DOI: 10.7860/JCDR/2021/49530.15245

Review Article

Nutrition Section

# Prevention of SARS-CoV-2 Infection with Antioxidants and Anti-inflammatory Action of Indian Spices: Light at the End of the Tunnel

SANDEEP NEGI[1], SONAL BHATT[2], LAKSHMI BALA[3]




## ABSTRACT

Today, we are living in the era of Coronavirus Disease-2019 (COVID-19), a pandemic that has affected almost the whole globe. It has rightly been called as the 'twenty-first-century plague' which has garnered considerable attention from researchers, pharma companies, policymakers, and media. Though vaccines are being deployed and people are eagerly receiving vaccination; the duration of conferred immunity, the possibility of re-infection of recovered/vaccinated individuals, the consequence of the new mutation in SARS-CoV-2 and its impact and challenge for the efficacy and degree of protection that a potential vaccine could provide is under question. In the absence of any definite answer, people are turning towards natural remedies and spices. India is known globally as the land of spices. Spices like ginger, garlic, black pepper, cardamom, turmeric, clove, cinnamon, etc., are known for their rich aroma, texture, and immunity boosting ingredients. These are rich sources of antioxidants such as flavonoids and alkaloids. The antioxidants present in them, neutralise the free radicals generated inside the body during viral infections and also prevent cellular damage. These exhibit anti-inflammatory activity and have the potential to combat "cytokine storm" in severe COVID-19 infection. Their potential has been realised by the public and has led to a tremendous increase in global demand and consumption. The present review enlists the active ingredients present in important spices and addresses their antioxidants, anti-inflammatory, and anti-viral action. Traditional Indian spices that are not only a cardinal part of the diet but are affordable, easily available can be viewed as the light at the end of the tunnel to combat the current COVID-19 conditions as a preventive measure.


**Keywords:** Clove, Curcumin, Cytokine storm, Garlic, Ginger, Severe acute respiratory syndrome coronavirus 2

## INTRODUCTION

Severe Acute Respiratory Syndrome Coronavirus-2 (SARS CoV-2) which is responsible for the global cause of Coronavirus Disease-2019 (COVID-19) has the property to constantly change itself through mutation. Today, with the help of genetic analysis it is possible to identify multiple variants of SARS-CoV-2. Most of the mutations are harmless while some result in forms that spread more quickly, cause more serious illness, or resist drugs. World Health Organisation (WHO) has given Greek alphabet naming scheme for such "variants of concern" and "variants of interest". These different variants of viruses identified so far are:

1. UK variant (B.1.1.7 or 'Kent Variant' is referred to as "alpha"), detected in December 2020;
2. South Africa variant (B.1.351 or "beta"), also detected in December 2020;
3. Brazil variant (P.1 or "gamma"), identified by January 2021;
4. Two more variants (B.1.427 and B.1.429) were first identified in California in February 2021 [1];
5. Another highly transmissible variant (B.1.617) responsible for the second covid wave in India during April 2021 with notable triple-variant (B.1617.1or "kappa" and B.1.617.2 or "delta") [2]. These different variants rendered the virus more transmissible posing greater public health risks.

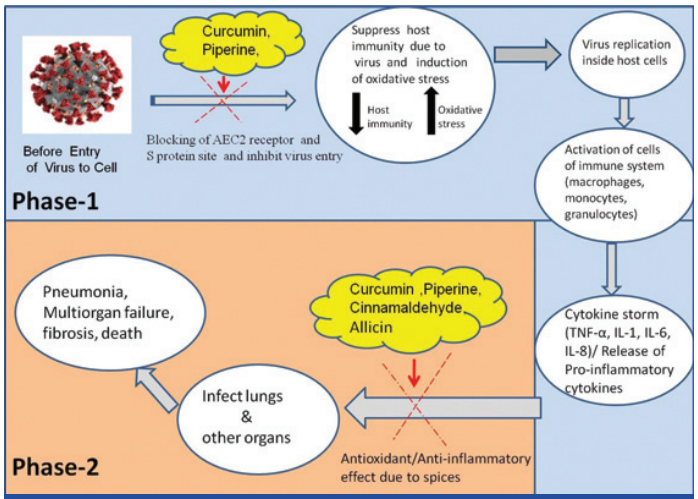
Presently, there are no proven effective therapies for COVID-19 to prevent infection or stop transmission of disease. Within a month of the onset of the pandemic, the United States (US) Food and Drug Administration (FDA) issued an emergency use authorisation for the use of repurposed approved drugs such as hydroxychloroquine, chloroquine (antimalarial drug), ritonavir, and lopinavir (a combination of antiretroviral drugs), remdesivir (an experimental Ebola drug) and steroids, interferon-beta, several immunomodulators, and anti-inflammatory drugs for the treatment of hospitalised patients with COVID-19. This lead to a surge in clinical trials of many approved drugs and the development of effective vaccines. The efficacy of different vaccines was reported to be different as per clinical trials:

1. Pfizer (91% against B.1.1.7);
2. Moderna (94% against B.1.1.7);
3. Oxford AstraZeneca (74% against B.1.1.7);
4. Johnson and Johnson (Janssen) (72% against B.1.1.7; 64% against B.1.351, P.1 and B.1.617);
5. Sputnik-V (92% against B.1.1.7);
6. Covaxin- India's 1st COVID-19 vaccine (78% against B.1.1.7) [3,4].

Several vaccines are deployed worldwide to ensure fair and equitable vaccination of mass for prevention of disease along with other safety measures as hand sanitisation, wearing of masks, and social distancing to combat this pandemic. However, many questions still remain unanswered about the real safety and efficacy of vaccines, the possibility of re-infection of recovered/vaccinated individuals, the duration of conferred immunity, the consequence of the new mutation in SARS-CoV-2, and its impact and challenge for the efficacy and degree of protection that a potential vaccine could provide. It has been observed that an individual's immunity plays an important role in combating infection of SARS-CoV-2 by reducing its pathogenic capacity within the host [5].

