



Impact of tea Polyphenols on Coronavirus Disease (COVID- 19) as Immunity Booster: A Review

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Abstract

Due to covid-19 pandemic, many countries imposed lockdown on their citizens to overcome the contamination of the virus. The global pandemic has caused severe threats to the physical health and daily life of peoples around the world and also leads a dramatic loss of human health worldwide and presents an unparalleled challenge to public health, food system and the world of work. More than 10,000 naturally occurring compounds are gathered in the large family of polyphenols having countless Biological and physiological health benefits for human health. This review focused on the polyphenols of green tea and Black tea particularly EGCG (epigallocatechin-3-gallate) and Theaflavins respectively. Tea polyphenols possess the binding sites present on SARS-CoV-2 and interaction properties in them especially with EGCG and theaflavin-3,3'-digallate(TF3). This review concludes the available researches and authenticity which displays the use of polyphenols as potential powers to treat COVID-19.

Keywords: Polyphenols, Green tea, Black tea, EGCG, Theaflavins, SARS-CoV-2.

Introduction

World Health Organization (WHO) has declared the “NOVEL CORONAVIRUS” (COVID-19) as pandemic it is spread rapidly to multiple countries all over the world. Before the discovery of novel Corona virus vaccine, all preventive measures were taken for keeping the massive population healthy and safe because COVID-19 targets on those who has poor or less immunity and especially those people who are over or under age [1]. Weak immunity is widely responsible for infections viz. Diabetes, cardiac issues, cancer and Current global Pandemic i.e. Coronavirus or COVID-19 or SARS-CoV-2 i.e. Severe acute respiratory syndrome. To overcome from the threats of COVID-19, it is advisable to be safe along with safety measures issued by WHO on time to time for the sake of strong immunity and to be shielded from COVID-19 [2,3].

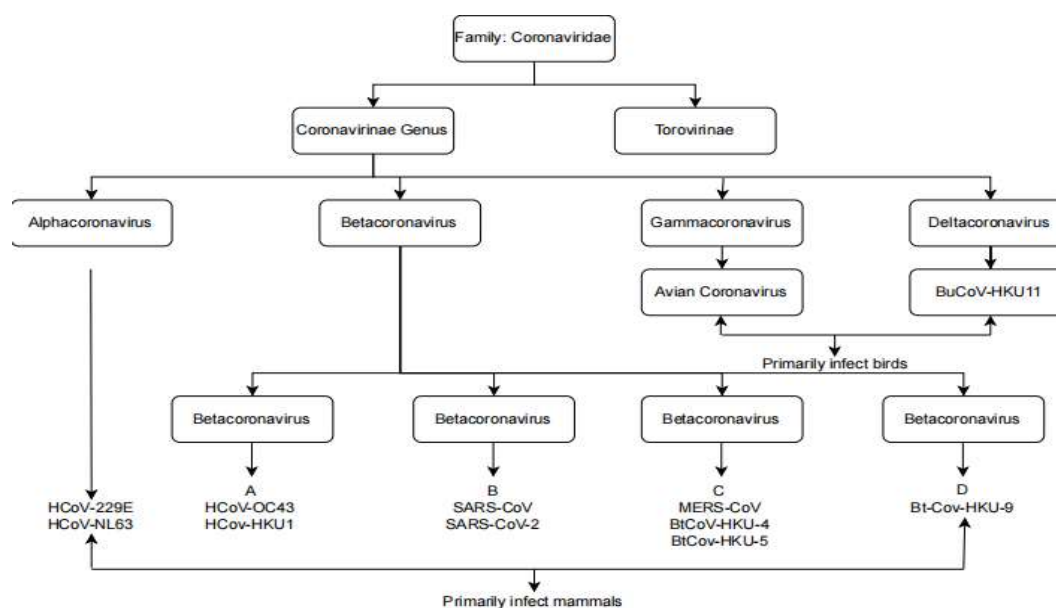


Fig. 1 Classification of Coronavirus

Modern studies shows that the body's immune system increased by the plant based foods and helps the intestinal bacteria by 85%, to get boost while the depletion of immunity gets sucked by the excessive intake of animal foods by the removal of beneficial bacteria from the body and causes inflammation, make diabetic, cardiac issues, Hepatitis-B and other disease. Drinking plenty of water and uses of minerals like Mg, Zn, Micro-nutrients, herbs, food rich in Vit. C, D and B12 can boost the health and overcome the viral infection. [4,5,6,7].

