

Phytochemicals: promising alternative molecules to fight against SARS-Cov-2 infection

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Abstract

The current pandemic coronavirus disease-2019 (COVID-19) has spread as wild fire globally by severe acute respiratory syndrome novel corona virus 2 (SARS-CoV2) and is probably the most convulsive global event in the history of mankind. There is a lack of effective antiviral agents for many coronavirus strains. Naturally existing phyto-molecules in plants provide a wealth of chemical diversity, including antiviral activity, and thus may have utility as therapeutic agents that can fight against coronaviral infections. This communication provides an insight about various phytochemicals which possess anti-SARS-CoV activity. The most commonly available dietary sources which contain phytochemicals (flavonoids) like quercetin, chrysin, rutin, curcumin possess antiviral. Several studies confirmed the antiviral activity of these phytochemicals against enveloped viruses including present SARS-CoV- 2.

Keywords: COVID-19 (SARS-Cov2), phytochemicals, quercetin, antiviral

Introduction

SARS (CoV-2) which caused coronavirus disease-2019 (COVID-19) is one of the most serious pandemics with widespread morbidity and mortality witnessed globally. Till date there is no effective vaccination and cure against SARS-CoV-2 though few vaccines proved in the containment of deaths. The COVID-19 pandemic has underscored the limitations of the current pool of approved antivirals and has emphasized the need for further discovery and development of therapeutic and prophylactic agents. Developing antiviral drugs is a challenge for the scientific community and pharmaceutical industry.

Repurposing of existing antiviral, anti-inflammatory or antimalarial drugs is an alternative for controlling SARS-CoV-2 with drugs in the present situation of COVID-19 pandemic. Further plants have been utilized throughout human history for a variety of

ailments and are considered inexhaustible sources of novel pharmacologically active compounds against viral, parasitic and protozoan infections. Several phytochemicals and their derivatives have already been approved for both viral and non-viral disease states in recent past. The Ministry of Ayush (India) also started clinical trials for COVID-19 with four Ayurvedic herbs: ashwagandha (*Withania somnifera* (L.) Dunal), guduchi (*Tinospora cordifolia* (Willd.) Miers), yasthimadhu (*Glycyrrhiza glabra* L.), and pipli (*Piper longum* L.) (Ministry of Ayush).

Several natural products have shown anti-SARS-Cov 2 activities both *in vitro* and *in vivo*. Phytochemicals or phytonutrients are plant secondary metabolites produced by the plants which possess therapeutic effects and beneficial to humans in treatment of diseases. Extensive biological investigations have revealed a broad spectrum of pharmacological and physiological activities such as anti-inflammatory, antioxidant, and anti-cancerous that led to its use in the formulation of promising drugs for the treatment of different diseases (Zhang *et al.*, 2015).

