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Review Article

Spices a Healthy and Sustainable Option to Rescue from Coronavirus

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Abstract

After the devastating Spanish Flu epidemics of 1918–1920, a new deadly virus strikes the world in late December 2019 and is first detected in China in early January 2020. There are 153 lakh active cases of corona virus worldwide (Worldometer data). Improving nutritional patterns is a successful strategy for combating coronavirus pandemic. The most effective natural antibiotics against viruses are spices like turmeric, ginger, black pepper and garlic.Curcumin, a hydrophobic polyphenol is an active constituent of turmeric rhizomes, has antioxidant, antiapoptotic and anti-fibrotic properties. It also has inhibitory effects on TLRs, NF-Kβ, cytokines, chemokines and bradykinin. Curcumin inhibited 3CLprotease and prevented SARS-CoV replication. It not only blocks ligand-receptor binding at entry point but blocks replication and gene expression of viruses. Ginger extracts containing compounds such as gingerol, shogoal and paradols have been found to be effective against SARS-CoV. These chemicals have anti-bacterial effect that can help to prevent nausea. They inhibit ACE2 gene receptor, in the same way that curcumin does. Piperine presents in black pepper slows the breakdown of curcumin in the liver, thus helping its absorption through intestine and increases its level in bloodstream. Garlic contains flavonoid (e.g. quercetin) and organosulfur (e.g.allicin and alliin) compounds that have immunomodulatory properties which inhibit the virus spread.

The inhibition potentials of turmeric, ginger, garlic and black pepper plant extracts are found to be healthy and sustainable option than anti-malarial drughydroxychloroquine and become very interesting towards the development of alternative medicine to fight COVID without side-effects.

Keywords:- *Black pepper, Coronavirus, Garlic, Ginger, Turmeric.*

Introduction

After 100 years of devastating outbreaks of Spanish Flu (during 1918-1920) which was caused by H_1N_1- influenza-A virus, another deadly virus attacks the world at the end of December, 2019 and is detected in China in early January 2020.On February 11, 2020, the International Committee on Virus Taxonomy named this virus "Severe Acute Respiratory Syndrome Coronavirus 2" (SARS-CoV-2). WHO designated this new disease as "COVID-19". The coronavirus disease has been declared as a pandemic by the world health organization (WHO) within few weeks of its emergence. According to the most recent update of the world meter data, more than 647 million COVID-19 cases have been reported worldwide, resulting in nearly 6.6 million fatalities that have affected 203 countries and

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territories. Following the first COVID-19 case in India on January 30, 2020, now it became 44.67 million cases and 530 thousand deaths as per the data of world meter.

Pathogenesis

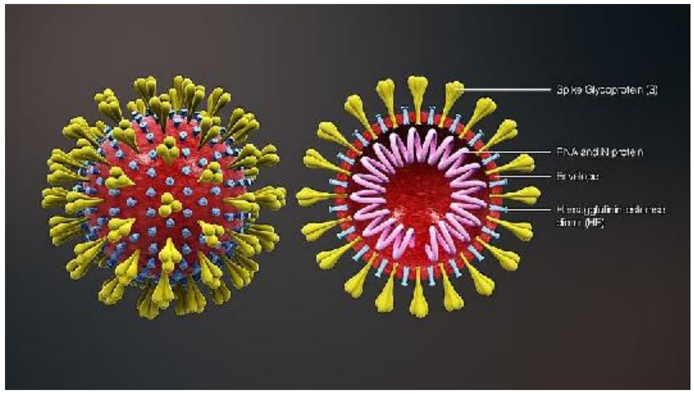

Fig-1: Structure of SARS-COV-2 in cross-section. *Source: https://www.scientificanimations.com.*

SARS-CoV-2 is a non-segmented enveloped positive-sense RNA virus. The initial viral RNA open reading frame encode 16 non-structural proteins and four crucial structural proteins are encoded by the remaining portion of the genome: spike glycoprotein(S), envelope (E), matrix (M), and nucleocapsid (N) protein(Cui *et al.*, 2019).Spike glycoprotein aids virus pathogenesis by binding to the cell surface receptor *i.e.* Angiotensin-Converting Enzyme 2 (ACE2) and allowing the virus to enter the host cell. The S protein has two domains. The S1 domain is involved in receptor binding and the S2 domain is associated with cell membrane fusion (He *et al.,* 2004). (Fig-1).According to data, the SARS-CoV2 protein binds to ACE2 with a higher affinity than the SARS-CoV protein. It consequently spreads rapidly among human populations. Cells in the lung, arteries, heart, kidney, and intestine all have ACE2 on their surfaces. (Hamming *et al.,* 2004). Men have higher levels of ACE2 in their alveolar cells than women, which may explain why men have a higher incidence of COVID-19.

Covid -19 And Drug Development Research

After so many test and trials India has rolled out a massive corona virus vaccination drives using two vaccine – 1. Covishield 2. Covaxin. First one has been developed by AstraZeneca and Oxford University. The second one has been developed by India in the collaboration with the Indian Council of Medical Research (ICMR) - National Institute of Virology (NIV). But unfortunately, this new vaccine shows some side effects like arm soreness, muscle aches, headaches and some instances of fever and chills.

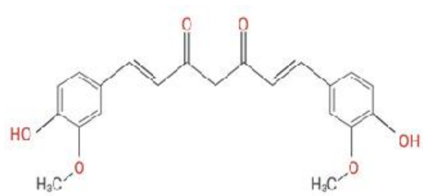

Fig-2: Molecular structure of curcumin. *Source: Wahab et al., 2020.*

A substantial population has shifted to the traditional medical system (herbal medicine) for their primary health care due to the inherent side effects of the synthetic chemicals used in allopathic drugs. Because of the accessibility, lack of side effects, low cost, and other benefits, ayurvedic medicine has emerged as a viable alternative to western medicine. India has historically been a rich source of spices due to its diverse agro-climatic regions.

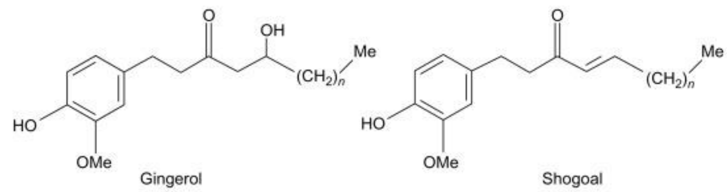

Fig-3: Molecular structure of gingerol and shogoal.
Source: Karunakaran and Sadanandan, 2019.