COVID-19 is a viral disease which is transmitted through the cough and sneeze of the infected person by emitting respiratory droplets to the other nearby person and enters to their mouth, nose or eyes. This transmission covers the respiratory system containing epithelial cells and the affected organ gets inflamed. This causes alveolar damage and leads to pneumonia [8,9].

This article focused on the various activities and properties of phytochemical agents containing various Polyphenols which are the major constituents of Green and Black tea [10,11,12]. The main class of Polyphenols on which this review is based are epigallocatechin gallate (EGCG) which is one of the richest Polyphenolic catechin found in *Camellia Sinensis* i.e., Green Tea and Theaflavins in Black tea respectively [13]. During COVID-19 pandemic both types of teas has proven its potential power against virus for its antiviral activity against Corona virus and proven its betterment rather than by treating through various synthetic chemical drugs [14]. It has been shown beyond doubts its supremacy as anti-inflammatory, anti-oxidative, antibacterial and anti-proliferative in addition of its antiviral effects [15,16,17], While on the other hand Black tea contains the Polyphenols known as Theaflavins and its derivative found in Black Tea are Theaflavin (TF1), Theaflavin-3-Gallate

(TF2A), Theaflavin-3'- Gallate (TF2 B) and Theaflavin-3-3'- Gallate (TF3) respectively [18,19,20,21].

Intake of Black tea improves postprandial blood sugar levels in normal and prediabetic adults and perform the role of antimicrobial activator to kill the growth of harmful bacteria and excess generation of free radicals diminished by Polyphenolic Black tea by neutralizing the harmful effects of elevated free radical level and also reduces the chances of onset of membrane chronic disorders [22,23,24,25].

This unique properties of both Polyphenols which are natural, simple, economical and environment friendly which enlightens the pathway and explains the importance in human health significantly on account of its antiviral activities as to enhance immunity by consuming them and to face the threats of infectious disease like COVID-19. [26,27]

Structure And Working Of SARS-CoV-2

Non-segmented, enveloped single stranded RNA (ss RNA) ranges between 26 to 32 Kb length are the specifications of Coronavirus [25,26]. It is the largest genome among the RNA virus. Electron microscopy structure of Coronavirus reveals the spherical shape of negative stained SARS-CoV-2 having studded outer surface and 60-140 nm of diameter and spikes of length 9-12 nm which give the degree of solar Corona virus to them because of its sun like structure [27,28].

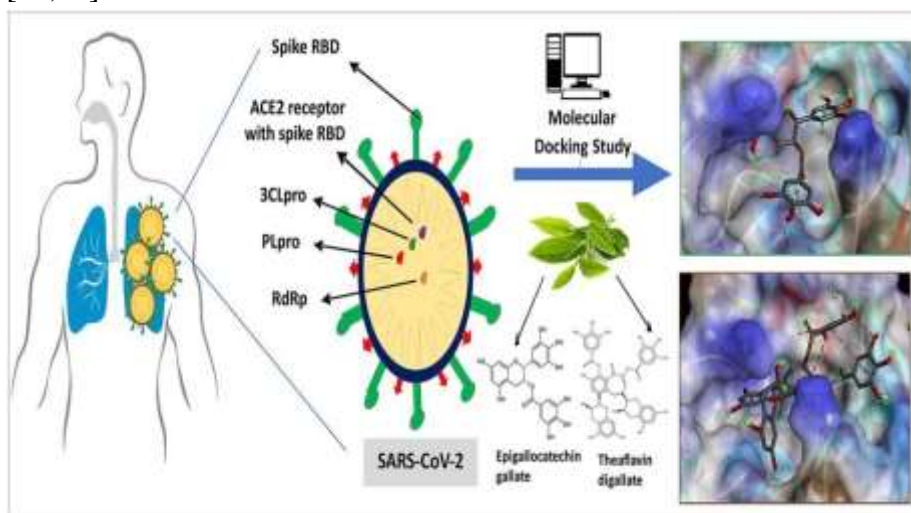


Fig. 2 Structure and Working of SARS-CoV-2

The virus firstly aims at the respiratory tract particularly to the lower one and ends up to the severe lung injury and the people having weak immunity and

among elders it leads to severe pneumonia and acute inflammation that blocks airpath [29] and then cause fatality by multi-organ failure. During infection two main phases are included