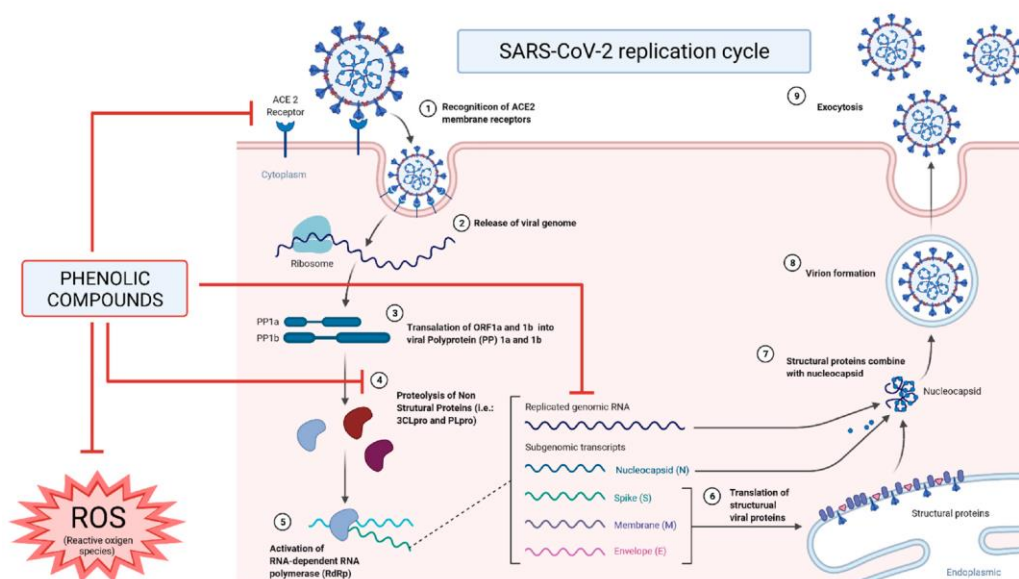


Figure 1. Mechanisms of action and inhibition of phenolic compounds against severe acute respiratory syndrome of coronavirus 2 (SARS-CoV-2) on its replication cycle and in the host's immune response (<https://doi.org/10.3390/foods10092084>)

The phytochemicals possessing antiviral properties include alkaloids, polyphenols, polysaccharides, flavonoids, lecithins, proteins, terpenes, lignans, coumarins, fructans, saponins, quinones, proanthocyanidins, steroids, thiosulfonates etc. Many of these bioactive compounds are known to active against MERS-CoV, SARS-CoV, and SARS-CoV 2 based

on their potential to destroy proteases of coronavirus structural proteins and polymerases essential for replication machinery of these viruses (Khaerunnisa *et al.*, 2020).

SARS-Cov 2 binds to angiotensin-converting enzyme 2 (ACE2) on the host cell surface membrane via a viral spike protein that recognizes ACE2 (Ni *et al.*, 2020). The major druggable targets of SARS-CoV-2 include 3-chymotrypsin-like protease (3CL^{pro}), papain like protease (PL^{pro}), RNA-dependent RNA polymerase, and spike (S) proteins (Wu *et al.*, 2020). Based on current information on mechanism and disease cycle, various therapeutic targets were identified to develop effective treatments against this novel virus. Therefore, the present communication summarizes phytochemicals which are abundantly present in human diet and available in Indian subcontinent as a source of antiviral agents and brings insights in the potential application of phytochemicals and their derivatives, which could help researchers to develop safe drugs against SARS-CoV-2.

Primary mode of action for phytochemicals includes the inhibition of virus entry into host cell by binding with the specific receptor sites in targeted cells and/or halting the replication process of these viruses by destroying viral polymerases and proteases essential to perform important task in viral replication (Fig. 1). Phytomedicines have also proven to boost up immunity against novel coronavirus. The list of commonly available phytochemicals with their probable mechanism of action reported is presented in Table 1.

Table 1: Phytochemicals with potential as anti-SARS-CoV-2 agents

Sl.No	Phytochemical	Inhibition (Target in Virus)	References
1.	Apigenin	3CL ^{pro}	Ryu <i>et al.</i> , 2010
2.	Chrysin	Restrict viral entry	Bhuiyan <i>et al.</i> , 2020
3.	Curcumin	3CL ^{pro}	Wen <i>et al.</i> , 2007
4.	Ellagic acid	RdRp inhibitor, TMPRSS2 inhibitor	Xu <i>et al.</i> , 2021
5.	Gallic acid	RdRp inhibitor, TMPRSS2 inhibitor	Singh <i>et al.</i> , 2020
6.	Glycyrrhizic acid	Virus replication	Hoever <i>et al.</i> , 2005
7.	Hesperetin	3CL ^{pro}	Lin <i>et al.</i> , 2005
8.	Kaempferol	M ^{pro}	Khan <i>et al.</i> (2021)
9.	Naringenin	M ^{pro}	Abdallah <i>et al.</i> (2021)
10.	Quercetin	PL ^{pro}	Abian <i>et al.</i> (2020)
11.	Rutin	PL ^{pro}	Pitsillou <i>et al.</i> (2020)
12.	Saikosaponin B2	Restrict viral entry	Cheng <i>et al.</i> , 2006

Conclusion

Plants provide a vast array of candidates for the treatment of COVID-19. Concerted efforts are needed to maximize resources, including phytochemicals, for the development of treatment agents for COVID-19 and other viral diseases to ease the blow of large viral outbreaks in the future. Phytochemicals are promising alternatives to fight against important viral diseases like SARS-Cov2.

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