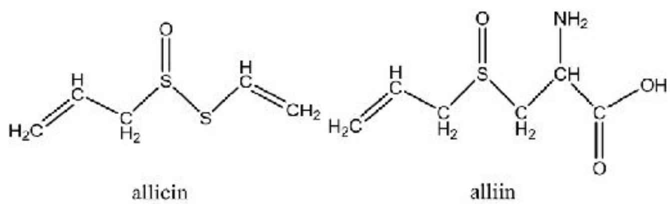

Fig 4. Garlic thiosulfinates (allicin-$C_6H_{10}OS_2$) and S-allyl cysteine sulfoxide (Alliin-$C_6H_{11}NO_3S$)

There are few extracted compounds of some spices like turmeric, ginger, black pepper, garlic have inhibition properties against coronavirus main protease.The dried, ground rhizome of the turmeric plant is used to extract the compound curcumin($C_{21}H_{20}O_6$)(Fig-2). Gingerol ($C_{17}H_{26}O_4$) and shogoal ($C_{17}H_{24}O_3$) are two components of the pungent ketones that give ginger its potent aroma (Fig-3). Garlic thiosulfinates (allicin-$C_6H_{10}OS_2$) and S-allyl cysteine sulfoxide (Alliin-$C_6H_{11}NO_3S$) are two important drug are isolated from the bulb of garlic(Fig-4). A naturally occurring alkaloid called piperine ($C_{17}H_{19}NO_3$) was discovered in the plants of both black and white pepper grains. (Fig-5).

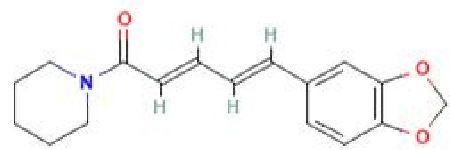

Fig-5: Molecular structure of piperine.
Source:https://pubchem.ncbi.nlm.nih. compound/Piperine#section=Structures

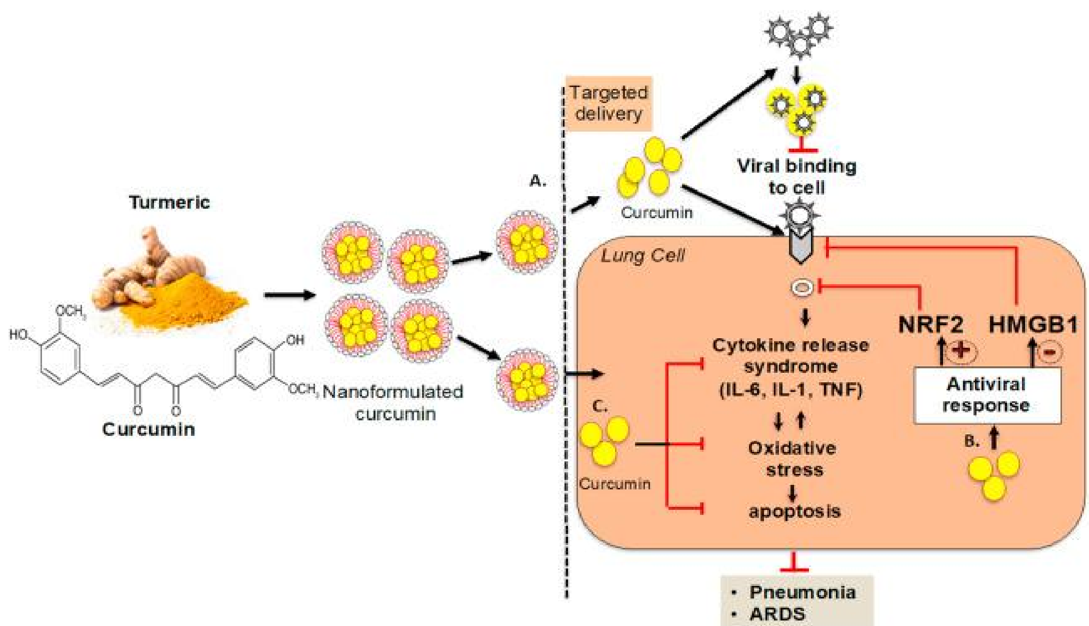

Fig-6: Molecular mechanism of curcumin *Source: Thimmulappa et al., 2021*.

Spices As A Fresh Choice:

As an effective agent, curcumin, gingerol, shogoal, piperine, and allicin could be considered to treat coronavirus. The active ingredients in turmeric, ginger, black pepper, and garlic are hydrophobic polyphenols. (Akbar *et al.,* 2018). They have antioxidant, anticancer, antibacterial, antiviral, and anti-diabetic properties along with anti-inflammatory effects (Fan *et al.,* 2015; Moghadamtousi *et al.,* 2014).

Therapeutic Effects of Turmeric and Ginger Against Corona Virus:

Antiviral:

The antioxidant extracted from turmeric prevents SARS-CoV2 (Covid-19) replication and inhibits chymotrypsin like protease(3CL^{pro}) in Vero E6 cells. In addition, it remarkably inhibits the cytopathogenic effect of SARS-CoV in Vero E6 cells (Wen *et al.,* 2007). The extracted drugs of turmeric is also efficient in combating other viruses such as the influenza A virus, HIV, enterovirus 71 (EV71), herpes simplex virus (HSV), hepatitis C virus (HCV), and human papillomavirus (HPV) through a variety of mechanisms, making them useful for antiviral therapies (Moghadamtousi *et al.,* 2014).It has been demonstrated that converting curcumin into carbon quantum dots can enhance curcumin's antiviral effects against enterovirus 71(EV71) in vitro and in vivo via various mechanisms (Lin *et al.,* 2019) (Fig-6).The intriguing feature of carbon quantum dots is their ability to neutralise human coronavirus (HCoV) by blocking the HCoV-229E entry receptor (Łoczechin*et al.,* 2019).Human respiratory syncytial virus (HRSV) attachment and penetration are inhibited by the aqueous extract of fresh ginger in human larynx epidermoid carcinoma cells and human lung carcinoma cell lines (Chang *et al.,* 2018). Fresh ginger has been shown to prevent viral adhesion and insertion into host cells by direct interaction with G and F proteins. Additionally, it promotes the release of interferon (IFN-α and IFN-β) from infected epithelial cells that resulted in inhibition of viral replication in the lower respiratory tract (Chang *et al.,* 2013).

Antiemetic:

Since ancient times, Asian nations have used ginger (*Zingiber officinalis*) and turmeric (*Curcuma longa* L.) as herbal remedies to treat vomiting. (Liu *et al.,* 2018, Bone *et al.*1990). A study done by Yao *et al.,* 2013 showed that curcumin and gingerol improved rat appetite during fluorouracil (5-FU)-induced chemotherapy. So, these plants can work well against vomiting caused by COVID-19.

