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Bio-active Compounds (Curcumin, Allicin and Gingerol) of Common Spices used in Indian and South-east Asian Countries Might Protect against COVID-19 Infection: A Short Review

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Authors' contributions

This work was carried out in collaboration among all authors. Author JA conceptualized the idea and has written the review article. Author TH edited the article throughout all stages. Author SP director provided overall support. All authors read and approved the final manuscript.

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ABSTRACT

Presently, our world is suffering with COVID-19 caused by novel coronavirus SARS- CoV-2. The high rate of mutation in SARS- CoV-2 helps viruses to become resistance against pre-existent anti-viral medications. Currently, there are no effective therapeutic strategies against COVID-19 infection except some vaccines. Curcumin, Allicin and Gingerol are natural bioactive compounds having anti-viral, anti-inflamatory, anti-pyretic, anti-fibrotic properties and were used as spices in food in South East Asian and Indian subcontinent that could be a potential treatment for COVID-19 disease. This review will help in understanding the biology and potential of bioactive compounds present in turmeric, garlic and ginger as therapeutic against COVID-19 infection. Computational study suggested that gingerol, curcumin, and allicin showed good interaction with proteins of SARS-CoV-2 and ACE2 receptor of host cell and might have an important role in impeding SARS-

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CoV-2 replication. Clinical trials have been conducted for nanocurcumin and gingerol. The fatality rate of people from South East Asia and Indian subcontinent eating highly spicy food is less as compared to people from America and Europe eating less spicy food. Further, this review will help people to do research on curcumin, allicin and gingerol against the treatment of COVID-19. All of the spices are commercially available, edible and might be used as precautionary home remedies against COVID-19.

Keywords: Curcumin; allicin; gingerol; COVID-19; SARS-CoV-2; bioactive compounds.

1. INTRODUCTION

The present pandemic in the world is coronavirus infectious diseases 2019 (COVID19) caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) having single stranded RNA genome of around 29 kb consist of 14 open reading frames (Orf) and belong to family β-coronavirus [1]. The SARS- CoV-2 has 4 structural proteins (nucleocapsid, membrane, envelope and spike protein). During COVID-19 infection, the spike protein (S) of SARS-CoV-2 binds with Angiotensin Converting Enzyme-2 (ACE2) receptor protein of host cell. The virus releases RNA into the cytoplasm and starts synthesizing proteins for the replication and transcription [2,3,4]. The genome sequence analysis revealed that novel coronavirus SARS-CoV-2 is very similar to the earlier reported corona virus like SARS-CoV. The ACE2 protein of host cell and spike protein of SARS-CoV-2 are the proposed drug target candidates as the spike protein binds with ACE2 receptor that facilitates entry of virus into host cell [5]. The SARS-CoV-2 lacks the proof-reading ability that leads to high rate of mutation and emergence of different types of variant. Recently, one variant of SARS-CoV-2 is found in U.K and it is spreading very fast to other parts of world. Because of this variant (VUI-2020/01) of SARS-CoV-2, a complete lockdown have been imposed in U.K till mid-February 2021 [6]. The mutation in the genome of virus act as blessing in disguise for viruses as they develop resistance against available antiviral therapy [7,8,9]. The mutation in coronavirus poses difficulty in developing vaccines and drugs against SARS-CoV-2 [10]. Aged, immune-compromised and people with other morbidities are the most susceptible towards COVID-19 due to physiological changes in immune system according to reports from different parts of the world [11]. Various pre-existing anti-viral drugs have been evaluated but only few of these have been approved for treatment of COVID-19. Studies on development of new drugs or therapy against COVID-19 are at early stage and there is need of more studies to be done on therapy of COVID-19 [12,13]. Till January, 2021, not a complete treatment against COVID-19 was available except some new authorized or approved vaccine from ICMR-Bharat Biotech (Covaxin), Serum Oxford vaccine (covishield), Astrazenece (AZD1222), Sinopharm (BBIBP-CorV), Sinovac (coronavac), Pfizer-BioNTech (BNT162b2) and Moderna (mRNA 1273). However, the present antiviral therapy has not been very successful due to resistance, side effects, cost, incomplete cure and non-compliance among patients. The drawbacks of these anti-viral therapy lead to development of a new non-synthetic antiviral agent from natural source as these agents are highly effective, safe, specific cellular targets, low cost. Recent study showed the anti-viral properties of natural compounds like curcumin [14]. The modern *in vitro, in vivo* studies and clinical trials have unravelled the potential for selected phytochemicals [15].

