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Protective Effect of Commonly Used Foods and Natural Products against COVID-19

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ABSTRACT

COVID-19 caused by the SARS-COV-2 virus has swiftly turned into a pandemic, leading to an ongoing health crisis worldwide. This disease has a zoonotic origin, and its symptoms range from asymptomatic, mild to severe, potentially leading to death. Given its pandemic nature, researchers around the world have expedited efforts to find the treatment. While synthetic drugs have been developed for treatment, their efficacy is still under evaluation, and their side effect is the primary concern. This situation necessitates the need to explore treatment options that are not only effective but also safe. Natural products could help COVID-19 prevention and treatment given their historical role in the treatment of other viruses such as HIV, MERS-CoV, and influenza. This study aims to evaluate the potential role of natural products against COVID-19, their mechanisms of action, and previous use against other viruses. This study aims to evaluate the potential role of natural products against COVID-19, their mechanisms of action, and previous use against other viruses. The comprehensive review focuses on natural products such as ginger, garlic, clove, black pepper, red pepper, black seeds, honey, turmeric, onion, ginseng, and thyme. The findings aim to contribute valuable insights to the development of anti-COVID-19 natural products.

Keywords COVID-19, corona virus, daily used foods, herbs, medicinal plants, natural products, prevention, viral diseases

Highlights

- Natural Remedies for COVID-19 Defense: Explore how everyday foods like garlic and turmeric could help protect against COVID-19, offering hope during the pandemic.
- Safe and Effective Alternatives: Look into the safety and effectiveness of natural products against COVID-19, suggesting they may be safer than synthetic drugs.
- Guidance for Future Treatment: Provide insights into how natural products have worked against other viruses, guiding the development of COVID-19 treatment.

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1. INTRODUCTION

Coronavirus disease, discovered in 2019 (COVID-19) has become a global public health problem that has affected 213 countries with over 6 million confirmed cases and 0.37 million deaths. Common symptoms found in these patients are; fever, shortness of breath, cough, acute respiratory infection in multiple organ failure in critical patients [1]. The most vulnerable are those who have impaired immune systems.

The severe acute respiratory syndrome coronavirus (SARS-CoV-2) is a novel coronavirus that belongs to the family Coronaviridiae of coronaviruses, responsible for causing the COVID-19[2]. According to studies, there is some similarity between SARS-CoV-2 and SARS-CoV, the virus that was found to cause the Middle Eastern respiratory syndrome (MERS) in 2012 and the severe acute respiratory syndrome (SARS) in 2002. Yet, SARS-CoV-2 is reported to have a significant genetic difference from other viruses due to its large RNA genome and positive-sense single-stranded RNA [3].

Treatment for this virus is hampered by viral resistance, adverse effects, viral re-emergence, and latency on most of the antiviral drugs that are currently on the market. Because of this predicament, numerous institutions, academics, professionals, and scientists are still striving for a COVID-19 resolution every day. It may be possible to tackle this fatal illness by understanding the mechanisms of action of complex plants and isolated chemicals obtained from plants. In this review study, the impact of natural products on COVID-19 is examined. These products include ginger, garlic, clove, black pepper, red pepper, black seeds, honey, turmeric, onion, ginseng, and thyme.

These natural products are used regularly, and all have certain biological activities. It is scientifically proven that all these natural products have a therapeutic effect against pulmonary fibrosis, pneumonia, acute respiratory distress syndrome, diffuse alveolar damage, lung and kidney injury. These symptoms are related to COVID-19. This review aims to evaluate the effect of these natural products against COVID-19 and other viruses and their mechanism of action.

1.1. Ginger

Ginger, a member of the *Zingiberaceae* family is closely related to turmeric, cardamom, and galangal. This herb originated in China and is used extensively in traditional Chinese medicine. It combats common flu, aids in digestion, and alleviates nausea. The distinctive aroma and flavor of ginger is due to the presence of an essential bioactive compound in it i.e. gingerol. This compound holds potent anti-inflammatory and anti-oxidative properties [4]. Studies suggest that Gingerol can help assuage the risk of infections. Using fresh ginger against the respiratory syncytial virus (RSV), which is a common cause of respiratory diseases, may also be efficient. A study was conducted on HRSV using hot water extracts of dried and fresh ginger. It involved testing the aforesaid in human upper and lower respiratory tract cell lining by plaque reduction assay. The analysis engaged whether or not ginger can incite anti-viral cytokines. The study revealed that comparatively, 300 µg/ml of fresh ginger can inhibit HRSV-induced plaque formation up to 19.7% in A549 and 27.0% in the HEp-2 cell line of the respiratory tract. Moreover, it was 12.9% effective

when given before viral inoculation. Therefore, research has proved the potential of ginger in inhibiting viral attachment and entry [5].