Anti-myodynia and anti-drowsiness:

In an animal study, curcumin and gingerol were given orally to mice and this improved their physical function and decreased their tiredness. (Huang *et al.,* 2015). The administration of both active ingredients reduced stress and exhaustion in subjects who are suffering from occupational stress-related disquiet and lethargy.By preventing the catabolic response in skeletal muscle through the inhibition of nuclear factor kappa B (NF-kB), gingerol and curcumin prevented sepsis-induced muscle wasting (Alamdari*et al.,* 2009). In healthy elderly subjects, it also prevented muscle loss, enhanced physical performance, and postponed the development and progression of sarcopenia. This findings suggest that turmeric and ginger may be useful in treating myalgia and fatigue caused by COVID-19.

Antioxidant:

In cases of severe COVID-19 infection, pneumonia may result in hypoxemia, which interferes with cell metabolism and lowers energy supply, resulting in acidosis and production of oxygen free radicals that disrupt the phospholipid layer of the cell membrane (Li *et al.,* 2020; Jafarzadeh *et al.,* 2021).Therefore, treatment with an antioxidant containing drug will be beneficial for those patients. As a result, patients suffering from COVID will be benefited from treatment with an antioxidant-containing drug. Several studies have shown that curcumin, gingerol, shogoal are powerful antioxidants (Abrahams *et. al,* 2019; Farzaei*et al.,*2018) (Fig: 7). A study found that curcumin reduced malondialdehyde (MDA) levels while increasing xanthine oxidase (XO) and total antioxidative capacity (TAOC) in rats with ventilator-induced lung injury (Wang *et al.,* 2018).

Prohibitory Effects on Cytokines and Chemokines:

The aqueous extract of ginger and turmeric reduced circulating Interleukin-6(IL-6) and tumour necrosis factor alpha (TNF-α)levels, which are key inflammatory mediators and are associated with an increase in inflammatory diseases (Derosa*et.al.,* 2016; Sahebkar *et al.,* 2016; Kim *et al.,* 2020). Acute respiratory distress syndrome(ARDS)is a clinical syndrome characterised by increased permeability pulmonary oedema, severe arterial hypoxemia, and impaired carbon dioxide excretion, ultimately leading to respiratory failure. Cytokines (TNF, IL-1, IL-6, IL-8, IL-10), chemokines such as macrophage inhibitory factor (MIF) and macrophage chemoattractant protein, arachidonic acid metabolites (prostanoids and leukotrienes), and oxyradicals are major inflammatory mediators in ADRS. Curcumin, shogoal and gingerol, on the other hand, have been studied in animal studies for their protective effects in a variety of pulmonary diseases such as chronic obstructive pulmonary disease (COPD), ARDS, pulmonary fibrosis, and asthma (Lelli*et al.,* 2017; Venkatesan *et al.,* 2007) (Fig-6, 7).

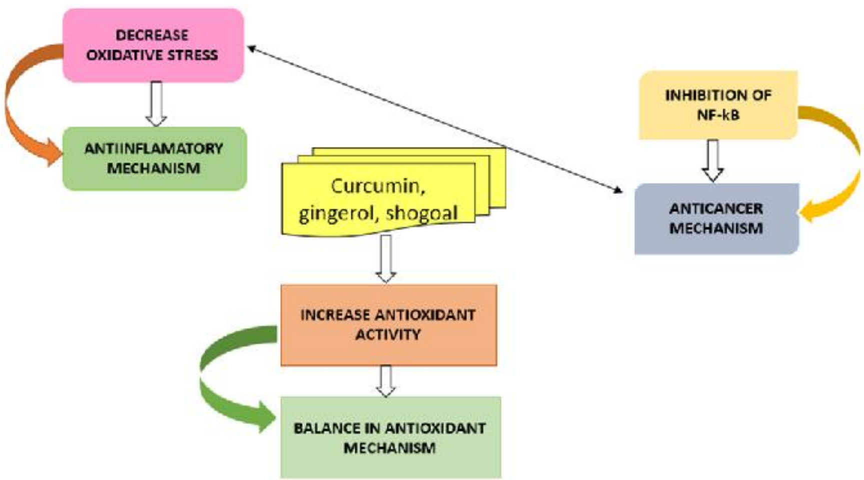

Fig-7: Antioxidant mechanism of turmeric and ginger extract

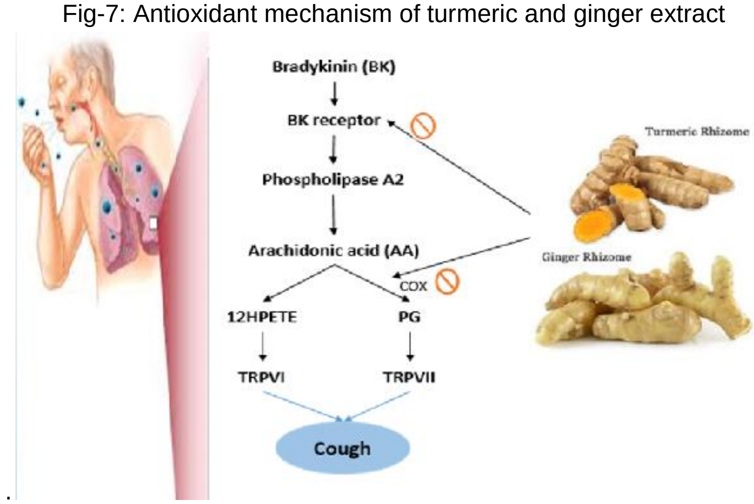

Fig-8: Effect of turmeric and ginger on bradykinin to supress cough

The molecular mechanisms towards down regulating the cytokines and chemokines are discussed here below.

i. Acute Lung Injury (ALI) is a model that is used for the Acute Respiratory Distressed Syndrome (ARDS) of animal study. Gingerol, shogoal, curcumin exhibit its effects by predominantly targeting proinflammatory factors by nuclear factor kappa B pathway (Ahn*et al.,* 2006; Karunaweera*et al.,*2015; Kim *et al.,* 2010). The extract of ginger and turmeric decreased IL-6 level, myeloperoxidase (MPO) activity, intercellular adhesion molecule-1 (ICAM-1) expression, and broncho alveolar lavage fluid (BALF) protein in ALI which are known as inflammatory indexes. This organic drugs inhibited the activation of NF-κB by upregulating phosphorylation of IκB-α(light polypeptide gene enhancer in B-cells inhibitor, alpha) in bone marrow-derived macrophages (BMDM). In ALI induced by intestinal ischemia-reperfusion in mice, the extract of this spices reduced IL-6 levels, myeloperoxidase (MPO) activity, intercellular adhesion molecule-1 (ICAM-1) expression, and Broncho Alveolar Lavage Fluid (BALF) protein, all of which are inflammatory indexes. They inhibited NF-kB activation by decreasing IB- phosphorylation in bone marrow-derived macrophages (BMDM). It has been proposed that curcumin and gingerol anti-inflammatory effects are due to their ability to modulate NF-kB activity.