The SARS-CoV-2 infection starts with its entry into host epithelial cells (lungs, intestine, etc.) via binding of its S (spike) protein with Angiotensin-Converting Enzyme 2 (ACE 2) receptor of host cells. Some of the active ingredients (andrographolide, berberine, curcumin, mangiferin, nimbin, piperine, thebaine, gallic acid, luteolin, naringenin, quercetin, resveratrol, and zingiberene and withaferin A, etc.) present in spices turmeric, garlic, pepper, cinnamon, etc., have been shown to have binding affinity for either the ACE2 receptor or SARS-CoV-2 S protein or both. These compounds might

inhibit the attachment of the SARS-CoV-2 virus to the host cell [6] [Table/Fig-1-3]. Further, the entry of the virus inside the cell generates a high amount of free radicals (e.g., superoxide anion radical, hydroxyl radical, singlet oxygen, hydrogen peroxide, peroxynitrite radical, hypochlorite, and nitric oxide radical). These are highly reactive and are capable of destroying biologically essential molecules in the nucleus and membranes of cells, such as DNA, proteins, carbohydrates, and lipid [7-9]. The natural antioxidants present in the body e.g., glutathione, vitamin C and E, superoxide dismutase, CYP etc., can donate an electron to a free radical and neutralise it, thus reducing or preventing its destructive potential of cellular damage [10,11]. With the enormous generation of free radicals, the natural antioxidants fall short and leads to oxidative stress. The miraculous treasure of various antioxidants present in spices prevents the cell from oxidative stress and serves as an immunity booster [10]. When a virus enters the host cell cytoplasm, it takes over the host's protein-synthesising machinery and translates its mRNA in the nucleus for the production of viral proteins. This promotes viral replication and the formation of mature viruses and their release. This leads to activation of cells of the immune system like macrophages, monocytes, and agranulocytes triggering the release of various types of chemokines, interferons, interleukins (IL-2, IL-6, IL-8, IL-10, IL-2R, IL-7, etc), colony-stimulating factors, and Tumour Necrosis Factor-α (TNF-α) [8,9]. The condition of hyperactive pro-inflammatory immune response is called "cytokine storm". This condition is responsible for the high degree of damages to host cells depending upon the severity and progress of viral infection. It also leads to life-threatening conditions like Acute Respiratory Distress Syndrome (ARDS), multiple organ failure, etc., and finally death of the patient. Congregated evidence for the anti-inflammatory action of spices in various pre-clinical and clinical studies is documented that may help in preventing cytokine storm [12]. Quercitin, lycorine, myricetin, caffeic acid, scutellarein, silvestrol, and tryptanthrin etc., have also shown antiviral activities in general [13].




**[Table/Fig-1]:** Role of Indian spices that may act in combating pathogenesis of SARS-CoV-2.

Efforts to carry out clinical trials in the more organised way should come in the forefront for developing Indian spices as an efficient and cheap preventive and treatment option against the devastating pandemic. This review addresses the important constituents present in the Indian spices which are anti-oxidant, anti-inflammatory, immunomodulatory, and may protect from 'cytokine storm' to act as an effective weapon for prevention of COVID-19.

## SPICES THAT BOOST IMMUNITY AGAINST COVID-19

### Ginger (*Zingiber officinale*)

It is well known and belongs to the family Zingiberaceae. It not only adds flavour and taste to the food but also has a wide range

| Spices | Constituents |
|---|---|
| Cinnamon | Eugenol, terpineol, proanthocyanidins, linalool, safrole, pinene, benzaldehyde, limonene, catechins, tannins, methyleugenol |
| Cloves | Eugenol, eugenyl acetate, isoeugenol, α-humulene, acetyleugenol, pinene, vanillin, flavonoids, β-caryophyllene, gallic acid, sesquiterpene, phenolic acids |
| Cardamon | Limonene, α-terpinyl acetate, 1,8-cineole, terpinolene, myrcene, limonene, caffeic acid, myrcene, quercetin, kaempferol, linalyl acetate, luteolin, pelargonidin, linalool, terpinolene |
| Coriander | Linalool, petroselinic acid, borneol, linoleic acid, geraniol, terpineol, palmitic acid, cumene, pinene, vaccenic acid, terpinene, quercetin, myristic acid, stearic acid, kaempferol, caffeic, ferulic, n-coumaric and vanillic acids, rutin, tocopherols, pyrogallol, oleic acid |
| Turmeric | Curcumin(diferuloylmethane), eugenol, bisdemethoxycurcumin, demethoxycurcumin, carotene, vanillic acid, ascorbic acid, p-coumaric, syringic, protocatechuic, caffeic |
| Ginger | 6-gingerol, 6-gingerdiol, paradol, geraniol, shogoal, geranial, borneol, gingerdione, linalool, camphene, zingerol, 6-paradol, zingiberon, bisabolene, β-phellandrene, cineole, citral (neral and geranial), zingerone, α-farnesene, zingiberene |
| Anise | Camphene, trans-, cis-anetholes, acetanisole, luteolin-7-glucoside, isoorientin, γ-hymachalen, pinene, estragole, anethole, para-anisaldehyde, methyl cavicol, linalool, eugenol, rutin, apigenin-7-glucoside |
| Fenugreek | Sesquiterpenes, diosgenin, choline, aromatic aldehydes, yamogenin, terpenes, tigogenin, carpaine, fenugreekine, 4-hydroxyisoleucine, gentianine, gitogenin, neotigogens, trigonelline |
| Black pepper | Piperine, camphene, terpenes, piperidine, sarmentine, lutein, β-carotene, zeaxanthin, capsanthin, limonene, isoquercetin, Capsaicin, caffeic acid, pinene |
| Garlic | Allicin, alliin, ajoene, diallyl sulfide, diallyl disulfide, diallyl trisulfide, allyl isothiocyanate, S-allylmercaptocysteine, S-allylcysteine, methiin, cycloalliin, isoalliin |
| Nutmeg | Catechins, eugenol, safrole, lignans, elemicin, myricetin, methylisoeugenol, orgentin, caffeic acid, myristicin, methyleugenol |
| Fennel seeds | Estragole, fenchone, anisaldehyde, sabinene, α-pinene, trans-anethole, limonene, β-myrcene, camphene β-pinene |