The SARS-CoV-2-related papain-like protease (PLpro) breaks down polyprotein a/b at several locations, releasing several proteins essential for viral survival and reproduction [6]. Molecular docking techniques revealed that the ginger's active components, 8-gingerol, 6-gingerol, 10-gingerol, and another class, effectively inhibit PLpro. Notably, 6-gingerol exhibited high affinity for a number of virus proteins necessary for the replication of SARS-CoV-2. Moreover, 6-gingerol interacts with the S protein and many RNA-binding proteins of SARS-CoV-2[7]. The results of docking analyses also showed that the compounds like gingerol, shogaol, geraniol, zingiberene, zingerone, and zingiberenol interact with important residues in the catalytic domain of the MPro, which allows them to prevent the spread of SARS-CoV-2 [8].

Findings from a Tunisian study showed that treating a few cases of COVID-19 using homemade remedies that contained ginger in combination with other herbs improved clinical manifestations [9]. In several regions of Africa, well-known treatments for COVID-19 that included ginger in blends of different plants have shown promising results. According to the findings of an Iranian clinical trial study, outpatients with suspected COVID-19 who received a combination medication of ginger and echinacea experienced fewer clinical symptoms compared to those receiving standard treatment [10].

1.2. Garlic

Garlic, an edible bulb from the lily plant family, serves d as a dietary supplement for high blood cholesterol levels, common cold, and for the prevention of various other diseases such as cancer. It is used in various forms; fresh, powdered, or in oil. Its supplements are also available in capsules and tablets.

This healthy ingredient is attributed to its antimicrobial, immunity-boosting, anti-oxidant, anti-inflammatory, and anti-stress properties. [11]. While it offers various health advantages, it's important to note its potential side effects, such as abdominal discomfort, diarrhea, and respiratory tract infections.

The glucosinolates present in garlic are responsible for its anti-biotic properties that help defend against bacterial, viral, and fungal infections in the body. Evidence suggests that this compound is potent against certain viruses such as herpes simplex types 1 and 2, human rhinovirus type 2, parainfluenza virus type 3, vaccinia virus, and vesicular stomatitis virus [12].

The main sources of sulphur in garlic are thiosulfinates (allicin), ajoenes (E- and Z-ajoene), S-allyl cysteine sulfoxide (alliin), 3-vinyl-(4H)-1,2-dithiin), vinyldithiins (2-vinyl-(4H)-1,3-dithiin, and diallyl (di and tri) sulphide. Garlic also contains several organosulfur compounds (OSCs) generated from alliin, including S-allyl-mercapto cysteine, S-allyl-cysteine,and N-acetylcysteine [13].

A serine-type Mproprotease with the kind of amino acids (such as Thr26, Thr24, and Asn119) found in the active site areas has been identified as the primary protease of the SARS-CoV-2 virus. Between types 1 and 2 of SARS-CoV, Mpro has a high degree of structural similarity. The infection rate may be significantly decreased by preventing the cleavage of the viral polyprotein since this protease is essential for viral replication and the

synthesis of functional protein as a result of SARS-proteolytic CoV-2's maturation [14].

In an in-silico study on the inhibitory impact of garlic against SARS-CoV-2, seven OSCs of alliin, S-(propyl /methyl/ allyl/ ethyl)-cysteine, S-ally-mercapto-cysteine, and S-propyl L-cysteine were taken into consideration as potential inhibitors of the Mpro of SARS-CoV-2 through H-bonds with this protease. Molecular docking studies revealed that, among other OSCs, alliin has a greater anti-viral capacity to prevent COVID-19. This bioactive substance, either by itself or in combination with the primary therapeutic medicine, would be an effective treatment to eradicate SARS-CoV-2 with the least amount of toxicity and adverse effects [15]. An effective in vivo inhibitory impact of 0.1 mL of garlic extract was found against SARS-CoV-1 growth, most likely as a result of the formation blocking of structural proteins and genetic materials [16].

1.3. Clove

Cloves are flower buds that are mostly used in preparing food, drugs, perfumes, and various cosmetics [17]. They are widely used due to their antioxidant, antimicrobial, and insecticidal properties.

There is insufficient research investigating the anti-viral properties of clove exclusively, but some studies highlight the synergistic effect of clove with other natural products for coronavirus treatment. One such study was carried out on 10 black patients (2 women, 8 men) who tested positive for COVID-19. The study involved treatment with medicinal plants through decoction preparation with three different protocols while taking two infusions in a day, morning and evening, having an interval of 8 hours. Cloves, ginger, mint leaves, lemongrass leaves, and eucalyptus were used in this study.

