

A Systemic Review: Structural Mechanism of SARS-CoV-2A and promising Preventive Cure by Phytochemicals

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ABSTRACT

The novel corona virus 2019-nCoV has recently emerged as a human pathogen in the city of Wuhan in China's Hubei province, causing fever, severe respiratory illness, and pneumonia disease recently named COVID-19 (1, 2).

The world experienced the outbreaks of corona virus infection that threaten global pandemic in 2002-2003 by Severe Acute Respiratory Syndrome (SARS) and in 2011 by Middle East Respiratory Syndrome (MERS). The genomic sequence of SARS-CoV-2 showed similar, but distinct genome composition of SARS-CoV and MERS-CoV. Phytochemicals are a powerful group of compounds, belonging to secondary metabolites of plants and including a diverse range of chemical entities such as polyphenols, flavonoids, steroidal saponins, organ Sulphur compounds, and vitamins. The potential biological benefits such as antioxidant, anti-inflammatory, anticancer, antibacterial, antifungal and antiviral activities.

The ideal technology would be vaccine that gives lifelong immunity with a single dose. When whole world community of scientist working hard to find out clinical solution of this problem so mean time we have to work with what we have in hand the best prevention approach and the phytonutrient could be a one of them.

Keywords: Social media platforms; Digital credit; Agricultural value addition; Artificial intelligence

INTRODUCTION

The novel corona virus 2019-nCoV has recently emerged as a human pathogen in the city of Wuhan in China's Hubei province, causing fever, severe respiratory illness, and pneumonia disease recently named COVID-19 (1, 2).

The world experienced the outbreaks of corona virus infection that threaten global pandemic in 2002-2003 by Severe Acute Respiratory Syndrome (SARS) and in 2011 by Middle East Respiratory Syndrome (MERS). The genomic sequence of SARS-CoV-2 showed similar, but distinct genome composition of SARS-CoV and MERS-CoV. [3-4]

The World Health Organization (WHO) also declared a global emergency on January 31st due to increasing concerns over its fast spread, and on March 11th the disease was recognized as a pandemic.

As of today, 26 Apr 2020 around 3million cases was reported that infected by corona virus with 200,000 deaths while 840,000

has been recovered. The distribution of total cases and daily projection of cases given in Figure-01

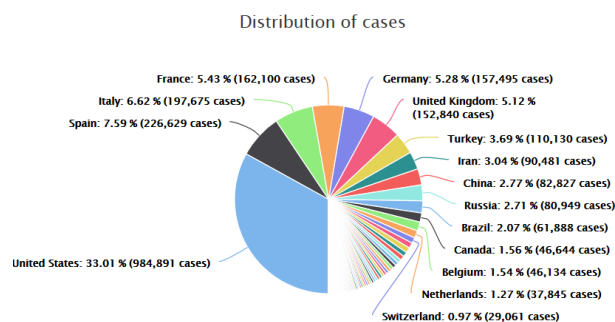


Figure 1: Worldwide distribution of COVID-19 cases [5].

On an average corona hit the 1.5% to 2020 global GDP and 0.2% to long-run global GDP. We forecast a muted long-term impact because damage to productive capacity will be small, plus

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economic confidence should quickly return once the virus subsides.[6-7]

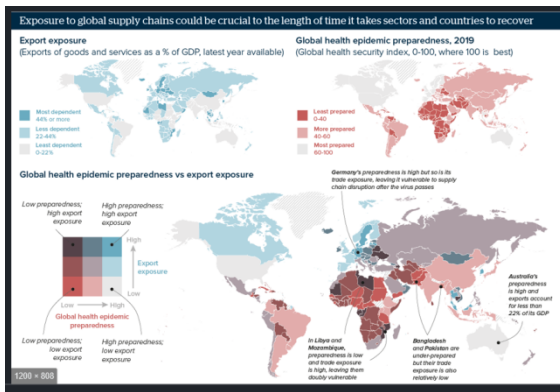


Figure 2: Health preparedness and trade affect COVID-19 exposure. <https://dailybrief.oxan.com/Analysis/GA251067/Health-preparedness-and-trade-affect-COVID-19-exposure>