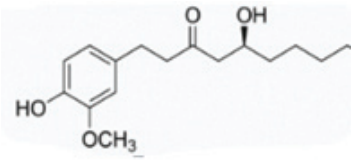
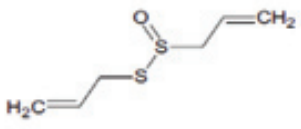
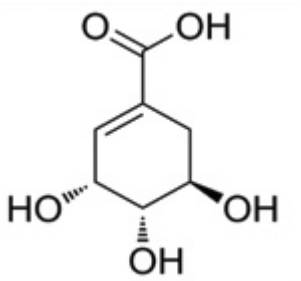
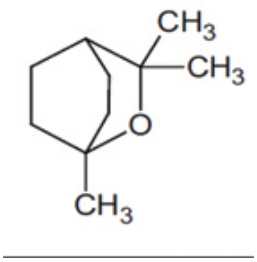
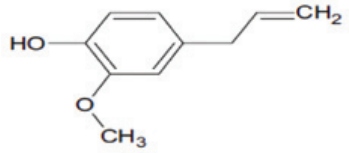
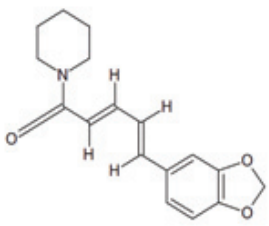
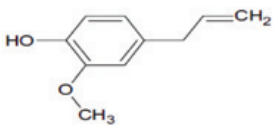
**[Table/Fig-2]:** Important constituents present in Spices [14, 15]

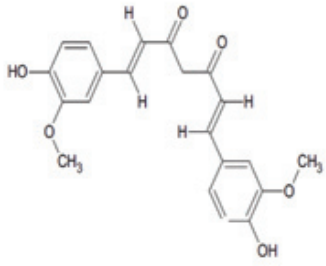
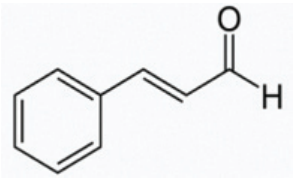
of medicinal properties. Since ancient times, ginger tea or ginger extract has been commonly used to treat common colds, flu, and sore throats [17]. Gingerol is an antioxidant that strengthens our immune system, has antiviral effects, and aids in the treatment of respiratory problems. It has recently been shown to be beneficial for COVID-19 patients [18], as it binds to many target virus proteins and decreases pathogenicity, according to Rathinavel T et al., (2020) [19]. Important enzymes such as alliinase, peroxidase, and myrosinase are also present. Allicin, alliin, and ajoene are sulfur-rich compounds that are among the main ingredients. It is an effective antioxidant agent since it includes compounds like superoxide dismutase and glutathione peroxidase, which play a key role in the body's defense mechanism against viral infections [20]. It has anti-inflammatory effects, functions as an analgesic, decreases blood cholesterol levels, and is helpful to people with heart disease.

Ginger hot water extract is very effective against the Respiratory Syncytial Virus (RSV), avian influenza, norovirus, and Feline calicivirus in studies (FCV). It stops viral plaques from forming in the airway epithelium cells and blocks viral attachment sites [21]. The aqueous ginger extract, garlic, and other herbs protect the food from contamination [22].

### Garlic (*Allium sativum*)

Garlic also has a wide spectrum of pharmacological effects, including cardioprotective, antioxidant, anti-inflammatory, anti-viral, anti-cancerous, and immunomodulatory properties, in addition to its food additive quality. Garlic, belongs to the family Amaryllidaceae, has been used as a medicinal herb in Ayurvedic medicine for antimicrobial and antiparasitic purposes

| Spices | Scientific Name | Family | Part used | Active Ingredient Present (with their structure) | Mode of action [14-16] |
|---|---|---|---|---|---|
| Ginger | Zingiber *officinale* | Zingiberaceae | Rhizome | 6-Gingerol  | • Alleviates cytokine storm (Downregulation of NF-κB, IL-6, and TNF-α)<br>• Reduces T cell activity in Allergic rhinitis |
| Garlic | *Allium sativum* | Amaryllidaceae | Bulb | Allicin (diallyl thiosulfinate)  | • Inhibition of inflammatory factors like NF-κB, ROS, 8-hydroxy-2'deoxyguanosine, 8-iso-prostaglandin F2α<br>• Increases the activation of NrF2<br>• Down regulates the proinflammatory cytokines and inhibit the nitric oxide synthase expression in macrophages.<br>• Possess antiviral effect on broad spectrum of viruses of HSV family, parainfluenza virus and human rhino virus. |
| Star anise | *Illicium verum* | Schisandraceae | Seed pod | shikimic acid  | • Reduces the expression of NF-κB |
| Cardamom | *Elettaria cardamomum* | Zingiberaceae | Seeds | 1,8-cineole  | • Blocks the interaction between NF-κB and target DNA<br>• Down regulate PGE2 and LTB4 in case of Bronchial asthma<br>• Down regulate NF-κB |
| Clove | *Syzygium aromaticum* | Myrtaceae | Flowers and buds | Eugenol  | • Modify the inflammatory signaling molecules such as NF-κB, TNF-α, IL-1, IL-6, COX-2, PGE2 |
| Black pepper | *Piper nigrum* | Piperaceae | Fruit | Piperine  | • Inhibition of NF-κB, extracellular signalregulated kinase1 or 2, I-κb-kinase α/β, cAM Presponse element binding and the expression of caspase-3 and ki-67<br>• Reduces the production of IL-1β, IL-6, TNF-α, COX-2, nitric oxide synthase-2 and NF-κB<br>• Neutralises Free Radicals (ROS) |
| Nutmeg | *Myristica fragrans* | Myristicaceae | Seeds | Eugenol  | • Modify the inflammatory signaling molecules such as NF-κB, TNF-α, IL-1, IL-6, COX-2, PGE2 |