Gouda and Bhandary (2019), reviewed the inhibiting function of turmeric on the expression of proinflammatory cytokines such as TNF-α, IL-1, and IL-6 in ALI and fibrosis. The downregulation or inhibition of IL-6 signalling in various inflammatory diseases appears to be the most significant molecular mechanism of curcumin on IL-6 activity (Ghandadi and Sahebkar, 2017). They also have an inhibitory effect on IL-17A, which is important in the inflammation of alveolar epithelial cells in ALI research.

ii. Several toll-like receptor (TLR) subtypes, including extracellular TLR 2, 4, 8, and intracellular TLR 9, are inhibited by curcumin, gingerol, and shogoal, which has therapeutic potential on inflammation, infection, autoimmune disorder, and ischemic disease. (Boozari *et al.,* 2019).Extracts from these two spices, when used in low concentrations (10, 20 μM), protected the human macrophages from apoptosis and cytokine production (TNF-α, IL-6) brought on by the 19-kDa Mycobacterium tuberculosis protein (P19).They also reduced the expression of TLR2/JNK, which may be involved in macrophage apoptosis (Li *et al.,* 2014). A severe influenza-A virus infection could result in ALI/ARDS, with significant morbidity and mortality. In contrast, the curcumin and gingerol both can decreased TLR-2/4 gene expression and prevented the phosphorylation of p38, JNK, and NF-kB in influenza-A virus-infected A549 cells. This two organic drug appears to regulate the TLR-MAPK/NF-kB signalling pathways involved in replication and influenza pneumonia.

iii. Alkaloids obtained from turmeric and ginger are found to have anti-apoptotic and anti-fibrotic effects in various organ injuries such as diabetes, nephrotoxicity, intestinal inflammation, and neurotoxicity via various mechanisms. In bleomycin-induced ALI, this organic compounds reduced the expression of p53, plasminogen activator inhibitor (PAI-1), chemokines, as well asIL-17-mediated apoptosis was inhibited, and cleaved caspase-3 was supressed in alveolar epithelial cells. The interaction of the inflammatory, fibrinolytic, and apoptotic pathways appears to be disrupted by curcumin(Gouda and Bhandary, 2018).

The Prohibitory Effects on Bradykinin to Subdue Cough:

In acute and chronic inflammatory diseases like respiratory tract infections and asthma, bradykinin plays a predominant role.Furthermore, it appears that bradykinin may cause coughing in these inflammatory diseases. Curcumin, gingerol and shogoalare the obstruction of activated protein-1 (AP-1) (Singh and Aggarwal, 1995).This inhibition ceased the expression of inter lukein-6 persuade by bradykinin in human airway smooth muscle cells (Huang *et. al.,* 2003; Jafarzadeh *et al.,* 2021). However, it has been demonstrated that those organic compounds have a higher affinity for the bradykinin 1 receptor (BK1) with strong obstruction activity as compared to the BK2 receptor (Fig: 8).

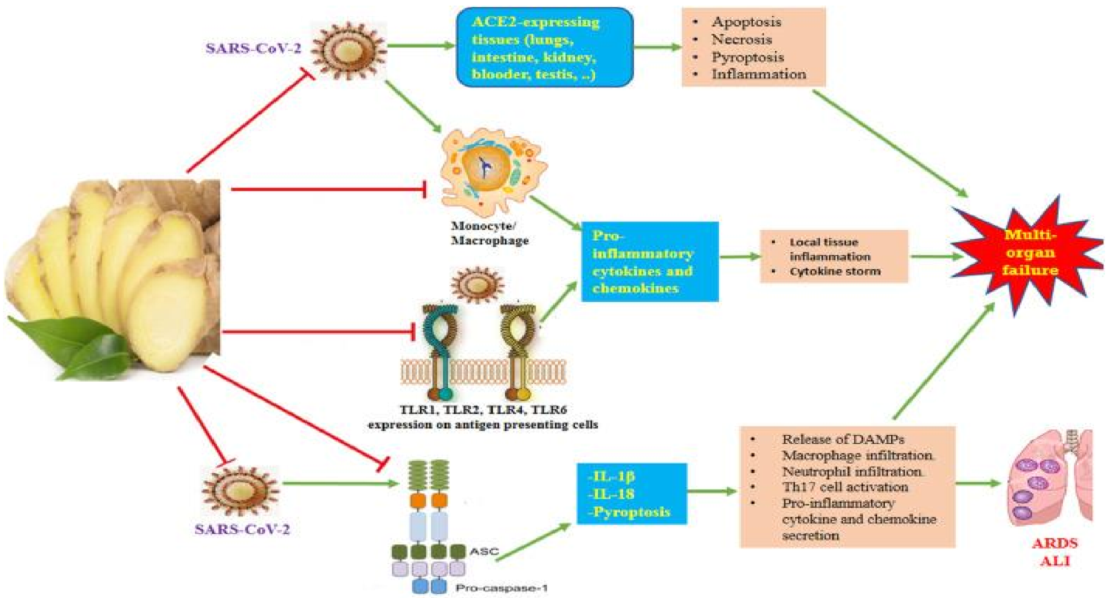

Fig-9: Molecular mechanism of ginger extract. *Source: Jafarzadeh et al., 2021*

Theraputic Effect of Garlic Against Coronavirus

1. Antiviral:

Garlic contains seven organosulfur compounds, including alliin, S-allyl cysteine, S-methyl cysteine, S-ethyl cysteine, S-propyl cysteine, S-propyl L-cysteine, and S-ally-mercapto-cysteine, which are thought to inhibit the 3 CL^{pro} of SARS-CoV-2 via hydrogen bonds (Khubber*et al.,* 2020). According to a study, allicin-containing supplements can help to prevent common cold virus attacks (Josling, 2001). However, among the seven OSCs, Alliin has the highest antiviral potential to prevent COVID-19 (Khubber*et al.,* 2020).

2. Immunomodulation:

Garlic shows immunomodulatory effect on human. Due to the transformation of organosulfur compounds (Chandrashekar *et al.,* 2011) it has been demonstrated that older garlic extract has stronger therapeutic potential than raw garlic extract (Chandrashekar *et al.,* 2012). Garlic extract stops the multiplication of interleukin (IL)-2 and interferon (INF)-ɣ gene expression in stimulated lymphocytes (Hanieh *et al.,* 2012).A study found that allicin can prevent immune-mediated liver damage in mice, most likely due to its immunomodulatory effects on T cells and adhesion molecules, as well as its inhibition of NF-kB activation (Bruck *et al.,* 2005) (Fig-10). Another finding suggested that allicin may have the ability to lessen the intestinal inflammation by having an immunomodulatory effect on intestinal epithelial cells(Lang *et al.,* 2004).