Additionally, it was recommended to take the herbal tea prepared with some of the aforesaid ingredients with lemon juice and honey. Surprisingly, their headaches alleviated after taking the infusion on the first day and their sense of smell and taste was restored by the fourth day. Several patients recovered within five days and others on the next day with their COVID-19 tests being negative [18].

Another study was conducted using herbs (Tulsi, Haldi, Giloy, Black pepper, Ginger, Clove, Cardamom, lemon, and Ashwagandha) to prepare an ayurvedic medicine called *Kadha*. The in-depth analysis of "*Kadha*" through molecular docking was used to test the effectiveness of phytochemicals against COVID-19. It was revealed that various phytochemicals present in "*Kadha*" bind strongly with CoVs proteins. So, they might regulate viral infection and proliferation. Moreover, results concluded that these phytochemicals possess anti-inflammatory properties that can enhance a person's immunity and have the ability to inhibit the virucidal infection caused by SARS-CoV-2 at different stages [19].

To understand Lipopolysaccharide induced lung inflammation, a study was conducted using mice. Aqueous extracts of clove at 0.5 µg/mL inhibited luminol-amplified chemiluminescence of resting neutrophils and myristate acetate-stimulated neutrophils. But it also significantly decreases MPO activity thus decreasing inflammation and inhibiting Reactive Oxygen Species production metalloproteinases activity. Another notable finding was that the neutrophil count fell from 61 to just 15 percent and

reduced protein leakage into bronchoalveolar lavage fluid.

Using infusions, decoctions, or herbal medicines containing clove with other herbs or spices can be beneficial against SARS-CoV-2 due to its exceptional properties, but no such study exists that shows the sole effect of clove against coronavirus.

1.4. Black Pepper

Black pepper (Piper Nigrum L) is a commonly used spice and has also been used as a traditional medicine in many cultures worldwide. The chief bioactive substance found in black pepper piperine, attributes to its functional properties. Scientefic evidence suggests that this spice offers health benefits, especially in areas of digestion. Studies also suggest that piperine has a role in providing help to the nervous system. It possesses anti-oxidants, anti-inflammatory and anti-microbial characteristics [20]. Research have shown that Black Pepper, and other medicinal plants such as dried Ginger, and Eucalyptus oil are proven to be useful for asthma, bronchitis, COPD, common cold, and sinusitis through human trials, making it a potential complementary therapy to the already prescribed treatments/regimen for COVID-19[21].

In a study, the binding modes of black pepper's chemical elements against COVID-19 were analyzed through an in-silico approach. Results showed that Piperdardiine and Piperanine appeared to be significantly active against COVID-19. Thus, black pepper should be regularly used to for the prevention of coronavirus [11].

Other than peperine, black pepper contains various other chemical constituents too, such as Sarmentosine, Sarmentine, Brachyamide B, Dihydropipericide, Piperine, Piperamide, Piperamine, Pipericide, N-Formylpiperidine, Guineensine, Pentadienoylpiperidine, Retrofractamide A, Chavicine, Isochavicine, Isopiperine, Nerolidol, β-caryophyllene, Tricholein, Trichostachine, Piperettine, Piperolein B, and Piperic acid [22].

In another study, an ayurvedic preparation using several medicinal plants was made. Through this study, chemical constituents of black pepper and other medicinal plants were identified against COVID-19 Coronavirus, in order to enter into the human body, makes its spike protein interact with ACE-2 receptors. Notably, 12 phytochemicals, including Pipericide, Retrofractamide A, Piperolein B, and Chavicine from black pepper, exhibited binding capacity with this spike protein. Furin, a protease assists the interaction of viral spike protein with ACE2. Of the 12 phytochemicals that showed binding with Furin, Chavicine from black pepper was also involved. Similarly, many of the phytochemicals explored showed notable affinity with SARS-CoV-2 ADP ribose phosphatase, also including Piperettine and Chavicine. Phytochemicals that were expected to interact with their main protease also had Piperettine and Trichostachine. Likewise, those chemical constituents interacting with the spike proteins on the SARS-CoV-1 also included Pentadienoylpiperidine, Piperettine, Piperine, RetrofractamideA, and Trichostachine. Piperine, known for its binding affinity with various inflammatory molecules, demonstrated anti-inflammatory characteristics, suggesting black pepper's efficacy in preventing COVID-19.