| | | | | | |
|---|---|---|---|---|---|
| Turmeric | *Curcuma longa* | Zingiberaceae | Rhizome | Curcumin  | • Binds to S protein and ACE2 receptor and inhibit virus entry inside cell<br>• Stimulates host interferon production to activate the host innate immunity<br>• Hinders phosphorylation of I-κBα and p65<br>• Acetylation and translocation of NF-κB to the nucleus.<br>• Inhibits NF-κB, cyclin D1, COX-2, TNF-α, STAT signaling pathways<br>• Neutralises free radicals and enhances the production of antioxidant enzymes. |
| Cinnamon | *Cinnamomum verum* | Lauraceae | Bark | Cinnamaldehyde  | • Inhibits the activation of I-κB NF-κB<br>• Suppress the NF-κB, TLR4 and NLRP3 signaling pathways<br>• Down regulates the production of prostaglandins |

**[Table/Fig-3]:** Different Indian spices and their active ingredient with their mode of action.
TNF: Tumour necrosis factor alpha (TNF alpha); NF-κB Nuclear factor-kappaB; COX: Cyclooxygenase; PGE: Prostaglandin E2, IL: Interleukin; ROS: Reactive oxygen species; DNA: Deoxyribonucleic acid

since ancient times. A variety of sulfur compounds are present which are the natural odour of garlic, the main one being allicin (diallyl thiosulfinate) [ 23]. Allicin has been shown to play a role in the formation of T-cells and B-cells [24]; it also stimulates the immune system's CD8+ cells and T lymphocyte cells [25] against a variety of viral infections, including influenza A and B, Human Immunodeficiency Virus (HIV), Herpes Simplex Virus-1 (HSV-1), viral pneumonia, and rhinovirus [26]. Garlic has been shown to have immunomodulatory effects by regulating the levels of cytokines and chemokines in the body [27], suggesting that it may be a promising candidate for countering the cytokine storm triggered by COVID-19. Garlic contains fructooligosaccharides, which are essential for immunomodulation. Its extract is thought to be anti-inflammatory, anti-atherosclerotic, and blood pressure-controlling [28].

## Blackpepper (*Piper nigrum*)

Black pepper is commonly known as Kali Mirch in India. Also, popular as 'spice king' which increases the texture and aroma of food as a spice. In Ayurveda, it can also be prescribed for bronchopulmonary conditions, fever, neurological disorders, and gastrointestinal problems [29]. Antioxidant, anti-viral, anti-inflammatory, anti-mutagenic, anti-parasitic, anti-bacterial, anti-asthmatic, anti-carcinogenic, anti-diarrhoeal, anti-ulcer, anti-thyroid, anti-apoptotic, anti-bacterial, anti-depressant, and immunomodulatory effects are some of its properties. It further enhances the therapeutic efficacy of various drugs, vaccines, and dietary supplements [30-33]. Piperine is a key component of black pepper that regulates the development of cytokines in various types of immune cells, including Th1, Th2, Th17, and Treg cells. It can also minimise inflammatory cell aggregation by preventing the expression of GATA3, IL-4, IL-6, IL-1, ROR, IL-17 A, and TNF in bronchoalveolar lavage fluid and increasing INF- and IL-10 secretion. It also promotes the growth of T and B cells, as well as macrophage cells [31,34,35]. Piperine is also harmful to cells. It reduces histamine release and serum immunoglobulin E, anti-OVA IgE, anti-OVA IgE1, and anti-OVA IgE1. It induces necrosis and inflammatory cell invasion. It also inhibits Th2/Th17 responses and activates mast cells. It inhibits NF-kB, c-Fos, the cAMP response bound element, and factor-2 transcription. It inhibits PKCa/ Extracellular signal-Regulated Kinase (ERK) 1/2 and decreases NF-kB/AP-1 activation, as well as PMA-mediated MMP-9 expression. It's also in control of p-glycoprotein inhibition and the CYP3A44 feature [36-37].

## Cardamom (*Elettaria cardamomum*)

Cardamoms are dried fruit capsules of the Zingiberaceae family. Its capsules are used to manage cataracts, nausea, gum infections, teeth and gastrointestinal, kidney diseases, asthma, diarrhoea, cardiac problems, for culinary and alternative medicine applications [38].

**Antioxidant properties:** Cardamom seeds are the storage of large-quality antioxidants, which scavenge free radicals by preventing the oxidation of other materials. Cardamom, according to Nair S et al., has a moderate degree of natural antioxidant properties due to the existence of phenol compounds such as quercetin, kaempferol, and luteolins [39]. Natural antioxidants are considered to be safer than synthetic antioxidants [40]. The essential oils in cardamom, including phytonutrients and vitamins, serve as antioxidants, scavenging free radicals and preventing cellular aging [40-41].

**Antimicrobial properties:** Cardamom's essential oil has powerful antimicrobial properties against various food microorganisms [42]. The growth of *Morgenella morganii* was significant inhibited by the use of cardamom oil. Antimicrobial effect was also shown by essential oil extracted from cardamon towards *Staphylococcus aureus, Escherichia coli, Streptococcus mutans, Salmonella typhi, Candida albicans, Bacillus pulmilus and Listeria monocytogenes* [43]. Most research focusing on the antibacterial activity of cardamom extracts and their essential oil was performed using the method of disc diffusion [44].

## Turmeric (*Curcuma longa*)

In India, it is popularly called "Haldi". The active ingredient is a polyphenolic compound known as curcumin, which acts as anti-inflammatory, anti-microbial, and has an immunomodulatory impact on our body [45]. It prevents the entry of viruses into the cell, inhibits the encapsulation of viruses and virus proteases, and modulates many cellular signaling pathways [46]. It is also effective in the therapy of osteoarthritis and rheumatoid arthritis. Turmeric has been suggested as a useful treatment of choice against COVID-19 [47]. The following are the primary effects of curcumin on respiratory disorders.