3. Anti-inflammation:

It has been demonstrated that garlic extract has anti-inflammatory potential. (Ban *et al.,* 2012). Lead compounds derived from allicin have been shown to be an excellent starting point for the creation of anti-inflammatory stimulants with fewer adverse effects. (Krishna *et al.,* 2012). According to one study, thiacremonone, a sulphur compound isolated from garlic, preventing neuroinflammation by inhibiting NF-kB activity (Lin *et al.,* 2012).

This bioactive component, alone or in combination with the main therapeutic drug, would be an effective therapy for SARS-CoV-2 eradication with the least amount of side effects and toxicity (Rajagopal *et al.,* 2020 and Pandey *et al.,* 2021).

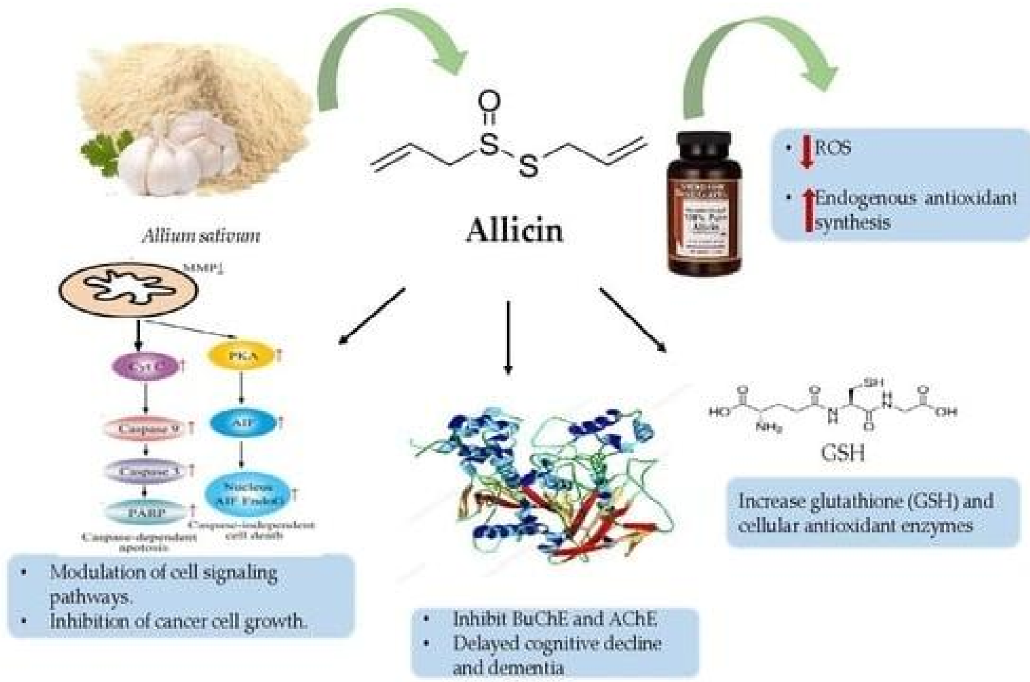

Fig-10: Molecular mechanism of allicin. *Source: Batiha et al., 2020*

Theraputic Effect of Blackpepper Against Coronavirus

Piperine ($C_{17}H_{19}NO_3$), a naturally occurring alkaloid, is found in black pepper. Black pepper is the good source of vitamin C, zinc (Zn), potassium, vitamin B2, vitamin B1, iron, and many other nutrients. T-cells, the soldiers who fight invading viruses, cannot become biologically active unless they are exposed to the pathogen along with the Human Leukocyte Antigen genes (comprises the major histocompatibility complex).Piperine enhances the bioavailability of Vitamin-C presents in ginger, turmeric, garlic, amla etc. and when it is used in combination with those, this is suggested as the best source of Vit-c supplements which will helps in the formation of WBC. Piperine in pepper slows the breakdown of curcumin in the liver, aiding absorption through the intestine and increasing blood levels. That means piperine increase the bioavailability of curcumin in human body.

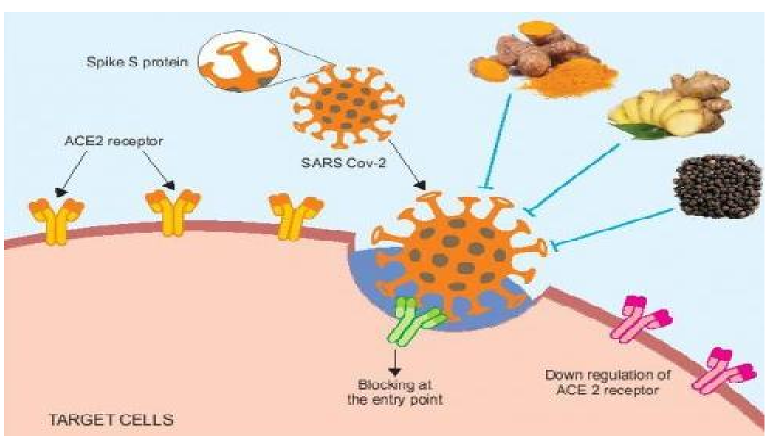

Fig-11: Downregulating of ACE 2 receptor by turmeric, ginger and black pepper
Source: https://cdn.downtoearth.org.in/library/medium/2020-10-29/0.45873000_1603969567_spices-page-001.jpg

Spices as Post Covid Treatments

People who have recovered from SARS-COV-19 are now facing a variety of serious health issues. The resulting scar tissue can cause long-term breathing problems due to decreased healing ability; blood clots and blood vessel problems, which can lead to heart attacks and strokes; seizures, and a variety of other problems that are still unknown.

Spices also shows its magical effect on the patients who are affected by coronavirus.

- Healing properties**:**

The organic compound of spices which are rich in anti-inflammatory, antioxidants, and anti-bacterial properties that aid in the healing of lungs tissue. This will help COVID19 patients with their breathing problems.

- Reduces the risk of cardiovascular diseases:

Curcumin improves heart health by improving the function of the endothelium, the lining of blood vessels and improves endothelial function.

- Antifungal properties:

The essential oils extracted from this spices exhibit anti-fungal properties and it also fights respiratory tract viruses.

- Reduces the risk of diabetes:

Adequate use of spices can reduce the cell-damaging effects of chronic hyperglycaemia in diabetic patients.

- Reduces the risk of brain damage:

Dietary turmeric enhances hippocampal neurogenesis and memory (Dong *et al.,* 2012). This effect could be due to curcumin-induced changes in the expression of genes involved in cell growth and synaptic plasticity (Dong *et al.,* 2012). It is prevalent to attribute the anti-inflammatory, antioxidant, and lipophilic ability of curcumin to its neuroprotective properties (Mishra and Palanivelu, 2008). As a result, it reduces the risk of brain damage in the COVID-19, particularly in the sensory organs such as the olfactory nerve.