To further authenticate its role as an anti-inflammatory, studies were conducted

on a cellular level. A study revealed the effect of one of the bio-active compounds, i.e. piperine from black pepper in inhibiting the adhesion of neutrophils on the endothelial monolayer. This is accomplished by preventing the expression of cell adhesion molecules such as VCAM-1 (vascular cell adhesion molecule-1), ICAM-1 (intercellular adhesion molecule-1), and E-selectin which is induced by tumor necrosis factor (TNF). It was discovered that piperine inhibits IκBα phosphorylation and degradation by lowering TNF-α stimulated IκB kinase activity when endothelial cells were treated with piperine. As a result, NF-KB translocation and activation were prevented, which restricted its ability to control the transcription of cell adhesion molecules [23]. By modulating the immune system, black pepper can be used effectively in the treatment of SARS-CoV-2.

1.5. Red Pepper

Capsicum is a genus of peppers that encompasses over 200 varieties including 5 main species [24, 25]. These peppers are commonly utilized either as food ingredients or as additives in various industries. These peppers are utilized both in culinary applications and as additives in various industries. Indians and Native Americans have been using peppers as a part of traditional medicine. It is also widely used in Chinese traditional medicine for common ailments. *Capsicum* species have been used to manage arthritis and stomachaches. The aforesaid therapeutic implications are due to the capsaicinoid, phenolic compound, and carotenoid constituents of peppers [24, 26].

Peppers can be yellow orange or even red. The pigment behind their distinct colors is carotenoids [27]. They protect various cells and tissues in our body from damaging radical oxygen species (ROS) because carotenoids have remarkable quenching abilities for singlet oxygen [28]. Carotenoids react with peroxyl radicals following a radical addition reaction thus protecting our bodies. Ina 2009 study involving astaxanthin, authors demonstrated that it can be used to reduce oxidative stress in diabetic nephropathy by decreasing the production of total RS [29].

The active substance responsible for the irksome and pungent effects of different species of peppers is Capsaicin [30]. It has anti-inflammatory, antimicrobial, and antifungal properties. The anti-inflammatory properties of *red peppers* are attributed to the capsaicin present in them. Capsaicin inhibits the production of pro-inflammatory cytokines [31].Red peppers might help manage risk factors for cardiovascular disease, other metabolic syndromes, and COVID-19 infection mortality[32, 33].

In addition to the compounds mentioned earlier, peppers contain other active components. A recent study was conducted using the molecular docking approach. The study analyzed some active compounds from selective medicinal plants. Among other compounds, quercetin and luteolin-7-glucoside from capsicum annum were also explored as an inhibitor of COVID-19 main protease. The study revealed that luteolin-7-glucoside, along with a few other active compounds seemed to comprise the best potential to act as one of the COVID-19 Mpro inhibitors [34].

1.6. Black Seeds/ Nigella Sativa l.

Black seeds are also titled Nigella Sativa L. It has dynamic benefits and aids in treating all afflictions as it is anti-fungal, anti-oxidant, anti-bacterial, anti-viral, anti-asthmatic, immunomodulatory, and so on.

N. sativa extract includes various significant components such as thymoquinone (27.8%-57.0%), ρ-simen (7.1%-15.5%), karvakrol (5.8%-11.6%), t-anetol (0.25%-2.3%), 4-terpineol (2.0%-6.6%), and longifoline (1.0%-8.0%) found to exhibit antiviral, anticancer, and antimicrobial properties [35]. A new study supports the positive effects of N. sativa extracts to reduce SARS-CoV-2 viral load by enhancing IL-8 induction [36].

According to a clinical study, 62% of patients with mild COVID-19 recovered more quickly on day 14 of treatment when Nigella sativa oil (NSO) supplementation was used. Compared to the control group, the typical recuperation period was also shorter. According to this study, the anti-inflammatory characteristics of Nigella sativa may be behind the reduction in COVID-19 symptoms (anosmia, chills, runny nose, and loss of appetite). Leukocytes and pro-inflammatory cytokines are released as a result of SARS-CoV-2 infection, resulting in the cytokine storm. This study claimed that by limiting the release of pro-inflammatory cytokines, NS exhibits immunostimulant and anti-inflammatory actions [37].

1.7. Honey

Honey is laden with nutritional components that makes it eminent for its health benefits. It is utilized quite a lot in traditional medicine. With antioxidant properties, honey is widely used in the treatment of various ailments like cancer, respiratory conditions, and even in neurological conditions [38]. One of the active components in honey that contributes to its antimicrobial properties is hydrogen peroxide. Its active component, hydrogen peroxide, contributes to its antimicrobial activity.

