

Review Article

Medicinal Spices for the Prevention and Treatment of Coronavirus Disease-2019

Chukwuebuka Egbuna^{1,2}; Muhammad Akram³; Rabia Anum⁴; Babatunde Oluwafemi Adetuyi⁵; Isayas Asefa Kebede^{6*}

¹Department of Biochemistry, Faculty of Natural Sciences, Chukwuemeka Odumegwu Ojukwu University, Uli, Anambra State, Nigeria

²Nutritional Biochemistry and Toxicology Unit, World Bank Africa Centre of Excellence, Centre for Public Health and Toxicological Research (ACE-PUTOR), University of Port Harcourt, Port Harcourt, Rivers State, Nigeria

³Department of Eastern Medicine, Government College University Faisalabad Pakistan

⁴SINA Health, Education and Welfare Trust Karachi Pakistan

⁵Department of Natural Sciences, Faculty of Pure and Applied Sciences Precious Cornerstone University, Nigeria

⁶School of Veterinary Medicine, Ambo University, Guder, Ethiopia

*Corresponding author: Isayas Asefa Kebede

School of Veterinary Medicine, Ambo University, Guder, Ethiopia.

Email: byisayas@gmail.com

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Introduction

COVID-19 is caused by the SARS-CoV-2 virus which infects the respiratory system and causes many health risks. This virus is a strain of coronaviruses that is distinguished by its containment of the genetic material RNA and on the surface the spikes that enable it to penetrate into cells through Angiotensin-Converting Enzyme 2 (ACE2), which is found in abundance on the surface of respiratory cells [94].

There are seven strains of the Covid virus; four of them cause slight symptoms, and the other three cause severe symptoms that may reach death [57]. The journey of the virus begins by adhering to ACE2, TMPRSS2 through its own spike, and then begins to penetrate the cells, especially the lung cells where the virus begins to multiply and the stage of symptoms appears. If

Abstract

By the end of 2019 and the year 2020, the COVID virus had spread, and in March 2020 the World Health Organization declared that COVID 2019 was an epidemic that invaded many Arab and foreign countries and threatened many lives. Since ancient times, medicinal plants have played an important role in treating many epidemic diseases. The Cochrane method confirmed that herbal plants are effective in treating respiratory epidemics such as SARS. In China, the National Health Committee explained the role of herbal plants in the treatment of Covid 19 in addition to the western treatment. Studies have shown that nutrition has an effective role in treating the virus, as foods rich in vitamin C are used to treat respiratory viruses. COVID-19 is one of the coronaviruses that cause infection of the respiratory system, and vitamin C may use for treatment. Foods rich in vitamin D are also used to raise the efficiency of the immune system and thus resist the viral infection. The pharmacy for the treatment and prevention of Covid 19 includes many plants such as fenugreek, curcumin, cinnamon, and black pepper. This review sheds the light on the medicinal plants with promising efficacy against COVID-19.

Keywords: COVID-19; Traditional medicine; Western medicine; SARA; Vitamins; Natural plants

the virus has not been detected at an early stage, this will lead to difficulty controlling it, and then clots occur, causing death [94]. Currently the entire world is suffering from the Covid19 infection as a pandemic disease which pressurized numerous countries to follow lockdown procedure for the sake of ensuring safety of their citizens [83]. During this time every country government is interacting their research teams to overcome with this problem that is created by the infection covid19. According to worldometers by November, 11, 2020 the world number of cases are 50636124, whereas in Pakistan 343189 COVID cases are reported [96]. Apart from all the strategies and treatment plan that is introduced, but medicinal plants are being used in the treatment of COVID-19.