Conclusion

All of these plant extracts have higher inhibition property than chloroquine and hydroxychloroquine. It has already been noted that these two anti-malarial narcotic compounds hinder COVID-19 proteolytic enzymes in vitro. But most of the nations do not approve those drug due to their intrinsic toxicity and adverse effects. Recently two vaccine are also developed. But those are also showing some side effects in human body. As a result, the implications of our findings for the development of complementary medicines by using those above compounds are very intriguing. In order to fight with the COVID-19, we anticipate swift action in this direction.

Conflicts of Interest

The authors declare that there are no conflicts of interest regarding the publication of this work.

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References

Abidi, A., Gupta, S., Agarwal, M., Bhalla, H. L. and Saluja, M., 2014. Evaluation of efficacy of curcumin as an add-on therapy in patients of bronchial asthma. *Journal of Clinical and Diagnostic Research*, 8(8), p.HC19-24.https://doi.org/10.7860/JCDR/2014/9273.4705

Abrahams, S., Haylett, W.L., Johnson, G., Carr, J.A. and Bardien, S., 2019. Antioxidant effects of curcumin in models of neurodegeneration, aging, oxidative and nitrosative stress: a review. *Neuroscience*, 406, pp.1-21.https://doi.org/10.1016/j.neuroscience.2019.02.020

Ahn, K.S., Sethi, G., Jain, A.K., Jaiswal, A.K. and Aggarwal, B.B., 2006. Genetic deletion of NADPH: quinone oxidoreductase 1 abrogates activation of nuclear factor-κB, IκBα kinase, c-Jun N-terminal kinase, Akt, p38, and p44/42 nitogen-activated protein kinases and potentiates apoptosis. *Journal of Biological Chemistry*, 281(29), pp.19798-19808.https://doi.org/10.1074/jbc.M601162200

Akbar, M.U., Rehman, K., Zia, K.M., Qadir, M.I., Akash, M.S.H. and Ibrahim, M., 2018. Critical review on curcumin as a therapeutic agent: from traditional herbal medicine to an ideal therapeutic agent. *Critical Reviews™ in Eukaryotic Gene Expression*, 28(1), pp. 17-24.https://doi.org/10.1615/CritRevEukaryotGeneExpr.2018020088

Alamdari, N., O'Neal, P. and Hasselgren, P.O., 2009. Curcumin and muscle wasting—a new role for an old drug?. *Nutrition*, 25(2), pp.125-129.https://doi.org/10.1016/j.nut.2008.09.002

Ban, J.O., Lee, D.H., Kim, E.J., Kang, J.W., Kim, M.S., Cho, M.C., Jeong, H.S., Kim, J.W., Yang, Y., Hong, J.T. and Yoon, D.Y., 2012. Antiobesity effects of a sulfur compound thiacremonone mediated via down-regulation of serum triglyceride and glucose levels and lipid accumulation in the liver of db/db mice. *Phytotherapy Research*, 26(9), pp.1265-1271.https://doi.org/10.1002/ptr.3729

Bone. M. E., Wilkinson. D. J., J. R. Young, McNeil. J., and Charlton. S., 1990. The effect of ginger root on postoperative nausea and vomiting after major gynaecological surgery. *Anaesthesia*, 45, pp. 669-671. https://doi.org/10.1111/j.1365-2044.1990.tb14395.x

Boozari, M., Butler, A.E. and Sahebkar, A., 2019. Impact of curcumin on toll-like receptors. *Journal of Cellular Physiology*, 234(8), pp.12471-12482.https://doi.org/10.1002/jcp.28103

Bruck, R., Aeed, H., Brazovsky, E., Noor, T. and Hershkoviz, R., 2005. Allicin, the active component of garlic, prevents immune-mediated, concanavalin a-induced hepatic injury in mice. *Liver International*, 25(3), pp.613-621.https://doi.org/10.1111/j.1478-3231.2005.01050.x

Chandrashekar, P.M. and Venkatesh, Y.P., 2012. Fructans from aged garlic extract produce a delayed immunoadjuvant response to ovalbumin antigen in BALB/c mice. *Immunopharmacology and Immunotoxicology*, 34(1), pp.174-180.https://doi.org/10.3109/08923973.2011.584066

Chandrashekar, P.M., Prashanth, K.V.H. and Venkatesh, Y.P., 2011. Isolation, structural elucidation and immunomodulatory activity of fructans from aged garlic extract. *Phytochemistry*, 72(2-3), pp.255-264.https://doi.org/10.1016/j.phytochem.2010.11.015

Cui, J., Li, F. and Shi, Z.L., 2019. Origin and evolution of pathogenic coronaviruses. *Nature Reviews Microbiology*, 17(3), pp.181-192.https://doi.org/10.1038/s41579-018-0118-9

Derosa, G. ,Maffioli, P. , Simental-Mendía, L. E. , Bo, S. , and Sahebkar, A., 2016. Effect of curcumin on circulating interleukin-6 concentrations: a systematic review and meta-analysis of randomized controlled trials. *Pharmacological Research*, 111, pp. 394–404.https://doi.org/10.1016/j.phrs.2016.07.004

Dong, S., Zeng, Q., Mitchell, E.S., Xiu, J., Duan, Y., Li, C., Tiwari, J.K., Hu, Y., Cao, X. and Zhao, Z., 2012. Curcumin enhances neurogenesis and cognition in aged rats: implications for transcriptional interactions related to growth and synaptic plasticity. *PloS one*, 7(2), p.e31211.https://doi.org/10.1371/journal.pone.0031211

El-SaberBatiha, G., Magdy Beshbishy, A., G. Wasef, L., Elewa, Y. H., A. Al-Sagan, A., Abd El-Hack, M. E., ... & Prasad Devkota, H. (2020). Chemical constituents and pharmacological activities of garlic (Allium sativum L.): A review. *Nutrients*, *12*(3), 872.https://doi.org/10.3390/nu12030872

Fan, Z., Yao, J., Li, Y., Hu, X., Shao, H., and Tian, X., 2015. Anti-inflammatory and antioxidant effects of curcumin on acute lung injury in a rodent model of intestinal ischemia reperfusion by inhibiting the pathway of NF-κB*. International Journal of Clinical and Experimental Pathology*, 8(4), p.3451.

Farzaei, M.H., Zobeiri, M., Parvizi, F., El-Senduny, F.F., Marmouzi, I., Coy-Barrera, E., Naseri, R., Nabavi, S.M., Rahimi, R. and Abdollahi, M., 2018. Curcumin in liver diseases: a systematic review of the cellular mechanisms of oxidative stress and clinical perspective. *Nutrients*, 10(7), p.855.https://doi.org/10.3390/nu10070855

Ghandadi, M. and Sahebkar, A., 2017. Curcumin: an effective inhibitor of interleukin-6. *Current Pharmaceutical Design*, 23(6), pp. 921–931.