Human pathogenic subtypes of CoV are associated with mild clinical symptoms. However, severe acute respiratory syndrome related corona virus (SARS-CoV) and Middle East respiratory syndrome corona virus (MERS-CoV) are the two notable exceptions. In 2012, MERS-CoV was first detected in Saudi Arabia. It was responsible for 2,494 confirmed cases, which led to 858 fatalities [8]. In 2002, a subtype of the beta-COV rapidly spread across Guangdong, China. This outbreak resulted in 8,000 infections and 774 fatalities in 37 countries [9]. The outbreak in 2020 has presented in the form of pneumonia. Initially, this virus was designated as 2019-nCoV. However, the International Committee on Taxonomy of Viruses designated it as the SARS-CoV-2 virus [10-13].

The aids epidemic offers an example the broad goal of course is to end the disease the highest leverage approach is prevention. The ideal technology would be vaccine that gives lifelong immunity with a single. When whole world community of scientist working hard to find out clinical solution of this problem so mean time we have to work with what we have in hand the best prevention approach and the phytonutrient could be a one of them.

Phytochemicals are a powerful group of compounds, belonging to secondary metabolites of plants and including a diverse range of chemical entities such as polyphenols, flavonoids, steroidal saponins, organ Sulphur compounds, and vitamins. The potential biological benefits such as antioxidant, anti-inflammatory, anticancer, antibacterial antifungal and antiviral activities. The high bioavailability and low cytotoxicity of natural phytochemical it would be great possible candidate in this situation. Here author intended to discuss the mechanism of antiviral properties of few phytochemical toward the SARS - COVID-19 and how it would be a preventive approach in the pandemic situation [14-17].

Clinical mechanism of SARS spike protein in host cell

Coronavirus (CoV) is a large family of positive-sense, single-stranded RNA virus that. Their viral RNA genome ranges from 26 to 32 kilobases in length [18]. The virus has four important

structural proteins which are (E) the envelope protein (M) the membrane protein (S) the spike protein and (N) the nucleocapsid protein, which are required to regulate the function and viral structure [19] among these virus S and N will help to attachment of virus with host cells. The attachment of virus to the host cells [20]

The S protein has three major sections which are the large ectodomain, a single-pass trans membrane anchor and a short intracellular tail. These play a major role in anchoring the host cells. Among these sections has two subunits which are the S1 receptor-binding subunit and S2 the membrane fusion subunit.

During infection, the S protein is cleaved into subunits, S1 and S2. S1 contains the receptor binding domain (RBD) which allows coronaviruses to directly bind to the peptidase domain (PD) of ACE2. S2 then likely plays a role in membrane fusion. [21]

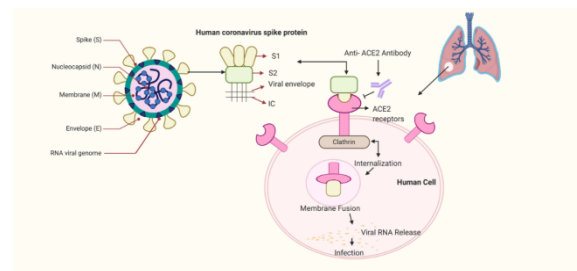


Figure 3: Mechanism of COVID-19 Virus infects to host cell [22].

Studies, suggests ACE2 needs to dimerism to be active. The resultant homodimer has two PDs, able to bind two COVID-19 S protein trimmers simultaneously. in the current study, the team identified that the structures could only bind if the PD interacts with the up RBD.

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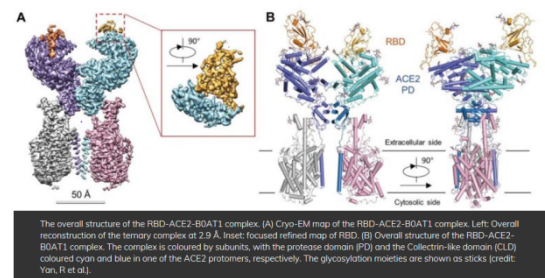


Figure 4: Mechanism of SARS Cov-2 spike protein association with host cell. <https://www.drugtargetreview.com/news/56895/scientists-demonstrate-how-covid-19-infects-human-cells/> 23

They further compared how SARS-CoV-2-RBD binding is different to other SARS-CoV-RBDs binding; showing that some changes in the sequence may make associations tighter in COVID-19, while others could reduce the binding affinity.