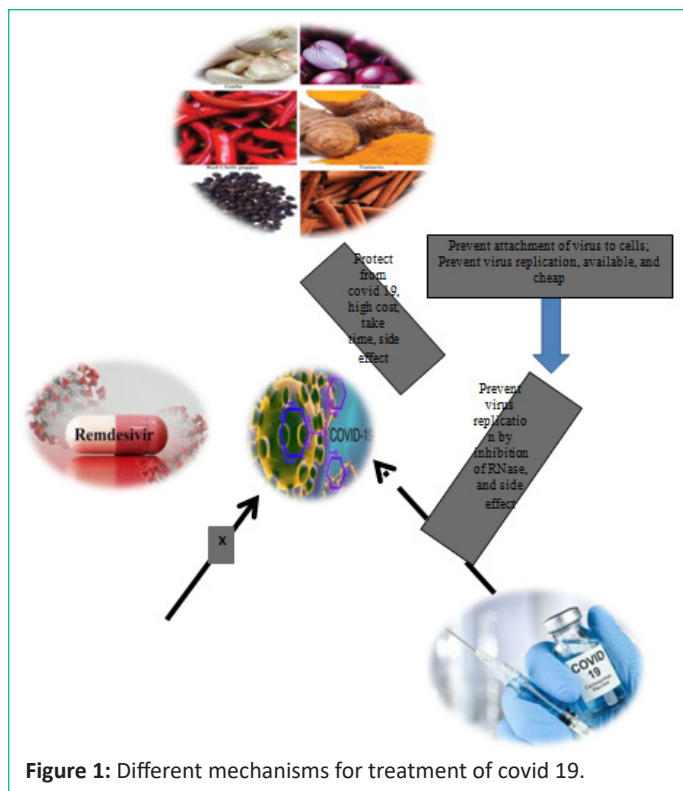


Figure 1: Different mechanisms for treatment of covid 19.

In light of the COVID-19 pandemic, scientists have sought to discover an effective vaccine, but this will require more time and studies, and that vaccine is likely to have side effects that may not appear except in the long run. Therefore, scientists turned to natural products and herbal plants in an attempt to find an effective treatment for this delinquent virus, and it yields effective fruits in treatment with the fading of the unwanted side effects of the chemical drugs. About 80% of world's population uses spices and condiments to prevent and manage different ailments. The herbs and spices are important for boosting immunity as shown in many studies. In this review, some medicinal plants that have proven effective in treating and preventing COVID-19 was highlighted (Figure1).

Ginger

Ginger, scientific name is *Zingiber officinalis*Rosc. (Zanjabeel or Adrak), is a fruitful herbaceous plant that grows in tropical areas. It has been used in alternative medicine in the treatment of many ailments such as hypertension, diabetes, dyslipidemia, headaches, colds, coughs, and sore throats (Bode & Dong, 2011). Ginger contains many bioactive constituents, including zingiberene, zingerone, gingerol, gingerdiol, shogaol, paradols, and curcumene. Ginger has many benefits as it is anti-bacterial and anti-fungal, anti-diabetic, anti-viral, and anti-inflammatory (Abdel-Moneim et al. 2013; Al Hroob et al. 2018; Hosseinzadeh et al. 2017). It is used as spice, a flavoring agent having a great medicinal importance belongs to the family *Zingiberaceae* [12] (Mohammad Sharrif Moghaddasi, 2012). It contains 1-3% weight of volatile oils, which is responsible to its unique flavor and particular aroma. The World Health organization (WHO) considers ginger as anti-emetic, cholagogic and anti-inflammatory properties [REF]. Other pharmacological properties that ginger possesses include antioxidant, antimicrobial, anti-asthma, expectorant, antipyretic and analgesic [19,32,74]. 6-shogaol interferes with the inflammatory cascade, inhibits Cyclooxygenase (COX), and the release of Prostaglandins (PGs) [64]. Further *invitro* studies showed that 6-gingerol and 6-shogaol present have anti-platelet aggregation activity [48]. Ginger also helps in the treatment of chronic diseases due to

its anti-inflammatory and immuno-modulatory effects [8]. Six weeks use of ginger reduces the inflammatory cytokine level plasma Interleukin-1 β (IL-1 β), Interleukin-6 (IL-6) and Tumour Necrosis Factor- α (TNF- α) and thus attenuates infection [REF]. Such strategies consideration follows in COVID-19 treatment [100]. Ginger as an immune booster basically inhibits the Human Respiratory Syncytial Virus (HRSV) as induced plaque formation on airway epithelium by blocking viral attachment [42]. A fresh ginger in high concentrations activates mucosal cells to secrete Interferon (IFN)- β which is responsible for the reduction in viral progression [3]. Sudanese people take ginger tea, or coffee as the local treatment for common cold and cough which is the major symptom of infection with corona virus as it provides protection and a quick recovery from the disease [52,69]. A randomized study trial indicated the effectiveness of ginger in the treatment of respiratory diseases [91]. Some scientific research has proven that ginger is effective in treating Covid 19 [68].