Gouda, M. M. and Bhandary, Y. P., 2019. Acute lung injury: IL-17A-mediated inflammatory pathway and its regulation by curcumin. *Inflammation*, 42(4), pp. 1160–1169.https://doi.org/10.1007/s10753-019-01010-4

Gouda, M.M. and Bhandary, Y.P., 2018. Curcumin down-regulates IL-17A mediated p53-fibrinolytic system in bleomycin induced acute lung injury in vivo. *Journal of Cellular Biochemistry*, 119(9), pp.7285-7299.https://doi.org/10.1002/jcb.27026

Hamming, I., Timens, W., Bulthuis, M. L., Lely, A. T., Navis, G. and van Goor, H., 2004. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. a first step in understanding SARS pathogenesis. *The Journal of Pathology,* 203(2), pp. 631–637. https://doi.org/10.1002/path.1570

Hanieh, H., Narabara, K., Tanaka, Y., Gu, Z., Abe, A. and Kondo, Y., 2012. Immunomodulatory effects of *Alliums* and *Ipomoea batata* extracts on lymphocytes and macrophages functions in White Leghorn chickens: *in vitro* study. *Animal Science Journal*, 83(1), pp.68-76.https://doi.org/10.1111/j.1740-0929.2011.00918.x

He, Y., Zhou, Y., Liu, S., Kou, Z., Li, W., Farzan, M. and Jiang, S., 2004. Receptor-binding domain of SARS-CoV spike protein induces highly potent neutralizing antibodies: implication for developing subunit vaccine. *Biochemical and Biophysical Research Communications,* 324(2), pp. 773–781. https://doi.org/10.1016/j.bbrc.2004.09.106

Huang, C. D., Tliba, O., Panettieri, R. A. Jr, and Amrani, Y., 2003. Bradykinin induces interleukin-6 production in human airway smooth muscle cells modulation by Th2 cytokines and dexamethasone. *American Journal of Respiratory Cell and Molecular Biology,* 28(3), pp. 330–338. https://doi.org/10.1165/rcmb.2002-0040OC

Huang, W.C., Chiu, W.C., Chuang, H.L., Tang, D.W., Lee, Z.M., Wei, L., Chen, F.A. and Huang, C.C., 2015. Effect of curcumin supplementation on physiological fatigue and physical performance in mice. *Nutrients*, 7(2), pp.905-921.https://doi.org/10.3390/nu7020905

Jafarzadeh, A., Jafarzadeh, S. and Nemati, M, 2021. Therapeutic potential of ginger against COVID-19: Is there enough evidence? *Journal of Traditional Chinese Medical Sciences,* 8 (4), pp. 267-279.https://doi.org/10.1016/j.jtcms.2021.10.001

Josling, P., 2001. Preventing the common cold with a garlic supplement: a double-blind, placebo-controlled survey. *Advances in Therapy*, 18(4), pp.189-193.https://doi.org/10.1007/BF02850113

Karunakaran, R. and Sadanandan, S. P., 2019. '*Zingiber officinale*: anti-inflammatory actions and potential usage for arthritic conditions.' In. *Bioactive Food as Dietary Interventions for Arthritis and Related Inflammatory Diseases (*2nd Ed.), Academic Press,pp. 233- 244.https://doi.org/10.1016/B978-0-12-813820-5.00013-1

Karunaweera, N., Raju, R., Gyengesi, E., and Münch, G. (2015). Plant polyphenols as inhibitors of NF-κB induced cytokine production-a potential anti-inflammatory treatment for Alzheimer's disease? *Frontiers in Molecular Neuroscience*, 8, p. 24. https://doi.org/10.3389/fnmol.2015.00024

Khubber, S., Hashemifesharaki, R., Mohammadi, M. and Gharibzahedi, S. M. T., 2020. Garlic (*Allium sativum* L.): a potential unique therapeutic food rich in organosulfur and flavonoid compounds to fight with COVID-19. *Nutrition Journal,* 19, p. 124https://doi.org/10.1186/s12937-020-00643-8

Kim M.K., Chung S. W. and Kim D. H., 2010. Modulation of age-related NF-kappa B activation by dietary zingerone via MAPK pathway. *Experimental Gerontology*; 45(6), pp. 419-426. https://doi.org/10.1016/j.exger.2010.03.005

Kim Y.G., Kim M.O. and Kim S, H., 2020. 6-Shogaol, an active ingredient of ginger, inhibits osteoclastogenesis and alveolar bone resorption in ligature-induced periodontitis in mice. *Journal of Periodontology*, 91(6), pp. 809-818. https://doi.org/10.1002/JPER.19-0228

Krishna, A. and Yadav, A., 2012. Lead compound design for TPR/COX dual inhibition. *Journal of Molecular Modelling*, 18(9), pp.4397-4408.https://doi.org/10.1007/s00894-012-1435-y

Lang, A., Lahav, M., Sakhnini, E., Barshack, I., Fidder, H.H., Avidan, B., Bardan, E., Hershkoviz, R., Bar-Meir, S. and Chowers, Y., 2004. Allicin inhibits spontaneous and TNF-α induced secretion of proinflammatory cytokines and chemokines from intestinal epithelial cells. *Clinical Nutrition*, 23(5), pp.1199-1208.https://doi.org/10.1016/j.clnu.2004.03.011

Lelli, D., Sahebkar, A., Johnston, T. P., and Pedone, C., 2017. Curcumin use in pulmonary diseases: state of the art and future perspectives. *Pharmacological Research*, 115, pp. 133–148. https://doi.org/10.1016/j.phrs.2016.11.017

Li, B., Yang, J., Zhao, F., Zhi, L., Wang, X., Liu, L., Bi, Z. and Zhao, Y., 2020. Prevalence and impact of cardiovascular metabolic diseases on COVID-19 in China. *Clinical Research in Cardiology*, 109(5), pp.531-538.https://doi.org/10.1007/s00392-020-01626-9

Li, M., Wu, Z., Niu, W., Wan, Y., Zhang, L., Shi, G. and Xi, X.E., 2014. The protective effect of curcumin against the 19-kDa *Mycobacterium tuberculosis* protein-induced inflammation and apoptosis in human macrophages. *Molecular Medicine Reports*, 10(6), pp.3261-3267. https://doi.org/10.3892/mmr.2014.2615

Lin, C.J., Chang, L., Chu, H.W., Lin, H.J., Chang, P.C., Wang, R.Y., Unnikrishnan, B., Mao, J.Y., Chen, S.Y. and Huang, C.C., 2019. High amplification of the antiviral activity of curcumin through transformation into carbon quantum dots. *Small*, 15(41), p.1902641.https://doi.org/10.1002/smll.201902641

Lin, G.H., Lee, Y.J., Choi, D.Y., Han, S.B., Jung, J.K., Hwang, B.Y., Moon, D.C., Kim, Y., Lee, M.K., Oh, K.W. and Jeong, H.S., 2012. Anti-amyloidogenic effect of thiacremonone through anti-inflammation in vitro and *in vivo* models. *Journal of Alzheimer's Disease*, 29(3), pp.659-676.https://doi.org/10.3233/JAD-2012-111709

Liu, Z., Huang, P., Law, S., Tian, H., Leung, W. and Xu, C., 2018. Preventive effect of curcumin against chemotherapy-induced side-effects. *Frontiers in Pharmacology*, 9, p.1374.