This virus belongs to β -corona virus, a large class of viruses prevalent in nature. Similar to other viruses, SARS-CoV-2 has many potential natural hosts, intermediate hosts and final hosts. Cytokine release syndrome is a vital factor that aggravates disease progression. A higher levels of IL-6 and IL-10, and lower levels of CD4+T and CD8+T are observed in COVID-19 patients parallel with the severity of the disease [7].

Mechanism of antiviral activities of phytochemical

Phytochemical compound works as a legend and - protein at the site where it was known to get involved in host cell binding. Their binding interaction is more stable than with that of recently available drug. Similarly, it was also seen that these molecules attach to those sites of ACE2 which were involved in serving a medium of viral entry. Thus, it is apparent from the present study that viral infection can be prevented by Phytochemicals.

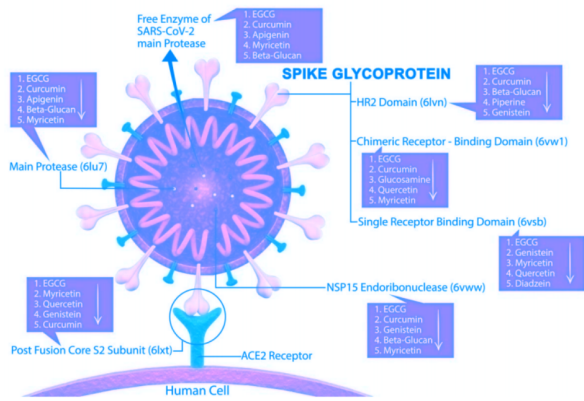


Figure 5: Phytochemical preventive mechanism toward -COVID19. <https://practical-evolutionary-health.com/> [26]

Phytochemicals bind to S this would rather serve dual inhibitory machinery by blocking host cell receptor to virus and viral protein entry. Moreover, some of the phytochemicals are more potent immuno stimulant and have been reported to induce autophagy, another important mechanism of viral clearance that promote elimination or neutralisation of viral infection [27].

Blocking Mechanism by the activity of viral RNA

Some of the myricetin, scutellarein, and phenolic compounds work as natural inhibitors against the SARS-Covid19. They show the different antiviral mechanisms against SARS-CoV that include inhibiting the viral 3CL protease and blocking the activity of viral RNA-dependent RNA polymerase[29]

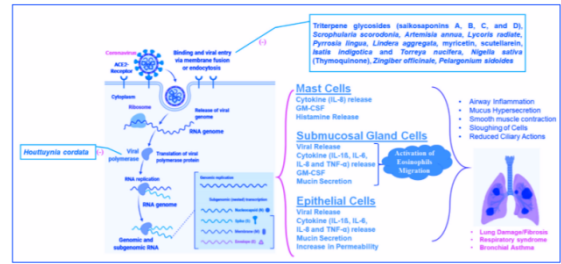


Figure 6: Schematic illustration of a viral transmission (Corona virus) replication cycle and infection on the pathogenesis of viral infection.

Molecular docking is a computational method which aims to identify non-Covalent binding between protein (receptor) and a small molecule (ligand/Inhibitor). Docking predicts the mode of interaction between a target protein and a small ligand for an established binding site.[28]

Phytochemical compound works as a legend. The SARS-CoV-2S is a surface glycoprotein. This protein plays important roles during viral attachment, fusion and entry into the host cells [33]. Biologically this protein exists in a heterotrimeric form with three separate polypeptide chains: chain A, B and C, forming each monomer [25]. Ligands to investigate their binding affinity with SARS-CoV-2S chain A as the receptor target protein [24-26].