1.Incubation. [non severe]

2.Massive Destruction [severe]

A successive immune response is responsible to eliminate the virus in the first phase in order to prevent biological tissues from the initialization of second phase of infection from transmission. That's why it is crucial to have good health, strong immunity power and healthy genetic background for the sake of the development of an endogenous protective immune response.[30,31,32].

On the other hand , in second phase spreading of virus and quantitative destruction of severe lungs inflammation by mediating through pro-inflammatory macrophages, granulocytes, inflammatory cytokines generation and IL-6 and IP-10 chemokines,[33,34] macrophage inflammatory protein such as MIP 1 α ,MIP 1 β and MCP 1.Due to this monocytes, macrophages and T cells are gets enclosed by these inflammatory molecules to the infected sites which on addition generates extra pro-inflammatory cytokines that causes dis-function of lungs by swelling of lungs and then cytokines stuck up the circulatory system and causes multi organ damage[35,36].

Inhibitory Effect of EGCG And Theaflavins On SARS-CoV-2

Coronavirus causes lethal effects on living tissues by causing common cold symptoms. Initially, the symptoms like fever, fatigue, dry cough and body ache by taking account of sore throat, headache and diarrhea appears. These proceeds later through breathing difficulty and hypoxia due to the secretion of pro-inflammatory factor IL-6,IL-17 and TNF - α elevation and the circulatory lymphocyte depleted[37,38,39].

SARS-CoV-2 Genome and sub genome have six open reading frames by the encoding of four major structural protein (M) and 3C like protease (3-Chymotrypsin like protease, 3CL pro) are effectively linked up to the virus replication and recognition. [40,41]

Recent research studies based on computational data support that EGCG and Theaflavin are inhibitors of SARS-CoV-2 3CL-protease and in silico molecular docking study with SARS-CoV-2 3CL-protease showed that EGCG and Theaflavins strongly binds with 3CL-protease, indicating that EGCG and Theaflavins probably suppress SARS-CoV-2 3CL-protease [42,43,44]

EGCG and 3CL Protease activity at different concentrations effectively inhibits 3CL Protease activity in dose dependent manner. The half inhibitory concentration of EGCG was found to be 7.58 $\mu\text{g/ml}$ which proves the inhibition of SARS-CoV-2 3CL Protease by EGCG [45,46].

During processing of tea leaves the oxidative coupling of Catechins produces major Polyphenolic compound called Theaflavins [47]. As many researches shown that the polyphenols of tea have broad spectrum antiviral activity [48]. Polyphenols have severe affinity to dock to the receptors and provides several interactions. In this way, Molecular docking is the way to understand the exact interaction of EGCG and TF3 with the possible binding sites of SARS-CoV-2 [49,50].

Inhibition in SARS-CoV-2 by Theaflavins have been studied by the addition of 3CL Protease. The results shows that TF effectively suppress 3 CL- Protease activity in dose dependent manner. The half inhibitory concentration of Theaflavins was found to be 8.44 $\mu\text{g/ml}$ which is higher than EGCG. This shows more effectiveness of Theaflavins for inhibition of SARS-CoV-2 [51,52].

Active Binding Sites For SARS-CoV-2 in TFS and EGCG

TFS AND EGCG have proven its inhibition towards 3CL Pro at mild concentration and acts as a good binding agent to the target the receptor binding domain which is a key part of a virus located on its spike that allows it to dock to body receptors to get entered into cells and leads to infection[67,68,69]. So, binding with TF to RECEPTOR BINDING DOMAIN (RBD) in SARS-CoV-2 through the hydrophobic interaction and hydrogen bonds with some points on viral S protein [53,54,55].