Curcumin's effect on pulmonary inflammation: In the inhibition of inflammatory cytokines, curcumin has its key task. Its presence stops essential signals that regulate the expression of various pro-inflammatory cytokine pathways, such as nuclear factor B and MAPKK. It has anti-inflammatory and anti-fibrotic effects. This

decreases the expression of chemokines and cytokines that are involved in lung infection, such as INFγ, MCP-1, IL-6, IL-10 [48-49]. It shows inhibitory effects against RSV infection by preventing viral replication, releasing TNF alpha, and down-controlling phosphor-NF-alpha-B [45-46].

Curcumin's effect on pulmonary fibrosis: Pathways mediated by the p38MAPK route for curcumin inhibit apoptosis [48].

Curcumin's impact on pulmonary oedema: The disorder where fluid accumulation takes place in the lungs is pulmonary oedema. In recent research related to SARS-CoV-2 infection has shown that its protein envelope stimulates protein kinase C, thus reducing the function of pulmonary epithelial sodium channels contributing to pulmonary oedema [50]. A study by Tian S et al., has shown that the use of curcumin reduces inflammation, leading to a decrease in the influx of fluid in the lungs of the rat [51].

Impact of curcumin on heart problems associated with COVID-19: The binding of the SARS-CoV-2 virus spike protein to the ACE2 respiratory epithelium cell receptor causes respiratory problems. In people with heart issues, these complications are more pronounced. The theory may be that AEC2 in cardio patients is more frequently expressed [52]. Curcumin prevents myocardial ischemia-reperfusion damage by reducing c-Jun N-terminal kinase and NF-B nuclear translocation phosphorylation. It also decreases immune cell penetration and the expression of binding molecules and pro-inflammatory mediators in vascular cells [53].

The impact of curcumin on kidney diseases: In COVID-19, the incidence of acute kidney injury is often manifested in patients with co-morbidities. The high incidence may be due to the high expression of ACE2 in the kidneys in patients with diabetes [54] and may be the reason for renal damage. In rat models, curcumin up-regulates AEC2 and ACE2 mRNA that contributes to increased blood flow in the kidneys [55]. By reducing inflammation caused by MCP-1, NF-κB, TNF, IL-1β, COX-2, and COX-1, at the stage of priming and activation, curcumin also decreases renal fibrosis. This lowers anti-inflammatory variables as well. It targets MAPK/ERK, TGF-β/smads, and PPAR-pathways in animal models [56].

### Clove (*Syzygium aromaticum*)

It is a dried flower bud, commonly used because of its strong taste and aroma to prepare spicy recipes. Also, eugenol, a bioactive compound present in cloves has been documented to have a broad range of medicinal properties such as analgesic, anti-inflammatory, immunomodulatory and better remedy for respiratory disorders as one of their phytoconstituents [57]. Furthermore, clove also has an important antiviral and antipyretic potency.

### Cinnamon (*Cinnamomum verum*)

It is a medicinal plant commonly known as Dalchini. It is used for fever, oedema, cough, and indigestion as a natural immunity booster [58]. Besides, due to its volatile bioactive components, cinnamon, the world's frequently consumed spice, has also been reported to have essential antioxidant, antitumour, and anti-inflammatory potency [59]. Cinnamaldehyde, cuminaldehyde, and eugenol are its major chemical constituents. Its bark consists of various beneficial compounds such as benzaldehyde, cinnamaldehyde, terpenes, and cuminaldehyde [60]. By increasing immunoglobulin and phagocytic index levels, it enhances immunity, i.e., cell-mediated and humoral immunity [58]. It is documented as a cell-mediated immunity regulator because of its NF-kB obstruction property that activates signaling components, PDK1 and NF-kB [35], CD29 and CD43 are also activated by cinnamon, which prevents cell migration and triggers the attachment of one cell to another cell. It decreases nitric oxide production and also regulates CD80 and CD69 levels and specific receptors such as TLR2 and CR3 that assist in pattern recognition. Cinnamon bark extract reduces the amount of IFN-alpha without affecting the level of IL-4 or IL-2. It also inhibits anti-CD3 antibodies induced by IFN-alpha and IL-4 at mRNA and secreted protein levels increase the secretion of IL2 protein at the cellular level, helping to reduce cell death. It inhibits IL-2 mRNA expression, inhibits anti-CD3 activation mediated by p38, JNK, ERK1/2, and STAT4, but does not degrade 1k B or STAT6 [49]. This shows the inhibitory effects of cinnamon on cytokine secretion and its role in the signaling molecules of activated T cells. It also leads to a decrease in the process of subG1 and increases the necrotic to apoptotic cell ratio. Its constituents cinnamaldehyde and cinnamophilinhave thromboxane A2, the receptor antagonist. It is anticoagulative and anti-atherosclerotic, preventing unwanted clumping of platelets [61]. SARS-CoV-2 inhibitors from Cinnamon have recently been identified through in silico studies [62].

### Star Anise (*Illicium verum*)

Star anise best known as Chinese star anise, is an aromatic member of the family Schisandraceae. It is of star shape, often reported to have numerous therapeutic applications because of its bioactive compounds, is commonly used as a culinary ingredient. It is one of the essential components of Chinese herbs and is well known for its antiviral effects. As an effective booster of immunity, it helps the body to fight many viral diseases. It is also the source of shikimic acid, the key molecule used in the manufacturing of oseltamivir (Tamiflu®), an antiviral drug for influenza A and influenza B. It has a wide range of other potentials properties in addition to its antiviral properties, such as antioxidant, antimicrobial, antifungal, etc. It is commonly used as a treatment in cough, asthma, dysentery, and in arthritis [63].

### Nutmeg (*Myristica fragrans*)

Because of its mysterious sweet and spicy taste, *Myristica fragrans* has been one of the key constituents in Indian cuisine since ancient times and has also been reported to have important medical values. Nutmeg is used as a pain reliever because it has myristcine, myrcene, safrol, camphene, sabinene, linalool, 1,8-cineole, and eugenol as its volatile constituent, and it also has properties to treat stomach disease, respiratory disorders, heart disease, as well as a brain tonic, liver tonic and immunity booster [64].