Honey administration as a dietary supplement is found to be effective in treating novel COVID-19. This deadly virus deteriorates the lungs and causes respiratory distress. Recent research suggests that honey could serve as a potential alternative to antiviral medications for treating certain viral infections, including the novel COVID-19. The investigators aim to study the efficacy of natural honey in treating COVID-19 [39, 40] patients in this randomized, multicenter, controlled trial, comparing honey in one arm to standard care in the other arm.

As an immunological stimulant, honey increases the growth of T and B lymphocytes, promotes phagocytosis, and controls the production of crucial pro-inflammatory cytokines from monocytes, such as tumor necrosis factor (TNF), interleukin 1 beta (IL-1), and IL-6. Additionally, honey also exhibits anti-inflammatory properties that stop the development of these pro-inflammatory cytokines. The antioxidant qualities of honey are thought to be responsible for its dual immunomodulatory functions [41].

Patients who died from COVID-19 had lower lymphocyte counts than survivors, which is correlated with the severity of the infection and the presence of lymphocytopenia [42]. These findings indicate that lymphocyte-mediated antiviral activity is ineffective against COVID-19. Despite lymphocytopenia, individuals with COVID-19 infection have shown indications of an accelerated release of pro-inflammatory cytokines (IL-1 and IL-6) during acute respiratory syndrome, which hastens the clinical course of the illness [43]. As a result, honey is expected to be essential in enhancing the immune system both as a supportive treatment for COVID-

19 patients and as a preventive step for healthy persons.

A study that looked at how honey's natural phenolic chemical compounds can affect SARS-COV-2 infection showed that the caffeic acid, caffeic acid phenethyl ester (CAPE), galangin, and chrysin that are all found in honey have a good chance of hindering the viral 3-chymotrypsin-like cysteine protease (3CLpro) enzyme, thus preventing the virus from replicating [44].

1.8. Curcumin

Turmeric, also known as "*Haldi*", is a plant native to Asia and Central America. Owing to its vibrant yellow color it is sometimes referred to as the "Indian saffron". The main constituent of turmeric responsible for its biological benefits is Curcumin [45].

Curcumin is an appropriate choice for the treatment of coronavirus infection because of its capacity to alter a variety of molecular targets. The potential of curcumin to regulate multiple molecular targets that support the adherence and internalization of SARS-CoV-2 in numerous organs, including the liver, cardiovascular system, and kidney, may have protective benefits against COVID-19 infection [46, 47]. Apoptosis, inflammation, and RNA replication are just a few examples of the cellular signaling pathways that curcumin may modify. The pathways linked to pulmonary edema and fibrosis in COVID-19 infection may likewise be suppressed by curcumin. To overcome the issue of limited bioavailability by oral administration, it is recommended that it be administered intravenously [48].

1.9. Cinnamon

Cinnamaldehyde, an aldehyde found in Cinnamomum bark, was used as a flavoring and in medicinal Cinnamaldehyde is the leading organic constituent of cinnamon oil found in Cinnamomum sp. Bark [49]. It is used as a flavoring and in therapeutic treatments according to its diverse pharmacological properties. In line with this, medicinal plants' development and exploitation that possess antiviral properties is an alternative way to control pathogenic viruses.

In a study, cinnamaldehyde at high concentrations demonstrated its ability to be anti-inflammatory in immune cells by blocking the activation of NF-kB in the immune cells. Moreover, cinnamaldehyde also demonstrated that it could lead to apoptosis in human peripheral blood mononuclear cells [50].

Because of its multiple targeting abilities, cinnamon, and its constituents can be advised in cases of SARS-CoV-2 infection. The use of chemical medications and their negative effects can be reduced by treating this viral hyper-inflammatory condition using cinnamon as an adjunctive medication. Cinnamon may be useful against SARS-Cov-2 theoretically due to its opener, diuretic, tonic, and antidote properties. Cinnamon's involvement in the treatment of this condition is supported by a number of pharmaceutical studies on its anti-viral, anti-inflammatory, antioxidant, organ-protective, and anti-depressant properties [51].

1.10. Onion

Allium vegetables, such as onion and garlic, have traditionally been used as medicinal and functional foods that possess countless health benefits. More than 25 active compounds are present in onion,

contributing to the prevention and cure of some infectious respiratory illnesses. Thus, onions have the potential to be used for enhancing and improving health. The extract of onion also has potential to be employed in therapy for asthma patients as it significantly reduces oxidant levels and increases antioxidants [52].

