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

Roli Jain*, Sandeep Shukla, Neeti Nema, Archna Panday, Hari Singh Gour

Department of Chemistry, Central University, INDIA

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

![Worldwide distribution of COVID-19 cases](image)

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...
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/6A251067/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.

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

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

They further compared how SARS-CoV2-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 \( \beta \)-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.

**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 |

**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, Zingiber officinale, 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 internalisation. 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 Scrophulariaceorodonia 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].

<table>
<thead>
<tr>
<th>Name of phytochemical</th>
<th>Mode of action</th>
<th>Structure</th>
<th>Source</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apigenin</td>
<td>Apigenin inhibited EV-A71 infection by suppressing viral internal ribosome entry site (IRES) activity.</td>
<td><img src="image" alt="Apigenin Structure" /></td>
<td>Fruit and vegetable parsley, celery, celeriac, and chamomile tea</td>
<td>[36]</td>
</tr>
<tr>
<td>Isatisindigotica</td>
<td>SARS-CoV 3CL protease inhibitor</td>
<td><img src="image" alt="Isatisindigotica Structure" /></td>
<td>Phenolic compound</td>
<td>[38]</td>
</tr>
<tr>
<td>Amentoflavone</td>
<td>SARS-CoV 3CL protease inhibitor</td>
<td><img src="image" alt="Amentoflavone Structure" /></td>
<td>Torreyanucifera japonae sister mag</td>
<td>[39]</td>
</tr>
<tr>
<td>Quercetin</td>
<td>Reduced RNA and protein synthesis and antioxidant activity.</td>
<td><img src="image" alt="Quercetin Structure" /></td>
<td>Red (grape) wines, leaves of radish (Raphanus sativus subsp. sativus) and fennel (Foeniculum vulgare), seeds of pepper (Capsicum annuum)</td>
<td>42,45</td>
</tr>
<tr>
<td>Kaempferol</td>
<td>Inhibit 3a ion channel of coronavirus</td>
<td><img src="image" alt="Kaempferol Structure" /></td>
<td>Raspberry (Rubusidaeus), capers (Capparisspinosa), Brussels sprout (Brassica oleracea), black bean (Phaseolus vulgaris) and fruit of grapes</td>
<td>46</td>
</tr>
<tr>
<td>Curcumin</td>
<td>By interference of viral replication machinery or suppression of cellular signaling pathways essential for viral replication</td>
<td><img src="image" alt="Curcumin Structure" /></td>
<td>Turmeric Indian spice.</td>
<td></td>
</tr>
</tbody>
</table>

**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 studies show 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-kB [22]. Inosine monophosphate dehydrogenase (IMP DH) enzyme due to rate-limiting activity in the de novo synthesis of guanine nucleotides is suggested as a therapeutic target for antiviral compounds.

Glycyrhrizin: Glycyrhrizin inhibits SARS-associated corona virus (SARS-CoV) replication in Vero cells with a selectivity index of 67. In addition to inhibition of virus replication, glycyrhrizin is able to inhibit adsorption and penetration of the virus during the early steps of the replicative cycle. The studies from show that glycyrhrizin 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 countering 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 preventative 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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