## CONCLUSION(S)

Nutrition plays a key role in maintaining good health. Spices when added to our food items in a suitable amount, provide taste as well as act as a source of antioxidants to our body to protect from attack of harmful microorganisms. They interfere to different inflammatory factors like cytokines, growth factors (TNF-α interleukin), COX, lipoxygenase, and NOX in the NF-κB pathway.

In ancient and modern India, these spices were commonly used to treat many diseases. Many Indian spices having above mentioned active ingredients have tremendous potential as an immune booster, antioxidants, and anti-inflammatory agents in preventing/alleviating SARS-CoV-2 infection.

## REFERENCES

[1] https://www.cdc.gov/coronavirus/2019-ncov/variants/variant.html. Accessed on 30th May 2021.
[2] https://www.cnbc.com/2021/05/10/who-classifies-triple-mutant-covid-variant-from-india-as-global-health-risk-.html. Accessed on 30th May 2021.
[3] Skowronski DM, De Serres G. Safety and efficacy of the BNT162b2 mRNA Covid-19 vaccine. Letter. N Engl J Med. 2021;384(16):1576-77. Doi: 10.1056/NEJMc2036242.
[4] http://www.healthdata.org/covid/covid-19-vaccine-efficacy-summary. Accessed May 30, 2021.

[5] Florindo HF, Kleiner R, Vaskovich-Koubi D, Acúrcio RC, Carreira B, Yeini E, et al. Immune-mediated approaches against COVID-19. Nat Nanotechnol. 2020;15(8):630-45.

[6] Maurya VK, Kumar S, Prasad AK, Bhatt MLB, Saxena SK. Structure-based drugdesigning for potential antiviral activity of selected natural products from Ayurveda against SARS-CoV-2 spike glycoprotein and its cellular receptor r. Virus Disease. 2020;31:179-93.

[7] Lobo V, Patil A, Phatak A, Chandra N. Free radicals, antioxidants and functional foods: Impact on human health. Pharmacogn Rev. 2010;4(8):118.

[8] Is Y, Woodside JV. Antioxidant in health and disease. J Clin Pathol. 2001;54(3):176-86.

[9] Bagchi K, Puri S. Free radicals and antioxidants in health and disease. East Mediterranean Health J.1998;4:350-60.

[10] Liu T, Stern A, Roberts LJ. The isoprostanes: Novel prostanglandin-like products of the free radical catalyzed peroxidation of arachidonic acid. J Biomed Sci 1999;6:226-35.

[11] Halliwell B. The antioxidant paradox. Lancet. 2000; 355, 1179-1180.

[12] Kunnumakkara AB, Rana V, Parama D, Banik K, Girisa S, Henamayee S, et al. COVID-19, cytokines, inflammation, and spices: How are they related? Life Sci. 2021;284:119201.

[13] Mani JS, Johnson JB, Steel JC, Broszczak DA, Neilsen PM, Walsh KB, et al. Natural product-derived phytochemicals as potential agents against coronaviruses: A review. Virus Res. 2020;284:197989. Doi: 10.1016/j.virusres.2020.197989.

[14] Kunnumakkara AB, Sailo BL, Banik K, Harsha C, Prasad S, Gupta SC, et al. Chronic diseases, inflammation, and spices: How are they linked? J Transl Med. 2018;16(1):01-25.

[15] Elengoe A. Indian spices boost the immune system against COVID-19. The Annals of the University Dunarea de Jos of Galati. Fascicle VI-Food Tech. 2020;44(2):189-206.

[16] Mrityunjaya M, Pavithra V, Neelam R, Janhavi P, Halami PM, Ravindra PV. Immune-boosting, antioxidant and anti-inflammatory food supplements targeting pathogenesis of COVID-19. Front Immunol. 2020;11:570122.

[17] Chang JS, Wang KC, Yeh CF, Shieh DE, Chiang LC. Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. J Ethnopharmacol. 2013;145(1):146-51. Doi: 10.1016/j.jep.2012.10.043.

[18] Safa O, Hassaniazad M, Farashahinejad M, Davoodian P, Dadvand H, Hassanipour S, et al. Effects of Ginger on clinical manifestations and paraclinical features of patients with Severe Acute Respiratory Syndrome due to COVID-19: A structured summary of a study protocol for a randomized controlled trial. Trials. 2020;21(1):841. Doi: 10.1186/s13063-020-04765-6.

[19] Rathinavel T, Palanisamy M, Palanisamy S, Subramanian A, Thangaswamy S. Phytochemical 6-Gingerol–A promising Drug of choice for COVID-19. Int J Adv Sci Eng. 2020;6(4):1482-89.

[20] Sharma L. Indian Spices: Hidden Treasure to manage Ailments. EPRA International Journal of Multidisciplinary Research. 2017;3(3):226-30.

[21] Kim SO, Kundu JK, Shin YK, Park JH, Cho MH, Kim YT, et al. [6]-Gingerol inhibits COX-2 expression by blocking the activation of p38 MAP kinase and NF-kappaB in phorbol ester-stimulated mouse skin. Oncogene. 2005;24(15):2558-67. Doi: 10.1038/sj.onc.1208446.

[22] Tripathi MK, Singh P, Sharma S, Singh TP, Ethayathulla AS, Kaur P. Identification of bioactive molecule from *Withaniasomnifera* (Ashwagandha) as SARS-CoV-2 main protease inhibitor. J Biomol Struct Dyn. 2020;01-14. Doi: 10.1080/07391102.2020.1790425.

[23] Gruhlke MC, Nicco C, Batteux F, Slusarenko AJ. The Effects of Allicin, a Reactive Sulfur Species from Garlic, on a Selection of Mammalian Cell Lines. Antioxidants (Basel). 2017;6(1):01-16. Doi: 10.3390/antiox6010001.

