5. | <i>Blumea laciniata</i> | Asteraceae | Respiratory syncytial virus | [89] |
| 6. | <i>Brazilian propolis</i> | Asteraceae | Influenza | [98, 99] |
| 7. | <i>Camellia sinensis</i> | Theaceae | HCV, influenza | [81] |
| 8. | <i>Curcuma longa</i> | Zingiberaceae | Influenza | [97] |
| 9. | <i>Eleutherococcus senticosus</i> | Araliaceae | Influenza virus A | [90] |
| 10. | <i>Geranium sanguineum</i> | Geraniaceae | Respiratory syncytial virus, Influenza | [88] |
| 11. | <i>Glycyrrhiza glabra</i> | Fabaceae | Influenza, SARS-COV | [85] |
| 12. | <i>Lycoris radiata</i> | Amaryllidaceae | SARS-CoV, Influenza | [84] |
| 13. | <i>Momordia charantia</i> | Cucurbitaceae | Influenza | [91] |
| 14. | <i>Nerium indicum</i> | Apocynaceae | Influenza, HSV | [92, 93] |
| 15. | <i>Piper nigrum</i> | Piperaceae | Influenza | [79] |
| 16. | <i>Radix glycyrrhiza</i> | Fabaceae | SARS-CoV-2 | [82, 83] |
| 17. | <i>Scutellaria baicalensis</i> | Lamiaceae | Influenza | [94-96] |
| 18. | <i>Urtica dioica</i> | Urticaceae | Influenza | [100, 101] |
| 19. | <i>Verbescum thapsiforme</i> | Scrophulariaceae | influenza viruses | [103] |

Covid-19 [19]. Several of the above-mentioned plants are being used as household remedies against viral infections especially those affecting the respiratory and/or digestive tract. The global problems could be addressed via local solutions and the indigenous resources need to be utilized in the current Covid-19 pandemic.

4. CONCLUSION

Medicinal plants are a promising alternative for the prevention and treatment of various diseases. China has utilized several medicinal plants as traditional medicines since the start of Covid-19. Several spices, herbs, and other medicinal plants are cultivated in Pakistan on large scale. Developing countries like Pakistan are continuously experiencing disease outbreaks (both viral and bacterial) and the current pandemic of Covid-19 could further aggravate the situation due to a large number of cases and co-infections [22]. In the current Covid-19 pandemic, the use of immune boosters and precautions could be the best options. The use of medicinal plants particularly spices and other food plants possesses important antiviral activities. Because of the presence of potential antimicrobial, immunostimulatory and immunomodulatory, antivirals, and other important properties, the mentioned medicinal plants are not

only recommended in the current situation but also need to be used against other infections prevalent in the country. These medicinal plants might have side effects if used inappropriately, therefore, further studies are needed to explore their effectiveness, amount of consumption along with the mode of consumption, and/or way of administration.

5. CONFLICT OF INTEREST

The authors declare no conflict of interest.

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