In this review, we have chosen three phytochemicals namely curcumin *(Curcuma longa*), gingerol (*Zingiber officinale*) and allicin (*Allium sativum*) as these compounds are commonly found in spices used in daily diet food of Indian subcontinent and South East Asian people with proven multiple biological and therapeutic activities. We have explored important search engines and databases like NCBI-PubMed, Scopus. In this review, the results of relevant studies and the effect of bioactive compounds (curcumin, allicin, gingerol) on viral diseases especially COVID-19 has been summarized. This review highlights the importance of bioactive compounds used in Indian subcontinent and South East Asian foods on COVID-19.

2. GINGER

Ginger is obtained from rhizome of *Zingiber officinale* having medicinal properties and used as spice in food. Gingerols, paradols, shogaols, zerumbones and zingiberene are the bioactive compounds found in Ginger. Gingerol ($C_{17}H_{26}O_4$)

commonly known as [6]-gingerol, is a major polyphenolic compound found in ginger having anti-microbial properties useful for human health. It has been used for the treatment of many common diseases including colds, flu, nausea, arthritis, asthma, and gastrointestinal complaints. Previous studies have shown that gingerol has been used against respiratory symptoms [16]. Computational studies have suggested that gingerol showed good interaction with proteins (main protease, Cathepsin K and SARS-CoV3C like protein) and less toxicity [17]. The docking analysis of 50 phytochemicals with Nsp15 of SARS-CoV-2 have been done and found that curcumin, gingerol, ursonic acid, sarsasapogenin, ajmalicine, piperine, novobiocin, aranotin, alpha terpinyl acetate, silymarin, rosmarinic acid bind to Nsp15 protein and might play a significant role in inhibiting replication of SARS-CoV-2 [18]. A randomized clinical trial is going on in Shahid Mohammadi Hospital, Bandar Abbas, Iran where a total of 84 COVID-19 patients were taken and categorised into two groups of 42 each (Intervention group and Control group). The intervention group (42 patients) will be given standard treatment with 1000 mg ginger thrice a day for 7 days and control group will be given standard treatment with placebo tablets at a dose as recommended to Intervention group [19].

3. ALLICIN

Allicin ($C_6H_{10}OS_2$) is a most biologically active organosulfur compound obtained from garlic (*Allium sativum*), which belongs to family Alliaceae. Previous studies have reported the antiviral properties of garlic against several viral diseases like Parainfluenza virus type 3, vaccinia virus, human rhinovirus type 2, influenza B, human cytomegalovirus (HCMV), herpes simplex type 1 and 2 [20]. The *in vivo* study exhibited that garlic extract showed inhibitory effect on multiplication of infectious bronchitis virus (IBV), a type of coronavirus which might be due to blocking of structural proteins and genetic materials [21]. Garlic has abundant sulphur containing amino acids and other compounds that might increase the activity of immune system by making macrophages or killer cells more active. As the COVID-19 infection has no effective cure or treatment, it has become more important to boost rev up build up the body's immune system to fight against SARS-CoV-2. Studies on immune cells showed that garlic extract significantly increases the CD4+ and CD8+ T cells which promote cellular immune system [22]. Another *in vivo* study conducted on garlic treated rats showed that garlic significantly increases T cell ($CD4^+$) and white blood cell count (WBC) which boosts the immune system [23]. Study conducted by Arreola et al. 2005 on garlic extract showed the reduction of expression of pro-inflammatory cytokines [24]. A computational study was conducted to demonstrate the binding potential of gingerol, curcumin and allicin towards proteins (main protease, cathepsin K, SARS-CoV 3 C-like protease) of SARS-CoV-2 and suggested that binding affinities of allicin with proteases was lower as compare to curcumin and gingerol [17]. In contrast to the finding of Oso et al. 2020, another computational study using molecular docking analysis with 7 natural compounds from *Allium sativum* and *Allium cepa* (S-Allylcysteine sulfoxide (Alliin), S-Propyl cysteine, S-Allylcysteine, S-Ethylcysteine, S-Allylmercaptocysteine, S-Methylcysteine, S-propyl L-cysteine) found that S-Allylcysteine sulfoxide (Alliin) have best binding efficacy (-5.24 kcal/mol) with the main protease of COVID-19 as compared to other compounds analysed. They suggested that S-Allylcysteine sulfoxide from garlic can be used as an effective inhibitor against the main protease which could be helpful in eliminating COVID-19 infection [25]. One more docking analysis of 17 organosulfur compounds present in the garlic showed strong interactions with ACE2 of host cell and the main protease of SARS-CoV-2. Allyl disulphide and allyl trisulfide expressed strongest activity against SARS-CoV-2. The above study also revealed the synergistic interactions of the 17 organosulfur compounds. The results suggested that the essential oil in garlic might be having anti-virus properties which contributes to checking the incursion of SARS-CoV-2 into the human body [26]. Based on the above studies, we suggest that *in vitro and in vivo* assays of *allium sativum* (garlic) may be done to clarify the importance as therapeutic against COVID-19.