Garlic

Garlic, botanical name *Allium sativum*L. (Lahsun), is another most common spice used for various disease due to its great medicinal importance. It contains mostly sulphur based compounds which are responsible for creating their aroma and other constituents. The main constituents are diallyl polysulfides, vinylthiini, ajoene, S-allyl cysteine, alliin and few non-sulphur compounds like enzymes, saponins and maillard reaction products [6,66]. It shows remarkable pharmacological properties as anti-inflammatory and antiviral properties which helps on curing cardiovascular, cancer, common cold, influenza virus and other diseases [34]. It acts as an immunity booster and is effective against virus, bacterial and fungal organisms. It is highly enriched in antioxidants with free radical scavenging activity. It shows antiviral activity and reduces the symptoms of cold, flu, cough, other symptoms related to influenza and thus might be helpful in COVID-19 infection [101].

Keyaerts et al have demonstrated that garlic has a vital role as an antiviral for Covid 19 [40]. Also, Thuy et al recognized that garlic is an important source in fighting Corona virus infection [88]. It is prescribed in the management of recurrent upper respiratory tract infections and chronic bronchitis [23]. The presence of allicin in garlic act as broad-spectrum antibiotic like as it increases T cells and B-cell differentiation [7]. Garlic improves the immune system by activating white blood cells like Natural Killer (NK) cells and macrophages and provides protection with the help of its contained natural fructans [13]. A study trial showed that garlic extract is effective in the treatment of respiratory diseases [63].

Fenugreek

Fenugreek is a natural antioxidant and commonly used spices in the kitchen as well as a medical ingredient in various medicine in Ayurveda to strengthen the immune system. It is highly enriched in vitamin E and used to preserve pickles [36]. Its botanical name is *Trigonella foenum-graecu* L. and belongs to the family *Leguminosae*. It has been used as medicinal herb since a long time. The major medicinal properties of fenugreek include lactation aid, hypocholesterolemic, gastric stimulant, diaphoretic, antitoxic, antibacterial, galactagogue, antidiabetic, anti-cancer and hepatoprotective [86]. The chemical constituents present per each 100 g seeds of fenugreek are 4.63g saponin and 43.8g protein [5] while other constituents are dietary fibers and polyphenols such as isovitexin and rhaponticin. Fenugreek showed significant results against colds, influenza, bronchial

disorders, catarrh, asthma, sinusitis, constipation, pneumonia, pleurisy, laryngitis, sore throat, lung congestion, emphysema and hay fever tuberculosis [REF]. The mucous solvent efficacy of the seeds provide relief in cough [REF]. It is highly beneficial to boost the immunity and for respiratory symptoms which are similarly found in covid-19 patients. A maximum dose of 300-500 mg/day in the form of capsules can help in getting rid of flu and cold-like symptoms [39].

Black Pepper

Black pepper (*Piper nigrum* L. (Kaali Mirch)) is considered the king of spices [38]. It is highly enriched in around 600 phytochemicals, including lignans, alkaloids/amides, terpenes, neolignans, etc. with numerous medicinal and pharmacological properties. Black pepper and its constituents possess various beneficial effects, such as antiviral, anti-bacterial, anti-inflammatory, anti-pyretic, anti-oxidative, antitumor, immuno-modulatory and other activities [18]. Due to the presence of the alkaloids, piperine and piperamides, it shows antiviral effects on respiratory tract infections and has a potential to fight with COVID-19 where the respiratory tract is drastically affected [16,53].

Research has indicated that black pepper is a powerful antioxidant used in the treatment of asthma and coughs and can prevent the attachment of viruses to the cells, so it may be an effective treatment in the case of infection with COVID-19. Studies have also confirmed that there is a convergence between the chemical composition of piperine and SARS-CoV-2 main protease, therefore, would be a strong inhibitor of virus attachment to the cells and thus prevent virus replication [26].