Researchers assert that onions, due to their anti-viral, antithrombotic, and anti-inflammatory properties, are a promising option for managing COVID-19 patients [53]. It is primarily utilized for its immunomodulatory, antioxidant, antibacterial, anti-inflammatory, antihypertensive, anticarcinogenic, antithrombotic, antimutagenic, and antidiabetic effects. Several research on onions has revealed that they may have potential antiviral action, mostly against respiratory illnesses. The effectiveness of onion in treating respiratory viral infections can be improved by nebulizing or inhaling it. Flavanoids possess chelating properties, therefore they might be used to target the numerous patterns in viral cell structure. Another benefit of onions is that, due to their anti-diabetic properties, even those with type diabetes can have them without any reluctance. Furthermore, proline, which is thought to stimulate proinflammatory cytokines and has antiviral effects against specific virus types, is considered to be present in onions [54].

Inulin is the long chain fructan present in onions. Inulin is a polysaccharide that is classified as a prebiotic. An experiment conducted on mice to examine the effect of inulin type fructan obtained from the green leafy part of welsh onion demonstrated anti-viral properties. It significantly decreased viral titers in the lungs and the bronchoalveolar fluid of mice with the virus compared to the control group mice. Fructans stimulated NO and the authors described their anti-viral properties as “host mediated” [55].

Quercetin, the major polyphenolic flavonoid found in onions and some other fruits and vegetables. Quercetin can be accumulated in various organs of the human body. Evidence confirms the significance of this bioflavonoid compound as an antiviral agent. It is beneficial against various health issues. It is most notably known for its anti-viral, anti-inflammatory, and anti-oxidant nature.

1.11. Ginseng

The coronaviruses are a group of enveloped RNA viruses that can cause respiratory illnesses of varying degrees in humans and other mammals. These viruses can be lethal like MERS-CoV and SARS-CoV or relatively harmless like the common cold. The novel coronavirus, COVID-19 has a relatively less fatality rate (3.4%) than MERS (34.3%) or SARS (9.6%).

There are two main types of ginseng: the Asian or better known as Korean ginseng (Panax ginseng) and the American ginseng (Panaxquinquefolius). Evidence shows that Korean Ginseng delivers more significant health benefits than the American variety.

In an experiment conducted on mice, they were intranasally infected with a lethal dose of common cold virus, either mixed with fermented extract of Ginseng or non-fermented ginseng extract. The study verified that fermented Ginseng extract is a more effective antiviral agent that completely inhibits viral replication due to the generation of new ginsenosidesaponin compounds [56].

Due to pyroptotic cell death and cytokine storms brought on by the enormous release of pro-inflammatory

cytokines, SARS-CoV-2 triggers a number of inflammasomes, causing severe COVID-19 in many patients with numerous organ damage. In COVID-19 patients, limiting inflammasome initiation and enhancing host immunity can be therapeutically beneficial. Ginseng and its components, ginsenosides, and saponins, can be promising herbal therapies to alleviate COVID-19 by blocking inflammasome activity. It is noteworthy that ginseng can reduce COVID-19 through specific techniques by preventing inflammasome action and boosting the host's antiviral defenses [57].

1.12. Thyme

Thyme is a medicinal plant or herb belonging to the family *Lamiaceae*. There are over 300 varieties of thyme with numerous therapeutic properties. *T. vulgaris* (common thyme), *Thymus zygis* (red thyme), and *Thymus hyemalis* (winter thyme) have been studied for their medicinal benefits. Thyme has been traditionally used in many herbal teas because of its potent antibacterial and healing properties.

In another study, the antiviral properties of extracts of thyme were studied against enveloped viruses and results showed that thyme extract prevents attachment of the virus to the host. Aqueous and ethanolic extract of *Thymus vulgaris* were shown to inhibit all enveloped RNA viruses, including SARS coronavirus [58].

Thyme can also be used as a natural symptomatic treatment of viral respiratory diseases due to its ability to reduce cough and relieve a sore throat. Thyme essential oil also has expectorant and antibacterial actions that help treat bronchitis. In a study conducted on T. zygis and T. hyemalis, these varieties' essential oils showed good antioxidant capacities. Thymol and linalool are their main constituents. T. zygisthymolchemotype contains higher amounts of thymol and thus is a very good anti-oxidant and anti-microbial. The anti-lipoxygenase effect of thyme essential oils due to thymol, limonene, bornyl acetate, p-cymene, camphor, and linalool considers its potential use as an anti-inflammatory agent [59].