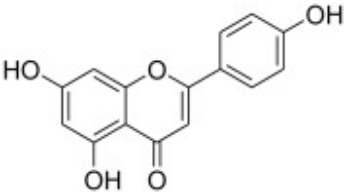
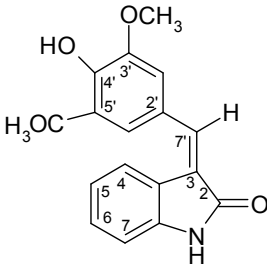
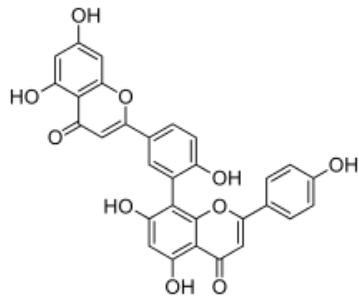
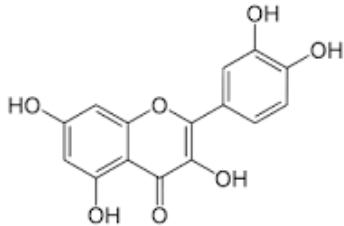
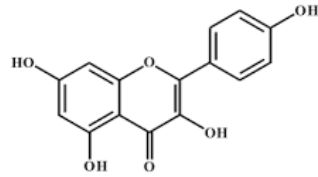
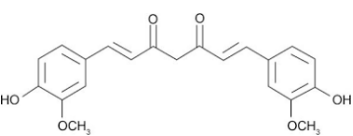
Activity of few Phytochemical -SARS covid-19

Medicinal plant compounds are already used to successfully treat numerous viral diseases. Currently no effective treatment is available for COVID-19. Phytochemicals could be an effective tool by increase the Immunity and can transform in to the clinical drug. Thus, it is necessary to further examine the topic of antiviral phytochemicals, highlighting drug delivery applications in overcoming the multiple biological barriers existing for antiviral agents to successfully reach their intended site(s) of action. Here author focus to explain about few phytochemical they could be a next possible treatment against the pandemic situation.

Ginger, Zingiberofficinale, is a widely used has been found active against Human Respiratory Syncytial Virus (HRSV)-induced plaque formation on the epithelium of the airways through blocking viral attachment and internalization. Interestingly, an extract of Pelargonium sidoides reduces rhinovirus infection through modulation of viral binding proteins on human bronchial epithelial cells [37]. For the management of acute bronchitis and acute respiratory tract infections [29].

It's reported these natural compounds effectively prevent the early stage of HCoV-22E9 infection, including viral attachment and penetration. saikosaponins (A, B2, C, and D), which are naturally occurring **triterpeneglycosides** isolated from medicinal plants such as Bupleurum spp. Heteromorpha spp., and Scrophulariascorodonia exert **antiviral activity** against HCoV-22E9. Natural inhibitors against the SARS-CoV enzymes, such as the nsP13 **helicase** and 3CL **protease**, have been identified as well and include **myricetin**, scutellarein, and

phenolic compounds from *Isatisindigotica* and *Torreyanucifera* (Table 1) [36-40].

Name of phytochemical	Mode of action	Structure	Source	Reference
Apigenin	Apigenin inhibited EV-A71 infection by suppressing viral internal ribosome entry site (IRES) activity.		Fruit and vegetable parsley, celery, celeriac, and chamomile tea	[36]
Isatisindigotica	SARS-CoV protease inhibitor	3CL 	Phenolic compound woad dyer's woad, or glastum,	[38]
Amentoflavone	SARS-CoV protease inhibitor	3CL 	Torreyanuciferajapaneasenutmag	[39]
Quercetin	Reduced RNA and protein synthesis and antioxidant activity.		Red (grape) wines, leaves of radish (<i>Raphanusraphanistrum</i> subsp. <i>sativus</i>) and fennel (<i>Foeniculumvulgare</i>), seeds of pepper (<i>Capsicum annuum</i>)	42,45
Kaempferol	Inhibit 3a ion channel of coronavirus		Raspberry (<i>Rubusidaeus</i>), capers (<i>Capparisspinosa</i>), Brussels sprout (<i>Brassica oleracea</i>), black bean (<i>Phaseolus vulgaris</i>) and fruit of grapes	46
Curcumin	By interference of viral replication machinery or suppression of cellular signaling pathways essential for viral replication		Turmeric Indian spice.	