Łoczechin, A., Séron, K., Barras, A., Giovanelli, E., Belouzard, S., Chen, Y.T., Metzler-Nolte, N., Boukherroub, R., Dubuisson, J. and Szunerits, S., 2019. Functional carbon quantum dots as medical countermeasures to human coronavirus. *ACS Applied Materials & Interfaces*, 11(46), pp.42964-42974. https://doi.org/10.1021/acsami.9b15032

Mishra, S. and Palanivelu, K., 2008. The effect of curcumin (turmeric) on Alzheimer's disease: an overview. *Annals of Indian Academy of Neurology*, *11*(1), p.13.https://doi.org/10.4103/0972-2327.40220

Moghadamtousi, S. Z., Abdul Kadir, H., Hassandarvish, P., Tajik, H., Abubakar, S. and Zandi, K., 2014. A review on antibacterial, antiviral, and antifungal activity of curcumin. *BioMed Research International*, 2014.https://doi.org/10.1155/2014/186864

Monteil, V., Kwon, H., Prado, P., Hagelkrüys, A., Wimmer, R.A., Stahl, M., Leopoldi, A., Garreta, E., Del Pozo, C.H., Prosper, F. and Romero, J.P., 2020. Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2. *Cell*, 181(4), pp.905-913.https://doi.org/10.1016/j.cell.2020.04.004

Ojha, L., Tüzün, B., and Bhawsar, J., 2020. Experimental and theoretical study of effect of allium sativum extracts as corrosion inhibitor on mild steel in 1 M HCl medium. *Journal of Bio- and Tribo-Corrosion.* 6.

Pandey, P., Khan, F., Kumar, A., Srivastava, A. and Jha N.K., 2021. Screening of potent inhibitors against 2019 novel coronavirus (Covid-19) from *Allium sativum* and *Allium cepa*: an in silico approach. *Biointerface Research in Applied Chemistry,* 11(1), p. 7981–93. https://doi.org/10.33263/BRIAC111.79817993

Pang, X. F., Zhang, L. H., Bai, F., Wang, N. P., Garner, R. E., McKallip, R. J., and Zhao, Z. Q., 2015. Attenuation of myocardial fibrosis with curcumin is mediated by modulating expression of angiotensin II AT1/AT2 receptors and ACE2 in rats. *Drug Design, Development and Therapy*, 9, pp. 6043–6054.https://doi.org/10.2147/DDDT.S95333

Rajagopal K, Byran G, Jupudi S, and Vadivelan R. 2020. Activity of phytochemical constituents of black pepper, ginger, and garlic against coronavirus (COVID19): an in silico approach.*International Journal of Research in Health and Allied Sciences*, 9(5), pp. 43–50. https://doi.org/10.4103/ijhas.IJHAS_55_20

Sahebkar, A., Cicero, A.F., Simental-Mendía, L.E., Aggarwal, B.B. and Gupta, S.C., 2016. Curcumin downregulates human tumour necrosis factor-α levels: a systematic review and meta-analysis of randomized controlled trials. *Pharmacological Research*, 107, pp.234-242.https://doi.org/10.1016/j.phrs.2016.03.026

San Chang, J., Wang, K. C., Yeh, C. F., Shieh, D. E., & Chiang, L. C. (2013). Fresh ginger (Zingiber officinale) has anti-viral activity against human respiratory syncytial virus in human respiratory tract cell lines. *Journal of ethnopharmacology*, *145*(1), 146-151.https://doi.org/10.1016/j.jep.2012.10.043

Singh, S. and Aggarwal, B.B., 1995. Activation of transcription tactor NF-κB is suppressed by Curcumin (Diferuloylmethane). *Journal of Biological Chemistry*, 270(42), pp.24995-25000. https://doi.org/10.1074/jbc.270.42.24995

Thimmulappa, R. K., Mudnakudu-Nagaraju, K. K., Shivamallu, C., Subramaniam, K. J. T., Radhakrishnan, A., Bhojraj, S. and Kuppusamy, G., 2021. Antiviral and immunomodulatory activity of curcumin: a case for prophylactic therapy for COVID-19, *Heliyon,* 7 (2),P.e06350. https://doi.org/10.1016/j.heliyon.2021.e06350

Venkatesan, N., Punithavathi, D., and Babu, M., 2007. Protection from acute and chronic lung diseases by curcumin. *Advances in Experimental Medicine and Biology*, 595, pp. 379–405.

Wahab, N., Lajis, N., Abas, F., Othman, I. and Naidu, R., 2020. Mechanism of anti-cancer activity of curcumin on androgen-dependent and androgen-independent prostate cancer. *Nutrients.,* 12, p. 679.https://doi.org/10.3390/nu12030679

Wang, X., An, X., Wang, X., Bao, C., Li, J., Yang, D., and Bai, C., 2018. Curcumin ameliorated ventilator-induced lung injury in rats. *Biomedicine and Pharmacotherapy*, 98, pp. 754–761.https://doi.org/10.1016/j.biopha.2017.12.100

Wen, C.C., Kuo, Y.H., Jan, J.T., Liang, P.H., Wang, S.Y., Liu, H.G., Lee, C.K., Chang, S.T., Kuo, C.J., Lee, S.S. and Hou, C.C., 2007. Specific plant terpenoids and lignoids possess potent antiviral activities against severe acute respiratory syndrome coronavirus. *Journal of Medicinal Chemistry*, 50(17), pp.4087-4095.https://doi.org/10.1021/jm070295s

Yao, Q., Ye, X., Wang, L., Gu, J., Fu, T., Wang, Y., Lai, Y., Wang, Y., Wang, X., Jin, H. and Guo, Y., 2013. Protective effect of curcumin on chemotherapy-induced intestinal dysfunction. *International Journal of Clinical and Experimental Pathology*, 6(11), p.2342.