

# COVID-19

The coronavirus pandemic known as COVID-19 is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). This is a highly pathogenic human coronavirus (CoV) first reported in Wuhan, China, where a pneumonia of unknown cause was detected in December 2019.

On January 30, 2020, the WHO declared the COVID-19 outbreak a global health emergency. On March 11, 2020, the WHO declared COVID-19 as a global pandemic, its first such designation since declaring H1N1 influenza a pandemic in 2009. As the death toll from the COVID-19 pandemic mounts, scientists worldwide continue their push to develop effective treatments and a vaccine for the highly contagious respiratory virus.

This novel CoV belongs to the *Coronaviridae* family, along with SARS-CoV and the Middle East respiratory syndrome coronavirus (MERS-CoV). The three of them are zoonotic viruses and have in common their ability to cause severe infection in humans. Highly pathogenic CoVs are enveloped, positive polarity, single-stranded RNA betacoronaviruses, and their genomes encode non-structural proteins (nsps), structural proteins, and several accessory proteins.

#### THE SYMPTOMS OF COVID-19







#### PREVENTION FROM COVID-19

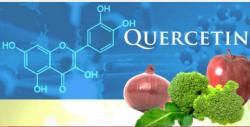












# **QUERCETIN**

Quercetin is a Flavonol—a subtype of potent substances called flavonoids that naturally occur in plants and offer a variety of beneficial health benefits to humans. In particular, quercetin is found in rinds, young shoots, and barks of plants, and is one of the most abundant flavonoids in our diets. Foods that commonly contain guercetin include onions, apples, grapes, berries, broccoli, citrus fruits, cherries, green tea, coffee, red wine, and capers. It is available as a dietary supplement in powder and capsule form. Typical dosages range from 500-1000 mg per day [1, 2].

The beneficial effects of flavonoids like quercetin come from their ability to function as antioxidants inside your body. Antioxidants are compounds that can bind to and neutralize free radicals. Free radicals are unstable molecules that may cause cellular damage when their levels become too high. Damage caused by free radicals has been linked to numerous chronic conditions, cancer, heart disease, and diabetes [3].

Quercetin as a supplement is generally well-tolerated, and side effects are uncommon at doses of 500-1000mg/day. The most common side effects are stomach upset, headache, and tingling of the arms and legs [4].

On its own, quercetin has a low bioavailability, which means your body absorbs it poorly. That's why the supplements may include other compounds, such as vitamin C or digestive enzymes like bromelain, as they may increase absorption [5].

Quercetin is a multipotent bioflavonoid with great potential for the prevention and treatment of disease [6]. Quercetin is said to be one of the most widely used bioflavonoids for the treatment of metabolic and inflammatory disorders [7].

Quercetin glycosides are metabolized, absorbed, and circulated as types of conjugates in the blood. Thereafter, quercetin-3-O- $\beta$ -D-glucuronide (Q3GA), a major metabolite of quercetin, is distributed throughout the body where it may exert beneficial functions in target tissues [8].

The over-the-counter availability and relatively good safety profile serve as the advantages of Quercetin

### **QUERCETIN** for the Treatment of COVID-19

Currently humans are immersed in a pandemic caused by the emerging severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which threatens public health worldwide. The pandemic of coronavirus disease 2019 (COVID-19) caused by the novel severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) presents an unprecedented challenge to identify effective drugs for prevention and treatment. Therefore, effective prevention and treatment medications against human coronavirus are in urgent need. In the past decades, many natural compounds have been reported to possess multiple biological activities, including antiviral properties.

The rapidly expanding knowledge regarding SARS-CoV-2 virology provides a significant number of potential drug targets. The most promising therapy is remdesivir. Remdesivir has potent in vitro activity against SARS-CoV-2 [9].

In principle, all CoV enzymes and proteins involved in viral replication and the control of host cellular machineries are potentially druggable targets in the search for therapeutic options for SARS-CoV-2 [10].

Various viral-based therapeutic options targeting various stages of virus entry and replication are being explored in the antiviral research.