Ashwagandha (*W. somnifera*): It has been reported *W. somnifera* compound, Withanone, docked very well in the binding interface of AEC2-RBD complex, and was found to move slightly towards the interface center on simulation.

Withanone significantly decreased electrostatic component of binding free energies of ACE2-RBD complex. Two salt bridges were also identified at the interface; incorporation of Withanone destabilized these salt bridges and decreased their

occupancies. We postulate, such an interruption of electrostatic interactions between the RBD and ACE2 would block or weaken COVID-19 entry and its subsequent infectivity [30].

Curcumin: Due to the lack of preventive and therapeutic options for many viral infections, numerous studies have been conducted to investigate the antiviral potential of various natural compounds [31-33], Accumulated evidence indicated curcumin plays an inhibitory role against infection of numerous viruses including hepatitis viruses, influenza viruses and emerging arboviruses like the Zika virus (ZIKV) or chikungunya virus (CHIKV), human immunodeficiency virus (HIV), herpes simplex virus 2 (HSV-2) and human papillomavirus (HPV) [21]. Various study shows The mechanisms involve either a direct interference of viral replication machinery or suppression of cellular signaling pathways essential for viral replication, such as PI3K/Akt, NF- κ B [22]. Inosine monophosphate dehydrogenase (IMPDH) enzyme due to rate-limiting activity in the de novo synthesis of guanine nucleotides is suggested as a therapeutic target for antiviral compounds.

Glycyrrhizin: Glycyrrhizin inhibits SARS-associated corona virus (SARS-CoV) replication in Vero cells with a selectivity index of 67. In addition to inhibition of virus replication, glycyrrhizin is able to inhibit adsorption and penetration of the virus during the early steps of the replicative cycle. The studies from show that glycyrrhizin induces nitrous oxide synthase in Vero cells and that virus replication is inhibited when a nitrous oxide donor (DETA Nonoate) is added to the culture medium [40,44].

Quercetin: Quercetin compound with phenolic group occurs widely in nature, found in berries, fruits, grains, onion, kale and vegetables. It neutralizes potentially damaging free radicals through the donation of a hydrogen atom. The antioxidant activity is a key interest in current situation. Computer modeling techniques to identify these molecules as conceivably block the "ACE2 receptors" on cells to which the corona virus that causes COVID-19 attaches, much like a key fits into a lock. Once the virus enters a cell it hijacks the cellular machinery and uses it to reproduce and crank out more viruses. Based on its molecular structure, quercetin could be a "key" that fits the lock and blocks other "keys" [46].

Studies reveals kaempferol has high bioavailability. In particular, The fact that these drugs not only block the 3a channel, thus counteracting virus production, but that they also interfere with other steps of the viral life cycle emphasizes the importance of multi-target phytochemical. The glycosides of kaempferol seem to be highly potent candidates for development as anti-coronaviral agents [46].

CONCLUSION

This is a unfortunate truth that a lot of world population will contract SARS-CoV infection. While specific treatment is not yet coming soon, individual preventive and protective measures drive the personal risk of getting the disease. Due to high bioavailability, efficacy phytochemicals is a promising preventive option in this situation. Include phytochemical rich food like curcumin, Ginger below the daily intake limit could be prevent the un-effected population of world by the pandemic situation.

Author not support to take any kind of those .more attention, research development and clinical trial would be need to became a rising clinical option and development of safe drugs. Author promotes to avoid COVID-19 in addition to a healthy diet, following precautions provided by the Centers for Disease Control and Prevention can help keep you safe.

CONFLICTS OF INTEREST

The authors report no conflicts of interest in this work.