Clove

Clove (*Syzygium aromaticum* (Laung)) is an ancient precious spice used for different therapeutic purposes since a long time [21,67]. It contains carbohydrates, protein, vitamins (A, C, E and K), thiamin, riboflavin, folate, niacin, dietary fibers, and minerals. In addition, also it is highly enriched in phenolic compounds, including eugenol, thymol, eugenol acetate, gallic acid and β -caryophyllene [30,45]. Its pharmacological activities include analgesic, antioxidant, antitumor, antiviral, antifungal, anti-inflammatory, antibacterial activity, hepatoprotective, antidiabetic and chemopreventive (Kamel et al. 2016). Due to the presence of eugenin, clove shows antiviral activity with an effective dosage of 5 μ g/mL [47]. It suppresses the viral DNA polymerase enzyme and thus inhibits the synthesis of DNA [31,76]. Studies have shown that clove has a viral inhibitory activity in dengue [70]. It can also be used for cold and cough, bad breath, oral hygiene and abdominal discomfort [2].

Red Chilli Peppers

Chilli peppers contain capsaicin, an important constituent which shows improvement in various gastrointestinal and cardiovascular problems by lowering the blood pressure, reducing the cholesterol level and preventing clot formation [54]. Its botanical name is *Capsicum annum* L. and belongs to the family *Solanaceae*. It boosts the immune system and thus shows significant results in relieving respiratory symptoms associated with infections [28]. Its antioxidant activity acts to remove free radicals and thus prevent various heart and neurodegenerative diseases [REF]. Capsaicin is known to alleviate flu, post nasal dribbling, chest congestion and allergic rhinitis [17] which are similar in Covid-19 cases. Hence the intake of capsaicin might be of significant value in ameliorating the respiratory disorders.

Curcuma Longa

Curcuma longa is a herbal plant known to have multiple medicinal properties because it contains metabolic secondary compounds that have antioxidant properties, mainly curcumin. It was used in the treatment of many diseases, such as diabetes and heart disease, and has proven effective in reducing the effects of infection with Coronavirus by strengthening the immune system to confront the virulent virus. Curcumin works to increase ACE2, but also reduces the release of the pro-inflammatory mediators TNF- α and IL-1 β , thus controlling the inflammatory response during viral infection. In addition, curcumin has recently reported to mitigate inflammation and oxidative in the lung of rats challenged with cyclophosphamide (LPS) (Saghir et al. 2020), adding support to its potent anti-inflammatory and antioxidant activities.

Curcumin harmonizes the replication and the cellular events of SARS-CoV-2, it similarly manifests the pathophysiological events of COVID-19. Experimental evidence revealed the efficacy of curcumin in patients with respiratory ailments, including influenza, inflammatory disorders, and coagulopathy. *In silico* investigations reported the ability of curcumin to interact with viral proteins, inhibit viral replication, growth and proliferation of disease. It protects the cellular and organ damage by enhancing the differentiation of immune cells. Further it also improves the activity of other drugs against the viruses [84]. There is a great potential in herbs and ancient spices to fight COVID-19 and regulate the Psychoneuroimmune (PNI) response. Psychological state i.e. mental status and immunity of the individual in this pandemic decide the outcome in numerous cases [87]. Curcumin as an immunity booster in this pandemic significantly reduce its effects and pro-inflammatory cytokines. Curcumin basically regulate the monoaminergic troupe that includes dopamine, glutamate, serotonin, and noradrenaline which ultimately reduce the stress, anxiety and depression [71,99].

A number of associated disorders in COVID-19 are reduced by curcumin through decreasing the regulators like STAT3. Increased pro-inflammatory cytokines weakens the immunity of the individuals [49]. It enhances the hematopoietic differentiation of immune cells [93] and thus reduces the pandemic effects. Curcumin boosts the immunity; excellent anti-depressant improves the neurogenesis and hippocampus functioning [84,99].