Thyme contains a variety of compounds, including the monoterpenoid phenols thymol and carvacrol, which have the potential to be employed in a variety of therapeutic and management approaches. Within the scope of COVID-19, a study examined the biological and pharmacological aspects of carvacrol. This compound's powerful antioxidant and immunomodulatory actions are anticipated to boost host cellular immunity and interact with ACE2 receptors, perhaps blocking SARS-CoV-2 entry into host cells. Carvacrol also interferes with viral protease thus limiting viral spike (S) glycoprotein adherence to the host cell [60]. In another study, Thymol was docked to the S1 receptor binding site S, which serves as the primary focus for new antiviral agents, in order to determine its antagonistic effect relying upon binding. As a natural substance with antiviral activity and molecular docking strategies, it demonstrated efficacy in inhibiting the viral spike protein and holds promise as a novel phytochemical therapeutic agent for COVID-19 [61].

Table 1. Potential Natural Products against COVID-19

Name	Active Ingredients	Mechanism	Reference
Gonger (Zingiberofficinale)	Gingerols, Shogaols, and Paradols	-8 compounds found in rhizomes of Alpiniaofficinarum and ginger were acknowledged as possible inhibitors of SARS-CoV-2 PLpro -Constituents from ginger (8-Gingerol, 10-Gingerol) are significantly active against COVID19	[62] [11]
Garlic (Allium sativum)	Ajoene>Allicin>Allyl methyl >Thiosulfinate>Methyl allylthiosulfinate	-The anti-viral properties of *A. sativum* were recognized due to the presence of particular contents in this order: ajoene>allicin>allyl methyl >thiosulfinate> methyl allylthiosulfinate	[63]
Clove (Syzygiumaromaticum)	Beta-caryophyllene, Vanillin, Eugenol, Acetyl eugenol, Crategolic acid, Eugenin, Methyl salicylate, Kaempferol, Rhamnetin, Eugenitin, Oleanolic acid, Stigmasterol, Campesterol, Gallic acid, and Flavonolglucosides	-Substantial binding affinity with various CoVs proteins -Inhibit the virucidal infection caused be SARS-CoV-2 on different stages	[19]
Black pepper (Piper nigrum L)	Piperine, Piperamide, Piperamine, Pipericide, Sarmentosine, Sarmentine, Brachyamide B, Dihydropipericide, N-Formylpiperidine, Guineensine, Pentadienoylpiperidine, Tricholein, Trichostachine, Piperettine, Piperolein B, Retrofractamide A, Chavicine, Isochavicine, Isopiperine, Nerolidol, β-caryophyllene and Piperic acid	-May demonstrate anti-inflammatory characteristics and may prove to be effective in preventing COVID-19	[19]

Name	Active Ingredients	Mechanism	Reference
Chilli Pepper (Capsicum frutescens)	Quercetin and Luteolin-7-glucoside	-Inhibitor of COVID-19 Main protease	[34]
Nigella Sativa (Black seeds)	Thymoquinone (TQ)	-Antiviral activity against cytomegalovirus, HIV, hepatitis C, influenza virus. - TQ mutates the phosphorylation of Ser-304 and Ser-328 of p47(PHOX) -Augment macrophage number and interferon production	[64]
Honey (Apis)	Hydrogen peroxide	-Inhibits influenza virus replication - Prevents the activation on inflammatory nuclear factor-κ B (NF- κ B) signaling pathway - Reduces TNF-α, IL-1β, IL-12 p70, MIP-1α, MIP-1β, MMP-9, MMP-1, FGF-13, IL-1ra, and IL-4 release	[65]
Turmeric (Curcuma longa.)	Curcumin	- Inhibits HCV entry by affecting membrane fluidity (alter virus binding and fusion) - Prevents the replication and budding of RSV - inhibitor of NF-κB, eIF-2α dephosphorylation, proteasome and COX2 - Targets HIV-1 protease, integrase and cellular NF-κB protein for the downregulation of HIV-1 replication - Represses the transcription of viral genome - Halts activity of Ebola virus by not allowing the release of pro-inflammatory cytokines like IL- 6 and IL-1, and tumor necrosis factor- alpha - Disturbs LPS-stimulated expression and diminishes the secretion of MIP-2, IL-1β, KC and MIP-1α in colonic epithelial cells (CEC) and in macrophages	[66]

Name	Active Ingredients	Mechanism	Reference
Onion (Allium cepa)	Fructans Quercetin	-Enhances the production of neutralizing antibodies against influenza A virus -Simulatory effect on NO production which inhibits the early stages of viral replication	[67]
Ginseng (Panax ginseng)	Ginsenosides	-Decreases virus-induced cytokine secretion and reactive oxygen species (ROS) formation - Possesses an immunomodulatory effect by balancing Th1 and Th2 immune responses - Suppresses the production of RSV-induced TNF-α in murine dendritic and macrophage-like cell lines - Inhibits the production of proinflammatory cytokines IL-6, IL-8, and TNF-α	[68]
Thyme (Thymus vulgaris)	Thymol P-cymene α-terpinolene	- Inhibits all enveloped RNA viruses including SARS coronavirus	[69]

2. CONCLUSION

Amidst the ongoing COVID-19 pandemic, where the reliable treatment options are limited, supplementary natural therapies are advised. In this regard, there is a growing interest in exploring and studying the antiviral and immunomodulating effects of different natural products.