4. CURCUMIN

Curcumin ($C_{21}H_{20}O_6$) is a polyphenolic yellow compound obtained from *curcuma longa* and used as spice in foods around the worldwide, especially in South East Asian and Indian subcontinent. It is cheap, easily available and has anti-viral, anti-oxidant, anti-inflammatory, anti-carcinogenic properties as has been observed in several *in vitro*, *in vivo* studies on various disease [27,28,29]. It is also used as medicine in Ayurveda, Siddha

medicine, traditional Chinese medicine and Unani medicine in Asia countries for centuries [30]. China found that the use of Traditional Chinese Medicine (TCM) is effective against COVID-19 [31]. Studies suggest the role of curcumin as potential anti-viral agent against various viral infections [32]. Furthermore, curcumin showed anti-viral activity against enveloped virus same as coronavirus by changing the features of the lipid bilayer [33]. Curcumin can reduce the growth of influenza A virus by activating Nrf2 signalling and inducing the production of anti-oxidants [34]. Consequently, curcumin might act as potential antioxidant agent against oxidative stress produced in lungs during SARS-COV-2 infection. Reports showed that curcumin could constrain the viral replication as evident by the reduction in virus titres and plaque numbers. This study suggested the possible role of curcumin as a capable anti-viral agent [35]. Interferons (IFNs) play a role in inhibiting viral infections and the production of IFN can be increased by bioactive agents. There are several findings showing the consequence of curcumin on IFNs in various viral diseases [36,37,38]. Curcumin limits viral growth by meddling with vital steps of viral attachment to host cell and replication of virus [39]. Curcumin exhibits inhibitory ability on the proliferation of diverse viruses like dengue virus, hepatitis B virus, Zika virus and chikungunya virus (CHIKV) [40,41,42,43]. Previous studies demonstrated that curcumin has a potential to inhibit the enzyme of other coronavirus SARS-CoV [44,45]. Recent studies showed that curcumin may lessen Influenza A virus which promoted lung infection by hindering the NFκB signalling pathway and constraining the production of inflammatory cytokines. Thus, curcumin may have a role in reducing lung infection accompanied with COVID-19 [46]. Previous studies on monocytes and macrophages found that curcumin can hamper the production of cytokines macrophage inflammatory protein-1α (MIP1α), monocyte chemoattractant protein-1(MCP1), IL8, IL1β and TNFα [47,48]. Additionally, several studies found inhibitory properties of curcumin on IL-1 of bone marrow cell, IL-6 of rheumatoid synovial fibroblasts, IL-8 of oesophageal cell and alveolar epithelial cells [49,50,51,52]. Therefore, curcumin might be considered as good candidate to check increased secretion of cytokines during COVID-19. Chen et al. 2013 demonstrated that Curcumin inhibits inosine monophosphate dehydrogenase (IMPDH) which has an important role in de novo biosynthesis of guanine during replication of virus [33]. Therefore, Curcumin might be effective in impeding the replication of SARS-CoV-2 virus as it inhibits IMPDH of SAR-Co-V. Inhibitory effects of curcumin against SARS-CoV and respiratory diseases associated virus guarantee the potential of curcumin against COVID-19. The varied mechanisms of curcumin against different viruses could help to use curcumin as a model against SARS-CoV-2.