[24] Salman H, Bergman M, Bessler H, Punsky I, Djaldetti M. Effect of a garlic derivative (alliin) on peripheral blood cell immune responses. Int J Immunopharmacol. 1999;21(9):589-97. Doi: 10.1016/s0192-0561(99)00038.

[25] Reinhart KM, Talati R, White CM, Coleman CI. The impact of garlic on lipid parameters: A systematic review and meta-analysis. Nutr Res Rev. 2009;22(1):39-48. Doi: 10.1017/s0954422409350003.

[26] Sawai T, Itoh Y, Ozaki H, Isoda N, Okamoto K, Kashima Y, et al. Induction of cytotoxic T-lymphocyte and antibody responses against highly pathogenic avian influenza virus infection in mice by inoculation of apathogenic H5N1 influenza virus particles inactivated with formalin. Immunology. 2008;124(2):155-65.

[27] Donma MM, Donma O. The effects of allium sativum on immunity within the scope of COVID-19 infection. Med Hypotheses. 2020;144:109934. Doi: 10.1016/j.mehy.2020.109934.

[28] Arreola R, Quintero-Fabián S, López-Roa RI, Flores-Gutiérrez EO, Reyes-Grajeda JP, Carrera-Quintanar L, et al. Immunomodulation and anti-inflammatory effects of garlic compounds. J Immunol Res. 2015;3(4):401630. Doi: 10.1155/2015/401630.

[29] Stojanovic-Radic Z, Pejcic M, Dimitrijevic M, Aleksic A, V Anil Kumar N, Salehi B, et al. Piperine-A major principle of black pepper: A review of its bioactivity and studies. Applied Sciences. 2019;9:01-29.

[30] Nahak G, Sahu RK. Phytochemical evaluation and antioxidant activity of Piper cubeba and Piper nigrum. J Appl Pharm Sci. 2011;1:153-57.

[31] Damanhouri ZA. A review on therapeutic potential of Piper nigrum L. (Black Pepper): The king of spices. J Med Aromat Plants. 2014. https://doi.org/10.4172/2167-0412.1000161.

[32] Srivastava AK, Singh VK. Biological action of Piper nigrum e the king of spices. Eur J Cell Biol. 2017. https://doi.org/10.5281/zenodo.839039.

[33] Peterson CT, Rodionov DA, Iablokov SN, Pung MA, Chopra D, Mills PJ, et al. Prebiotic potential of culinary spices used to support digestion and bioabsorption. Evidence-Based Complementary and Alternative Medicine. 2019;8973704.

[34] Balkrishna A, Solleti SK, Singh H, Tomer M, Sharma N, Varshney A. Calcioherbal formulation, Divya-Swasari-Ras, alleviates chronic inflammation and suppresses airway remodelling in mouse model of allergic asthma by modulating pro-inflammatory cytokine response. Biomed. Pharmacother. 2020. https://doi.org/10.1016/j.biopha.2020.110063.

[35] Gautam S, Gautam A, Chhetri S, Bhattarai U. Immunity against COVID-19: Potential role of Ayush Kwath. J Ayurveda Integr Med. 2020. https://doi.org/10.1016/j.jaim.2020.08.003.

[36] Zhai WJ, Zhang ZB, Xu NN, Guo YF, Qiu C, Li CY, et al. Piperine plays an anti-inflammatory role in Staphylococcus aureus endometritis by inhibiting activation of NF-kB and MAPK pathways in mice. Evid Compl Altern Med. 2016;8597208. https://doi.org/10.1155/2016/8597208.

[37] Bui TT, Piao CH, Hyeon E, Fan Y, Van Nguyen T, Jung SY, et al. The protective role of Piper nigrum fruit extract in an ovalbumin-induced allergic rhinitis by targeting of NFkBp65 and STAT3 signalings. Biomed. Pharmacother. 2019;109:1915-23. https://doi.org/10.1016/J.BIOPHA.2018.11.073.

[38] Khan AU, Khan QJ, Gilani AH. Pharmacological basis for the medicinal use of cardamom in asthma. Bangl J Pharmacol. 2011;6(1):34-37.

[39] Nair S, Nagar R, Gupta R. Antioxidant phenolics and flavonoids in common Indian foods. J Assoc Physicians India. 1998;46(8):708-10.

[40] Saeed A, Sultana B, Anwar F, Mushtaq M, Alkharfy KM, Gilani AH. Antioxidant and antimutagenic potential of seeds and pods of green cardamom (Elettaria cardamomum). Int J Pharm. 2014;10(8):461-69.

[41] Ashokkumar K, Murugan M, Dhanya MK, Warkentin TD. Botany, traditional uses, phytochemistry and biological activities of cardamom *[Elettaria cardamomum* (L.) Maton]–A critical review. J Ethnopharmacol. 2020;10:01-40.

[42] Kubo I, Himejima M, Murari H. Antimicrobial activity of flavour components of Cardamom. J Agric Food Chem. 1991;39:1984-86.

[43] Bano S, Ahmad N, Sharma AK. Phytochemical screening and evaluation of anti-microbial and anti-oxidant activity of Elettaria cardamom (Cardamom). J Applied Natural Sci. 2016;8(4):1966-70.

[44] Gradinaru AC, Aprotosoaie AC, Trifan A, Spac A, Brebu M, Miron A. Interactions between cardamom essential oil and conventional antibiotics against Staphylococcus aureus clinical isolates. Farmacia. 2014;62(6):1214-22.

[45] Zahedipour F, Hosseini SA, Sathyapalan T, Majeed M, Jamialahmadi T, Al-Rasadi K, et al. Potential effects of curcumin in the treatment of COVID-19 infection. Phytother Res. 2020;01-10. https://doi.org/10.1002/ptr.6738.

[46] Gupta H, Gupta M, Bhargava S. Potential use of Turmeric in COVID-19. Clin Exp Dermatol. 2020;45(7):902-03. Doi: 10.1111/ced.14357.

[47] Emirik M. Potential therapeutic effect of turmeric contents against SARS-CoV-2 compared with experimental COVID-19 therapies: In silico study. J Biomol. 2020;01-14. Doi: 10.1080/07391102.2020.1835719.