After the analysis of various research on the pharmacological properties of onions, it can be concluded that onion possesses antiviral, antioxidant, as well as immune-stimulating properties, which can be attributed to the presence of bioactive compounds like Quercetin and fructans. The therapeutic effect of onion extract in Asthma and Influenza indicates that onion can treat viral diseases. However, further research is required to confirm the efficacy of onion in treating all viral diseases.

The critical analysis of the antiviral properties of ginseng against viruses that target the human respiratory system confirms the efficiency of ginseng in the prevention and treatment of viral diseases. This information can further be utilized in studies or experiments to validate the efficacy of ginseng against COVID-19. The therapeutic effectiveness of ginseng against viral diseases can provide a gateway for new research and experiments to establish a cure or preventive treatment for COVID-19.

Evidence suggests that black seeds can assist in increasing macrophage number and interferon production. Antiviral properties of honey against influenza virus,

herpes simplex virus, COVID-19, RSV, HIV, and VZV were proved by different research and clinical trials. Clinical trials of multiple research projects showed that curcumin can act as an entry inhibitor of rHCV, IAV (Orthomyxoviridae), JEV (Flaviviridae), MNV, ZIKV (Flaviviridae). In HIV its effect is a protease inhibitor, integrase inhibitor, and Tat protein inhibitor. Replication inhibition effects are seen in RSV (Pneumoviridae).

Research findings indicate that cinnamon may have little to moderate effectiveness as an antiviral food. It's not virucidal but can enhance antiviral activity in the treatment of influenza A virus. Researches are still in the process to prove its anti-viral properties.

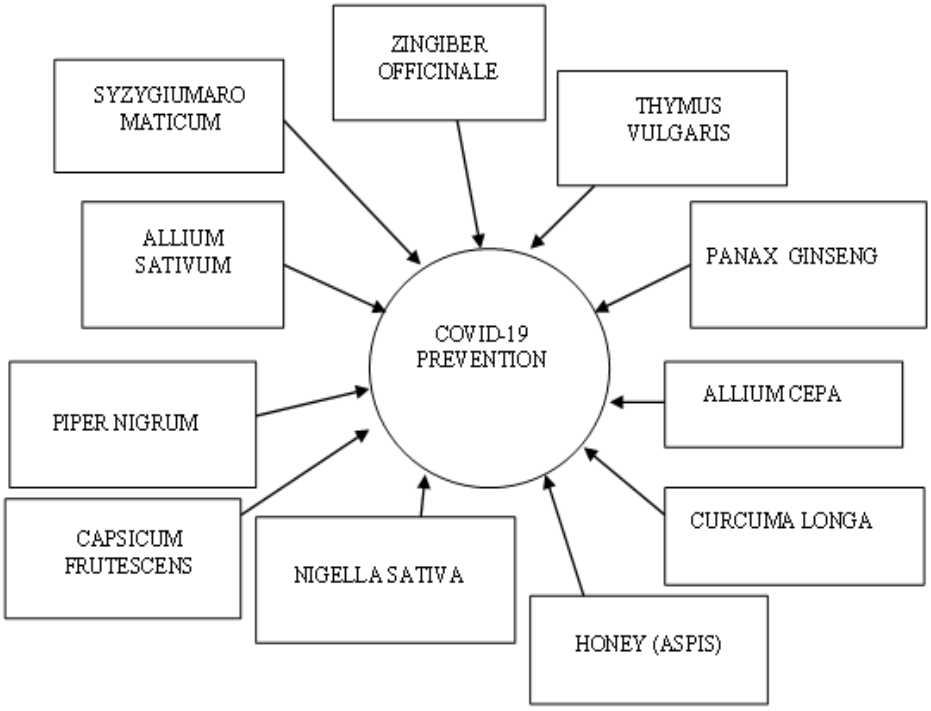

Figure 1. COVID-19 and Natural Foods

CONFLICT OF INTEREST

The author of the manuscript has no financial or non-financial conflict of interest in the subject matter or materials discussed in this manuscript.

DATA AVALIABILITY STATEMENT

The data associated with this study will be provided by the corresponding author upon request.

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