Recently a docking analysis was used by Das et al. 2020 to screen the possible inhibitors of the SARS-CoV-2 among 33 molecules and proposed that curcumin binds to the SARS-CoV-2 protease but has less efficiency than compounds like ritonavir (control drug), lopinavir (control drug), rutin (natural compound), hesperidin (natural compound), emetine (anti-protozoal) and indinavir (anti-viral drug) [53]. The *in silico* studies conducted on herbal compounds found that citrus and galangal compounds showed superior binding affinities to each receptor (spike protein-RBD, PD-ACE2 and SARS-CoV-2 protease) compared to those of the compounds of *Curcuma sp*. and sappan wood [54]. Another molecular docking was performed to examine essential compounds of Ayurveda that might have the potential to enhance immune system and obstruct the entry of virus in host cell. In contrast to other *in silico* studies, Maurya et al. 2020 predicted that curcumin and nimbin showed strong interaction with both spike proteins and ACE2 proteins as compared to other selected synthetic drugs (Hydroxychloroquine, Nafamostat, Captopril) and natural product (Withaferin, Mangiferin, Andrographolide, Piperine, Berberine, Thebaine, Quercetin, Resveratrol, Luteolin, Zingiberene, Naringenin, b-Caryophyllene, Citronellol, Eugenol, Gallic acid) [55]. The presumed inhibitory potential of gingerol, curcumin and allicin against main protease, cathepsin K and SARS-CoV 3 C-like protease predicted using molecular docking and simulation analysis suggested that curcumin has highest binding affinities and binding free energy with all the selected proteases. Therefore, the above studies suggest that curcumin could be potential therapy for the prevention of COVID-19 [17].

Dandapat et al. 2020 conducted another molecular docking and simulation study of curcumin and catechin and suggested that both bind with spike proteins and ACE2 proteins. The binding energy of curcumin is 7.9 Kcal/mol and 7.8 Kcal/mol and that of catechin is 10.5 Kcal/mol and 8.9 Kcal/mol for spike protein and ACE2, respectively which showed that curcumin binds with a lesser affinity than that of Catechin. The binding of these compounds (curcumin and catechin) to spike proteins alter the binding of spike proteins to ACE-2 proteins on host cell for inhibition of virus entry [56]. Rajagopal et al. 2020 conducted molecular docking studies on bioactive compounds from natural resources and currently recommended drugs and suggested that the G score values of cyclocurcumin (6.77 kcal/mol) was higher than that of remdesivir (6.38 kcal/mol), curcumin (6.13 kcal/mol), nelfinavir (5.93kcal/mol) and hydroxychloroquine (5.47 kcal/mol). Further, cyclocurcumin significantly binds with the main protease of SARS-CoV-2 as compared to other compounds/drugs [57]. Kumar et al. 2020 screened around 50 phytochemicals for their binding potential with Nsp15protein of SARS-CoV-2 using molecular docking approach and predicted that phytochemicals like curcumin, sarsasapogenin, gingerol, ajmalicine, ursonic acid, novobiocin, piperine aranotin, silymarin, alpha terpinyl acetate and rosmarinic acid bind to Nsp15 protein and might play an important role in inhibiting replication of SARS-CoV-2 [18].

Regardless of the beneficial effects of bioactive compounds against various diseases, the restricted bio-availability of curcumin may be a challenging subject [58]. The bio-availability of bioactive compounds can be improved by several ways like analogs of curcumin, encapsulation of curcumin, phospholipid complexes, liposomes, curcumin conjugated with nanocarrier [59,60,61]. Researchers are using Nano formulation of curcumin in clinical studies to overcome the drawbacks of bioavailability. A clinical trial is conducting on 40 COVID-19 patients (20 intervention group and 20 placebo group) of Shahid Mohammadi Hospital in Bandar Abbas, Iran to identify the effect of nanocurcumin on COVID-19 patients. The patients were administered 40 mg of curcumin nanomicelles, four times per day for two weeks and the placebo group were taken as control. The effectiveness of curcumin nanomicelles treatment will be evaluated on days 0, 7 and 14 post treatment by measuring IL-4, IL-17, IFN-Y and TGF-β and gene expression of t-bet, FoxP3, GATA-3, and ROR- γT to assess the shift of T helper1, T helper2, T helper 17, T regulator [62] Another clinical study was conducted on the 40 COVID-19 patients (20 intervention group and 20 placebo group) and 40 healthy patients group in Imam Reza Hospital, Iran to know the effects of Nanocurcumin on COVID-19 patients. Patients were administered with 160 mg of Nano-curcumin daily for 14 days and the placebo capsule were given to control group. Before treatment, the expression and production of cytokines (IL-6, IL-18, IL-1β and TNF-α) were found to be higher in COVID-19 patients as compared to healthy control group and after treatment with Nano-curcumin, the expression and production of IL-1β and IL-6 were significantly decreased as compared to healthy group. Conversely, IL-18 mRNA expression and TNF-α production were not affected by Nano-curcumin treatment [63]. Additionally, curcumin modified the various outcome of SARS-CoV-2 infection [64,65].