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REFERENCES

1. Nimesh Singh and Archana Panday. Corona Virus: A Review Article to Identify Novel Drug for Treatment. International journal of Science & Research. 2020;9(4):2319-7064.
2. Chan JF, Yuan S, Kok KH, To KK, Chu H, et al. A familial cluster of pneumonia associated with the 2019 novel coronavirus indicating person-to-person transmission: a study of a family cluster. The Lancet. 2020;395(10223):514-23.
3. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, Zhang L, Fan G, Xu J, Gu X, Cheng Z. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. The lancet. 2020;395(10223):497-506.
4. Cyranoski D. Did pangolins spread the China coronavirus to people? Nature. 2020.
5. COVID-19 Coronavirus Pandemic. <https://www.worldometers.info/coronavirus/>
6. Andersen K, Caldwell P. Morningstar's View: The Impact of Coronavirus on the Economy. 2020.
7. Health preparedness and trade affect COVID-19 exposure. Oxford Analytica Daily Brief. 2020.
8. Scientists demonstrate how COVID-19 infects human cells. Drug Target Review. 2020.
9. Wang LS, Wang YR, Ye DW, Liu QQ. A review of the 2019 Novel Coronavirus (COVID-19) based on current evidence. International journal of antimicrobial agents. 2020 Mar 19:105948.
10. Organization WHO. Coronavirus disease 2019(COVID-19) Situation Report-40. 2020.
11. Chan JF, To KK, Tse H, Jin DY, Yuen KY. Interspecies transmission and emergence of novel viruses: lessons from bats and birds. Trends in microbiology. 2013;21(10):544-555.
12. Zhu N, Zhang D, Wang W, Li X, Yang B, et al. A novel coronavirus from patients with pneumonia in China, 2019. New England Journal of Medicine. 2020.
13. Thevarajan I, Nguyen TH, Koutsakos M, Druce J, Caly L, et al. Breadth of concomitant immune responses prior to patient recovery: a case report of non-severe COVID-19. Nature medicine. 2020;26(4):453-455.
14. Forni C, Facchiano F, Bartoli M, Pieretti S, Facchiano A, et al. Beneficial role of phytochemicals on oxidative stress and age-related diseases. BioMed research international. 2019.
15. Panche AN, Diwan AD, Chandra SR. Flavonoids: an overview. Journal of nutritional science. 2016;5.