Binding effect of EGCG on SARS-CoV-2 done by the formation of RBD-ACE2 complex in the process of binding of EGCG on SARS-CoV-2 [74,75]. Spike protein, cell membrane receptor is the active site through which the virus gets attached into the host cell for replication [56].

SARS-CoV-2 is responsible for proteolytic function which is a matured stage of virus contains enzyme named 3CL Pro which cleaves at least 11 sites on poly-protein named 1a and 1ab respectively of viral genome to cleave NSP4-NSP16. [57]

RNA dependent RNA polymerase, exo and endonuclease, 2'-O-methyl transferase are the important class of protein in viral genome. Among all, 3CL Pro is the most important target drug against COVID-19 [58,59].

Impact Of Theaflavin And EGCG As Immunity Booster

Our immune system is a constitution of different structure like white blood cells, antibodies, complex protein, networks and organs. Some parts of the system act as a inhibitor against virus and bacteria to prevent them to reach to brain while

others hunt and remove from the body [60,61]. In this order developing a strong immunity helps to identify the stranger virus. Boosting of immune health helps to fight from other common bugs like cold or flu virus and COVID-19 pandemic comes prior of all [62,63,64].

Green tea contains flavonoids, antioxidants and anti-inflammatory properties which deals themselves as an immunity booster [86,87]. Its flavonoids reduce bad cholesterol and blood clotting while anti-oxidative and anti-inflammatory properties helps to get rid of skin problems by making glow on it along with mind clearance, increases alertness, relieves stress and reduces mood swings. [65,66,67]

A cup of black tea consumes daily enhances immunity and reduces chronic risk [67]. It also leads to the prevention of body cells and tissues from oxidative stress but also destroys free radicals and boosts immunity [68]. Polyphenols are less toxic than other drugs, which makes them active antiviral candidates [69]. A large number of polyphenols have been characterized, including Theaflavin (TF1), Theaflavin-3-O-gallate (TF2a), Theaflavin 3-O-gallate (TF2b), Theaflavin 3,3'-digallate (TF3), myrcetin, EGCG, hesperidin, and quercetin. Polyphenols have been assessed for their potential to serve as SARS-CoV-2 RdRp inhibitors. In docking experiments, selected polyphenols have been found that the active site of SARS-CoV-2 RDRP has been interacted with it to indicates its potential to serve as an inhibitor. EGCG proves its efficacy to block porcine respiratory and reproductive infection with syndrome virus (PRRSV) to control both before and after infection, and a total concentration of 125 μ M EGCG was sufficient to entirely prevent viral cell infectivity [70,71,72,73]

Conclusion

In this review we studied to determine that drinking green tea has enormous health benefits, such as cancer prevention and treatment of infective diseases. Epigallocatechin-3-gallate (EGCG) is the major Catechin component in green tea, having 50–80% of the catechins in a brewed cup of green tea, and in one cup of green tea it contains approx. 100-300 mg of EGCG . In black tea, Theaflavins is the important constituent, and it has also shown several beneficial effects.

It has been concluded that EGCG absorption is relatively high, and its maximum plasma concentration exceeds 1 μ g/mL It is evident that EGCG inhibits the enzymatic activity of the Coronavirus 3CL protease. Moreover, EGCG has been reported to regulate the potential targets, such as RNA-dependent RNA polymerase and the viral spike protein. According to studies it has been found that one minute exposure black tea decreases the virus level to an undetectable level less than 1/1000 of untreated control and used as an

convenient agent for the preventive measure of COVID-19 virus while green tea shows reduction in the infectivity of Sars-CoV-2.

It is proved that green tea and black tea contains a high percentage of EGCG and Theaflavins, it would be valuable to examine the effect of green tea and black tea on the spread of SARS-CoV-2. In addition, further clinical trials will be required to reveal the effect of tea consumption on COVID-19 prognosis. By taking reference of green tea and black tea that both are important source of nutritional immunity and also several viral infectious diseases by their innate immunity response.

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