5. DISCUSSION

Dietary factors have a significant role in the regulation of various diseases in human beings. Spices are used in Indian subcontinent and south East Asian to enhance flavour of food and believed to promote human health. Some commonly used spices like turmeric, garlic and ginger are used in our daily diet to enhance the flavour of food and the bioactive compounds present in these spices boost our immune system and help immune cells in defending our body from infection as mentioned in Fig. 1. Worldwide, doctors are recommending to boost immunity through nutritional supplementation in the battle against COVID-19. Computation studies on spices like Onion, Garlic, Peppermint, Fenugreek, Chilli and Ginger showed strong binding of the bioactive compounds present in these spices with main protease and spike protein of SARS-coV-2 and suggested their possible inhibitory effect against SARS-CoV-2. All of the spices are commercially available, edible and might be used as precautionary home remedies against COVID-19 under the pandemic situation. Finally, these spices are reported for *in vitro* studies [66]. WHO releases COVID-19 weekly epidemiological update on every week and the updates of 22ndNov.,2020 showed that the percentage of death in seven days (16thNov.,2020 to 22nd Nov.,2020) were 49% for Europe, 33% for America, 9% for Eastern Mediterranean, 7% for South East Asian

Table 1. Depicts the studies on Anti-SARS-CoV-2 effects of curcumin and other phytochemicals in different regions of India

S. No.	Observation and conclusion	Compounds studied	Techniques used	References
1	Curcumin could bind to the active site of the SARS-CoV-2 protease but with less efficient than other compounds like rutin ritonavir, emetine, hesperidin, lopinavir and indinavir	Control Drugs (Penciclovir, Ritonavir,Hydroxychloroquine, Lopinavir Natural compounds (Demethoxycurcumin, EGCG, EGC, Hesperidin, Myricitrin, Puerarin, Scutellarin, Rutin, Quercitrin, Capsaicin, Ursolic acid, Glabiridin, Apiin, Rhoifolin, Glycyrrhizin, Vitexin) Anti-fungal drugs (Fluconazole, Itroconazole) Anti-viral drugs (Azidothymidine, Indinavir, Tipranavir, Saquinavir) Anti-nematodal and Anti - protozoal drugs (Diethylcarbamazine, Primaquine, Mepacrine Artemisinin, niclosamide, Emetine)	Molecular docking	Das et al. [53]
2	citrus and galangal compounds showed superior binding affinities to each receptor (SARS-CoV-2 protease, Spike glycoprotein-RBD ,and PD-ACE2)) compared to those of the compounds of *Curcuma sp*. and sappan wood	Control drug (Nafamostat, lopinavir) Natural compound (ACA, Galangin, DMC, BDMC, Tangeretin, Hespiretin, Nobiletin, Hesperidin, Naringenin, Brazilein, Brazilin)	Molecular docking	Utomo & Meiyanto, [54]
3	Curcumin and nimbin exhibits strong interaction with both spike glycoprotein of SARS-CoV-2 virus and ACE2 receptor of host cell as compared to other selected synthetic drug/ natural product	Synthetic drug (Hydroxychloroquine, Nafamostat, Captopril) Natural Product (Curcumin, nimbin, Withaferin, Piperine, Mangiferin, Thebaine, Berberine, Andrographolide, Quercetin, Luteolin, Resveratrol, Naringenin, Zingiberene, b-Caryophyllene, Citronellol, Eugenol, Gallic acid)	Molecular docking	Maurya et al. [55]
4	Curcumin have higher binding affinities and binding free energy than gingerol and allicin with all the selected protease that suggest curcumin potential as a prevention of COVID-19.	Curcumin, gingerol, allicin	Molecular docking and molecular dynamic simulation	Oso et al. [17]
5	Curcumin binds to RBD domain of viral S-protein and ACE2 receptor of host cell with less affinity than that of Catechin	Curcumin, Catechin	Molecular docking and molecular dynamic simulation	Dandapat et al. [56]