16. Kumar S, Pandey AK. Chemistry and biological activities of flavonoids: an overview. *The scientific world journal*. 2013.
17. Hassan SA, Sheikh FN, Jamal S, Ezeh JK, Akhtar A. Coronavirus (COVID-19): a review of clinical features, diagnosis, and treatment. *Cureus*. 2020;12(3).
18. Schoeman D, Fielding BC. Coronavirus envelope protein: current knowledge. *Virology journal*. 2019;16(1):1-22.
19. Walls AC, Park YJ, Tortorici MA, Wall A, McGuire AT, Veasler D. Structure, function, and antigenicity of the SARS-CoV-2 spike glycoprotein. *Cell*. 2020.
20. Campbell GR, Pasquier E, Watkins J, Bourgarel-Rey V, Peyrot V, Esquieu D, Barbier P, de Mareuil J, Braguer D, Kaleebu P, Yirell DL. The glutamine-rich region of the HIV-1 Tat protein is involved in T-cell apoptosis. *Journal of Biological Chemistry*. 2004;279(46):48197-204.
21. Vellingiri B, Jayaramayya K, Iyer M, Narayanasamy A, Govindasamy V, et al. COVID-19: A promising cure for the global panic. *Science of the Total Environment*. 2020;4:138277.
22. Scientists demonstrate how COVID-19 infects human cells. *Drug Target Review*.
23. Pandey P, Rane JS, Chatterjee A, Kumar A, Khan R, Prakash A, Ray S. Targeting SARS-CoV-2 spike protein of COVID-19 with naturally occurring phytochemicals: An in silico study for drug development. *Journal of Biomolecular Structure and Dynamics*. 2020;1-11.
24. Belouzard S, Millet JK, Licitra BN, Whittaker GR. Mechanisms of coronavirus cell entry mediated by the viral spike protein. *Viruses* 2012;4(6):1011-1033.
25. Zhou Y, Simmons G. Development of novel entry inhibitors targeting emerging viruses. *Expert review of anti-infective therapy*. 2012;10(10):1129-1138.
26. DeLano WL. The PyMOL molecular graphics system. <http://www.pymol.org>. 2002.
27. Jena AB, Kanungo N, Nayak V, Chainy GB, Dandapat J. Catechin and Curcumin interact with corona (2019-nCoV/SARS-CoV2) viral S protein and ACE2 of human cell membrane: insights from Computational study and implication for intervention.
28. Chandel V, Raj S, Rathi B, Kumar D. In Silico Identification of Potent COVID-19 Main Protease Inhibitors from FDA Approved Antiviral Compounds and Active Phytochemicals through Molecular Docking: A Drug Repurposing Approach.
29. Ahmad A, Rehman MU, Alkharfy KM. An alternative approach to minimize the risk of coronavirus (Covid-19) and similar infections. *European Review for Medical and Pharmacological Sciences*. 2020;24(7):4030-2034.
30. Balkrishna A, POKHREL S, Singh J, Varshney A. Withanone from *Withania somnifera* may inhibit novel Coronavirus (COVID-19) entry by disrupting interactions between viral S-protein receptor binding domain and host ACE2 receptor.
31. Steinmann J, Buer J, Pietschmann T, Steinmann E. Anti-infective properties of epigallocatechin-3-gallate (EGCG), a component of green tea. *British journal of pharmacology*. 2013;168(5):1059-1073.
32. Praditya D, Kirchhoff L, Brüning J, Rachmawati H, Steinmann J, Steinmann E. Anti-infective properties of the golden spice curcumin. *Frontiers in microbiology*. 2019 May 3;10:912.
33. Mathew D, Hsu WL. Antiviral potential of curcumin. *Journal of functional foods*. 2018;40:692-699.
34. Zorofchian MS, Hajrezaei M, Abdul Kadir H, Zandi K. *Loranthus micranthus* Linn.: biological activities and phytochemistry. *Evidence-Based Complementary and Alternative Medicine*. 2013.
35. Yoshikawa TT, High KP. Nutritional strategies to boost immunity and prevent infection in elderly individuals. *Clinical infectious diseases*. 2001;33(11):1892-900.
36. World Health Organization: Available from: <http://www.who.int>. [Last accessed on 2013 Sep 18].
37. Li SY, Chen C, Zhang HQ, Guo HY, Wang H, et al. Identification of natural compounds with antiviral activities against SARS-associated coronavirus. *Antiviral research*. 2005;67(1):18-23.
38. Lin CW, Tsai FJ, Tsai CH, Lai CC, Wan L, et al. Anti-SARS coronavirus 3C-like protease effects of *Isatis indigotica* root and plant-derived phenolic compounds. *Antiviral research*. 2005;68(1):36-42.
39. Ryu YB, Jeong HJ, Kim JH, Kim YM, Park JY, et al. Biflavonoids from *Torreya nucifera* displaying SARS-CoV 3CLpro inhibition. *Bioorganic and medicinal chemistry*. 2010;18(22):7940-7947.
40. Fiore C, Eisenhut M, Krausse R, Ragazzi E, Pellati D, Armanini D, Bielenberg J. Antiviral effects of Glycyrrhiza species. *Phytotherapy Research: An International Journal Devoted to Pharmacological and Toxicological Evaluation of Natural Product Derivatives*. 2008;22(2):141-148.
41. Liou CJ, Cheng CY, Yeh KW, Wu YH, Huang WC. Protective effects of casticin from *Vitex trifolia* alleviate eosinophilic airway inflammation and oxidative stress in a murine asthma model. *Frontiers in pharmacology*. 2018 Jun 14;9:635.
42. Lalani S, Poh CL. Flavonoids as antiviral agents for Enterovirus A71 (EV-A71). *Viruses*. 2020;12(2):184.
43. Cinatl J, Morgenstern B, Bauer G, Chandra P, Rabenau H, et al. Glycyrrhizin, an active component of liquorice roots, and replication of SARS-associated coronavirus. *The Lancet*. 2003;361(9374):2045-6.
44. Lin LT, Hsu WC, Lin CC. Antiviral natural products and herbal medicines. *Journal of traditional and complementary medicine*. 2014;4(1):24-35.
45. <https://www.mcgill.ca/oss/article/health/quercetin-take-or-not-take>
46. Schwarz S, Saute D, Wang K, Zhang R, Sun B. Kaempferol Derivatives as Antiviral Drugs against the 3a Channel Protein of Coronavirus. 2014;80(02-03):177-182.