Allergy is a pro-inflammatory condition mediated by pro-inflammatory cytokines. Curcumin plays a significant role in clearing the congested airways and lungs and increases cellular antioxidant defenses. A study evaluates the effect of curcumin on IL-2, IL-5, Granulocyte Macrophage-Colony Stimulating Factor (GM-CSF), and IL-4 by lymphocytes in atopic asthmatic patients and their production and allergic response to dust mite. Showed marked inhibition of these mediators, indicating the potent anti-allergic and anti-inflammatory abilities of curcumin [43]. Mast cell degradation is further activated by immunoglobulin especially IgE which generates an allergic response. IL-10 induce the function of Treg Cell which suppresses the production of IgE. Curcumin has been demonstrated to significantly reduce the symptoms of allergic rhinitis by increasing serum IL-10 and decreasing IL-17 which is responsible for the severity of disease in asthma and lung hypersensitivity [51].

Research studies have been made to study the effect of curcumin on the SARS-CoV-2 and it showed anti-viral activity, and Lin and Ying (2020) confirmed that curcumin is effective in treat-

ing pneumonia resulting from infection with the virus. Since curcumin contains phyto-chemical compounds that have anti-viral and anti-inflammatory properties, it is possible to classify it as an effective treatment in cases of infection with SARS-CoV-2 [98].

Black Cumin

Black cumin (*Nigella sativa* L., family *Ranunculaceae*) is a thriving annual plant that grows in North Africa. It contains many chemical compounds such as thymoquinone, cymene, carvacrol, thymohydroquinone, dihydrothymoquinone and thymol. [25,62]. It is used in a wide range of disease conditions, including jaundice, conjunctivitis, rheumatism, diabetes, anorexia, gastrointestinal problems, intrinsic haemorrhage, asthma, cough, bronchitis, fever, bronchitis, influenza and others [44]. Black cumin has shown great therapeutic benefits in patients with viral hepatitis [51] and its main constituent thymoquinone possesses strong antioxidant and anti-inflammatory activities (Galaly et al. 2014; Mahmoud et al. 2014). Very recently, thymoquinone has been reported to ameliorate inflammation and protect the lung against the deleterious effect of repeated administration of Lipopolysaccharide (LPS) (Saghir et al. 2021). It suppresses the viral load by enhancing the number of CD4⁺ T-cells and macrophages and increasing the production of IFN [79]. Black cumin contains secondary metabolites and 30%–45% fixed oil [50]. Ethanolic extract of the seed in a ratio of 1:4 showed anti-inflammatory effects on lungs [REF]. A double-blind randomized control trial showed that the soft gel capsules of cold-pressed *N. sativa* oil containing 0.7% thymoquinone improved asthma control with a trend in pulmonary function improvement [97]. *N. sativa* seeds relieve the respiratory symptoms especially cough and help in the reduction of inflammation [REF] and thus can be used in COVID. Ulasli et al. (2017) showed that the extract of *Nigella sativa* has an anti-SARS-CoV-2 effect where it reduced its reproduction, and the research confirmed that it is effective against other coronaviruses [89].

Fennel

Fennel whose scientific name is *Foeniculum vulgare* Mill. is indicated for respiratory illness and complaints associated with cold, flu and cough [82]. It contains majorly essential oils including trans-anethole, estragole, and limonene [10] other constituents are stilbenes. WHO recommended dose of its intake is 1.5 to 2.5 g in 200 ml of boiling water (brew for 15 min) three times a day. Ethanolic extract of the fennel seeds show anti-inflammatory and analgesic activity in rats whereas aqueous extract along with ethanolic extract has myorelaxant properties used in guinea-pig trachea for broncho-dilatory effect. Its ethanolic extract with essential oil has effects that are similar to theophylline [82]. Hence the drug is safe and can be used in COVID-19 to relieve its symptoms.

Onion

The scientific name of onion is *Allium cepa*, majorly served in Salads. It is antibacterial [77] and numerous studies shows that it also acts as an antiviral and can be used in respiratory ailments [14,15], through the presence of proline which activates the pro-inflammatory cytokines [37]. Inhalation improves its antiviral potential. Flavanoids present in onion act as a chelating agent and helps in targeting virus in the cell [60]. Diabetic patients can also take onion as it as antidiabetic activity [92].