S. No.	Observation and conclusion	Compounds studied	Techniques used	References
6	Cyclocurcumin significantly bind with the active site of SARS-CoV-2 main protease as compared to other compounds/drugs (curcumin, hydroxychloroquine, nelfinavir and remdesivir)	Control drug (hydroxychloroquine, nelfinavir and remdesivir) Natural product (curcumin, Cyclocurcumin, dihydroxydimethoxyflavone , Andrographolide, Bis-demethoxycurcumin, Demethoxycurcumin, Curcuphenol, 14-deoxy12 hydroxy andrographolide, curlone, 14deoxyandrographolide, Turmerone, cinnamateester, Stigmasterol, βSitosteryl fatty acid esters, beta-Sitosterol	Molecular docking	Rajagopal et al. [57]
7	Phytochemicals like curcumin, sarsasapogenin, ursonic acid, ajmalicine, novobiocin, silymarin and aranotin, piperine, gingerol, rosmarinic acid, and alpha terpinyl acetate bind to Nsp15 viral protein and they might play a key role in inhibiting SARS-CoV-2 replication	Positive control Nelfinavir, Hydroxychloroquine Phytochemicals Sarsasapogenin, Ursonic acid, Novobiocin, Aranotin Ajmalicine, Beta sitosterol , Alpha amyrin , Silymarin, Pomolic acid Carnosol Rutin, Naringin, Arjunolic Asiatic acid, Reserpine Betulinic acid, Platanic acid, Berberine, Taspine, Alphitolic acid, Taxifolin, Luteolin, Apigenin Myricetin, Wogonin, pigallocatechin Chlorogenic acid, Afromosin, Gliotoxin, Psoralen, Carinatine, Rhinacanthin, Caffeic acid, Coriandrin, Scopoletin, Cordycepin, Ricinoleic acid, Alpha asarone, Valproic acid Allicin	Molecular docking	Kumar et al. [18]
8	The effectiveness of curcumin nano micelles will be evaluated by measuring cytokines (IL-4, IL-17, IFN-Y, TGF-β)	curcumin nano micelles and placebo tablets were given to 20 intervention group and 20 placebo group each in Shahid Mohammadi Hospital in Bandar Abbas, Iran	Clinical trial	Hassaniazad et al. [19]
9	After treatment with Nano-curcumin, the expression and secretion of IL-6 and IL-1β were significantly decreased as compared to healthy group. However, IL-18 mRNA expression and TNF-α concentration were not influenced by Nano-curcumin	Nano-curcumin given to 20 patients of Intervention group and placebo given to 20 patients of control group	Clinical trial	Valizadeh et al. [63]
10	S-Allylcysteine sulfoxide (Alliin), showed the best binding efficacy (-5.24 kcal/mol)with the main protease of COVID-19 as compared to other compound analysed	S-Allylcysteine sulfoxide (Alliin), S-Propyl cysteine, S-Allylcysteine, S-Ethylcysteine, S-Allylmercapto-cysteine, S-Methylcysteine, S-propyl L-cysteine	Molecular docking	Pandey et al. [25]
11	A randomized clinical trial is going on and	standard treatment with ginger based herbal tablets given to	Clinical trial	Safa et al. [19]

S. No.	Observation and conclusion	Compounds studied	Techniques used	References
	the primary outcome is recovery rate of clinical symptoms, including fever, dry cough, tiredness, and GI symptoms as well as paraclinical features,	42 patients of Intervention group and standard treatment with placebo tablets given to 42 control group		
12	The bioactive compounds present in commonly used spices like Onion, Garlic, Peppermint, Fenugreek, Chilli and Ginger showed strong binding with main protease and spike protein of SARS-coV-2	10 herbal compounds (Onion, garlic, ginger, turmeric, black piper, Red chilli, Fenugreek, Black cumin, cumin, peppermint)	Molecular docking and molecular dynamic simulation	Sen et al. [66]
13	17 organosulfur compounds found in garlic essential oil showed strong interactions with the amino acids of the ACE2 protein and the main protease PDB6LU7 of SARS-CoV-2	17 organosulfur compounds found in garlic essential oil	Molecular docking	Thuy et al. [26]