[48] Avasarala S, Zhang F, Liu G, Wang R, London SD, London L. Curcumin Modulates the Inflammatory Response and Inhibits Subsequent Fibrosis in a Mouse Model of Viral-induced Acute Respiratory Distress Syndrome. PLoSONE. 2013. https://doi.org/10.1371/journal.pone.0057285.

[49] Negi S, Bala L. Natural home remedies may act as Immunomodulators to protect against SARS-CoV-2 infection. J Exp Biol. 2020;8(Spl-1-SARS-CoV-2).S176-S189. http://dx.doi.org/10.18006/2020.8.

[50] DeDiego ML, Nieto-Torres JL, Jimenez-Guardeño JM, Regla-Nava JA, Castaño-Rodriguez C, Fernandez-Delgado R, et al. Coronavirus virulence genes with main focus on SARS-CoV envelope gene. Virus Research. 2014. https://doi.org/10.1016/j.virusres.2014.07.024.

[51] Tian S, Hu W, Niu L, Liu H, Xu H, Xiao SY. Pulmonary pathology of early-phase 2019 novel coronavirus (COVID-19) pneumonia in two patients with lung cancer. J Thorac Oncol. 2020;15:700-04. https://doi.org/10.1016/j.jtho.2020.02.010.

[52] Zheng Y. COVID-19 and the cardiovascular system. Nature Reviews Cardiology. 2020;17:259-60. https://doi.org/10.1038/s41569-020-0360-5.

[53] Li X, Fang Q, Tian X, Wang X, Ao Q, Hou W, Bai S. Curcumin attenuates the development of thoracic aortic aneurysm by inhibiting VEGF expression and inflammation. Mol Med Rep. 2017;16(4):4455-62. https://doi.org/10.3892/mmr.2017.7169.

[54] Ye M, Wysocki J, William J, Soler MJ, Cokic I, Batlle D. Glomerular localization and expression of angiotensin-converting enzyme 2 and angiotensin-converting enzyme: Implications for albuminuria in diabetes. J Am Soc Nephrol. 2006. https://doi.org/10.1681/ASN.2006050423.

[55] Xu X, Cai Y, Yu Y. Effects of a novel curcumin derivative on the functions of kidney in streptozotocin-induced type 2 diabetic rats. Inflammo pharmacology. 2018. https://doi.org/10.1007/s10787-018-0449-1.

[56] Sun X, Liu Y, Li C, Wang X, Zhu R, Liu C, Li Y. Recent advances of curcumin in the prevention and treatment of renal fibrosis. BioMed Research International. 2017; 2418671. https://doi.org/10.1155/2017/2418671.

[57] Dibazar SP, Fateh S, Daneshmandi S. Clove *(Syzygiumaromaticum)* ingredients affect lymphocyte subtypes expansion and cytokine profile responses: An in vitro evaluation. J Food Drug Anal. 2014;22:448-454.

[58] Niphade SR, Asad M, Chandrakala GK, Toppo E, Deshmukh P. Immunomodulatory activity of Cinnamomum zeylanicum Bark. Pharm Biol. 2009;47:1168-73.

[59] Goel B, Mishra S. Medicinal and Nutritional Perspective of Cinnamon: A mini-review. European Journal of Medicinal Plants. 2020;31:10-16.

[60] Valizadeh S, Katiraee F, Mahmoudi R, Fakheri T, Mardani K. Biological properties of Cinnamomum zeylanicum essential oil: Phytochemical component, antioxidant and antimicrobial activities. International Journal of Food Safety, Nutrition and Public Health. 2015;6:174-84.

[61] Tsui PF, Lin CS, Ho LJ, Lai JH. Spices and atherosclerosis. Nutrients. 2018. https://doi.org/10.3390/nu10111724.
[62] Prasanth DSNBK, Murahari M, Chandramohan V, Panda SP, Atmakuri LR, Guntupalli C. In silico identification of potential inhibitors from Cinnamon against main protease and spike glycoprotein of SARS CoV-2. J Biomol Struct Dyn. 2020;01-15. Doi: 10.1080/07391102.2020.1779129.
[63] Patra JK, Das G, Bose S, Banerjee S, Vishnuprasad CN, del Pilar Rodriguez-Torres M, Shin HS. Star anise *(Illicium verum)*: Chemical compounds, antiviral properties, and clinical relevance. Phytother Res. 2020;34:1248-67.
[64] Upadhyay RK. Thermal-Aroma-Organic-Carbon-Fusion therapy: An open air conventional method for clearance of nasal air passage, trachea, lungs and immunity boosting against Influenza Virus. Intern J Zool Invest. 2020;6:71-93.

**PARTICULARS OF CONTRIBUTORS:**
1. Research Scholar, Department of Biochemistry, Babu Banarasi Das University, Lucknow, Uttar Pradesh, India.
2. Research Scholar, Department of Nutrition, Babu Banarasi Das University, Lucknow, Uttar Pradesh, India.
3. Professor, Department of Biochemistry, Babu Banarasi Das University, Lucknow, Uttar Pradesh, India.

**NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:**
Dr. Lakshmi Bala,
Professor, Department of Biochemistry, Babu Banarsi Das University,
Lucknow-201206, Uttar Pradesh, India.
E-mail: lakshmi266@gmail.com

**PLAGIARISM CHECKING METHODS:** [Jain H et al.]
- Plagiarism X-checker: Mar 30, 2021
- Manual Googling: Jun 23, 2021
- iThenticate Software: Jul 31, 2021 (16%)

**ETYMOLOGY:** Author Origin

**AUTHOR DECLARATION:**
- Financial or Other Competing Interests: None
- Was Ethics Committee Approval obtained for this study? NA
- Was informed consent obtained from the subjects involved in the study? NA
- For any images presented appropriate consent has been obtained from the subjects. NA

Date of Submission: **Mar 20, 2021**
Date of Peer Review: **May 18, 2021**
Date of Acceptance: **Jun 24, 2021**
Date of Publishing: **Aug 01, 2021**