It contains chemical compounds, including isoalliin, methiin,

and propiin, quercetin and kaempferol, and because it is rich in quercetin, it has an anti-viral effect against Covid 19, as it works to prevent its reproduction and growth by preventing its entry into cells, and inhibiting some of the enzymes responsible for the reproduction of the virus. In addition, quercetin strengthens the immune system through secretion of interferon, modification of interleukin, and activation of programmed cell death [65].

Nutmeg

Commonly used spice nutmeg whose botanical name is *Myristica fragrans* Houtt. is of great value due to numerous therapeutic activities. It contains tocopherol, ascorbic acid, flavanoids, phenolic compounds. It possesses antioxidant [41] and antibacterial activity [33].

Cinnamon

Cinnamon, scientifically known as *Cinnamomum verum* J. Presl. belongs to family Lauraceae. It possesses antioxidant, antibiotic, anti-fungal, anti-viral, antibacterial activities [1]. It can be used by diabetic patients [4,46] and also reduce cardiovascular diseases [58]. It has anti-inflammatory effects [72].

Cinnamon contains Eugenol, which has an effective role in preventing the entry of the virus into cells by inhibiting endocytosis. It also works to inhibit the enzymes related to the formation of polypeptides and then prevent the virus from multiplying, so this is an effective treatment to eradicate the virus [22].

Curry Leaves

Curry leaves are in great demand in subtropics due to its health benefits and medicinal values and daily uses. The scientific name of this species is *Cinnamomum tamala* (Buch.-Ham.) T. Nees & Eberm. belongs to family Lauraceae. It possesses anti-inflammatory, anti-microbial, anti-diabetic, anti-diarrheal, antioxidant and immune-modulatory effects [73,90].

Cardamom

The scientific name of cardamom is *Elettaria cardamomum* (L.) Maton, belongs to the family (Zingiberaceae). It has anti-inflammatory, antibacterial, anti-fungal and anti-oxidant activities [9,80]. It increases HDL cholesterol level in blood and hence reduce hypertension. It can be used in the treatment of respiratory tract infections [29].

Ajwain

Ajwain (*Trachyspermum ammi* L., family Apiaceae) are aromatic plant seeds are commonly used for improving digestion. The active enzymes in ajwain improve flow of stomachic acid that help to relieve indigestion, bloating and gas [11]. It possessed antioxidant, anti-hypertensive and lowers the blood pressure, antihyperlipidemic activities along with hepato- and nephro-protective effects [78]. It can be used for dry cough and sore throat problems. Its antibacterial activity especially acts on the lower respiratory tract infections [27].

Drumstick

Drumstick (*Moringa oleifera* Lam) is a flourishing woody tree that grows in India, some African countries and some tropical places. It contains many chemical compounds Apigenin, Luteolin, Phytosterols, Quercetin, Terpenoids, Caffeic acid, which makes it have many medical purposes as it is used in the treatment of coughs, influenza, bronchitis, diabetes, high blood

pressure [56]. It also has an anti-viral effect because it is rich in many minerals and vitamins, especially vitamin C. Research has proven that Moringa has an anti-effect against the COVID-19 virus [81].

Conclusion

From this review, we can see the great benefits of medicinal plants, as multiple studies have proven that medicinal plants have an effective role in treating viruses, especially with regard to the prevailing Corona pandemic 19. These plants contain photo-chemical compounds that have the ability to prevent the virus from penetrating into cells or by stopping the reproduction process, and therefore are potential remedies against this highly infectious disease. Besides, these herbal medicines have no side effects, and by adding these to food, our immune system can be strengthened to a great extent to protect us from the risk of infection with the COVID-19 virus. However, further studies must be done to examine the mechanism by which each plant works separately, and to study the possibility of dispensing with chemical antivirals and to replace alternative medicine and herbal remedies instead.

Author Statements

Data Availability

All the datasets generated or analyzed during this study are included in this manuscript.

Conflicts of Interest

The authors declare that they have no conflicts of interest.

Authors' Contributions

All authors contributed to the study conception, design, data gathering, data analysis, manuscript write-up, and editing of the manuscript. All authors have approved the submission of the manuscript.

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