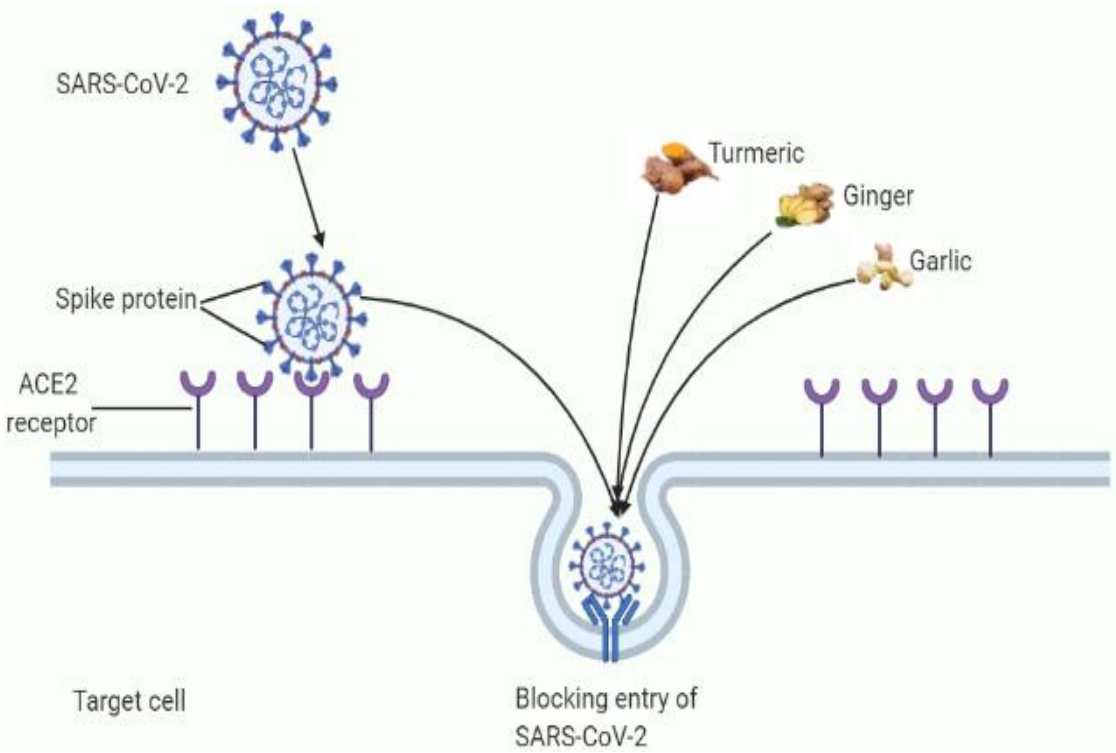

Fig. 1. Shows the bioactive compounds present in turmeric, garlic and ginger were used to boost immune system and help immune cells in defending our body from infection

countries, 2% for Africa and 1% for western pacific. The fatality rate COVID-19 of high spice food eating people from South-East Asia and Indian sub-continent is lower as compared to less spicy food eating people from America and Europe despite better health system in these developed countries. Although age, genetics and co-morbidities could play a significant role in the mortality [67,68]. People of the Indian subcontinent and south East Asian countries consume more spices as compared to American and European people and these common spices consist of turmeric, garlic and ginger which have a possible role to fight against SARS-CoV-2 and boost our immune system. Therefore, we suggest that use of spices might be a significant factor in the less mortality rate in Indian sub-continent and South East Asian countries compared to American and European countries despite better health system.

6. CONCLUSION

In this review, the promising anti-viral properties of 3 common spices namely turmeric, ginger and garlic used in Indian sub-continent and south East Asian dishes and effectiveness of bioactive compounds Curcumin, Allicin and Gingerol against the novel SARS-CoV-2 has been summarized in Table 1. Ginger, garlic and turmeric have been used as spices to enhance the flavour of food and believed to enhance immune system against viral/bacterial infections. The extracts of these spices have been used for centuries to treat a variety of ailments, ranging from wounds, pain, nausea, fatigue, chronic inflammation, etc. The competence of bioactive compounds to regulate several molecular targets makes it a possible candidate for the control of COVID-19. Till now, several *in silico* studies have been done on the potential of bioactive compounds (curcumin, allicin and gingerol) and some clinical trials have been done. Based on the *in silico* studies of these bioactive compounds, we feel that there is an urgent need of *in vitro* and *in vivo* studies on potency of curcumin, allicin and gingerol against COVID-19 infection. We also suggest that spices consisting of turmeric, garlic and ginger are having potential to fight against SARS-CoV-2 and could boost our immune system to fight against COVID-19 infection.

DISCLAIMER

The products used for this research are commonly and predominantly used products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

CONSENT

It's not applicable.

ETHICAL APPROVAL

It's not applicable.

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COMPETING INTERESTS

Authors have declared that no competing interests exist.

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