Quercetin is reported to be effective on treatment and prophylaxis of other SARS like coronavirus infections, as a strong antioxidant and scavenger flavonoid without any adverse events. It was shown that quercetin has the ability to chelate zinc ions and act as zinc ionophore. Therefore, quercetin could have antiviral activity against many RNA viruses. It has unique biological properties that may improve the reduction of infection risk.

After the 2003 SARS-CoV-1 coronavirus outbreak, researchers in China found quercetin and other

# Through several screening studies of natural compounds identified quercetin as a promising candidate targeting the SARS-CoV-2 through two mechanisms which are as follows:

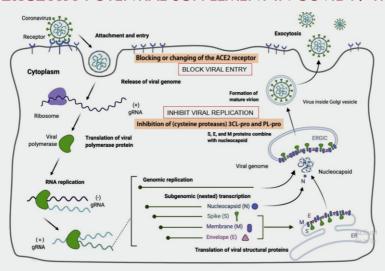
1. Prevention of virus from entering the host cell through inhibition of ACE-2 [12,13.14,15,16,17]

The interaction of Angiotensin Converting Enzyme-2 (ACE-2) with viral spike protein is a critical initial step for the entry of virus to the human host cell.

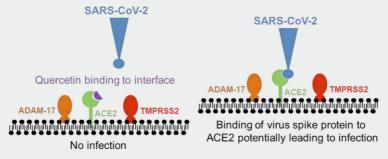
2. Inhibition of cysteine proteases, 3CLpro & PLpro [18, 19]

The viral main protease Mpro or 3-chymotrypsin like proteases (3CLpro) and papain like protease (PLpro) controls the activities of the coronavirus replication complex.

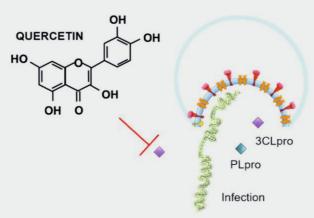
# **QUERCETIN POTENTIAL SUPPLEMENT IN COVID19 TREATMENT**



# **QUERCETIN BLOCKING OF VIRAL ENTRY** [18]



# **QUERCETIN INHIBITION OF VIRAL REPLICATION** [17]



#### **CURRENT CLINICAL TRIALS OF QUERCETIN in COVID-19 Treatment** [20]

# 1. Title: Effect of Quercetin on Prophylaxis and Treatment of COVID-19 (NCT04377789)

Aim Ouercetin Enrolment Evaluate the possible role of quercetin on prophylaxis and treatment of COVID-19 † 18 years and older, COVID-19-negative and -positive, 50 participants

IG 1: quercetin (1000 mg/day in COVID-19 patients)

IG 2: quercetin (500 mg/day in NO COVID-19 patients) Intervention

CG: no intervention (in NO COVID-19 patients) Duration: not specified

#### 2. Title: The Study of Quadruple Therapy Zinc, Quercetin, Bromelain and Vitamin C on the Clinical Outcomes of Patients Infected With COVID-19 (NCT04468139)

STUDY DESIGN	NCT04377789	NCT04468139
Study Type	Interventional (Clinical Trial)	Interventional (Clinical Trial)
Estimated Enrollment	50 participants	60 participants
Allocation	Non-randomized	N/A
Intervention Model	Parallel Assignment	Single Group Assignment
Masking	None (Open Label)	None (Open Label)
Primary Purpose	Prevention	Treatment
Trial Location	Kanuni Sultan Suleyman Training and Research Hospital, Istanbul, Turkey	Ministry of health, First health cluster, Riaydh, Saudi Arabia

www.clinicaltrials.gov

# VITAMIN C

Vitamin C is one of our most important antioxidants to mop up those free radicals when we're sick. Vitamin C can significantly reduce the incidence and severity of pneumonia, which is one of the major complications of COVID-19 [22]. There is a clinical trial (NCT04342728) exploring the role of Vitamin C and Zinc supplementation in COVID19 (COVID A to Z). There is evidence vitamin C and quercetin co-administration exerts a synergistic antiviral action due to overlapping antiviral and immunomodulatory properties. Also, the ability of vitamin C to recycle and enhance the benefits of guercetin. This combination can be used as a prophylaxis in high-risk populations and for the treatment of COVID19 patients as an adjunct to promising pharmacological agents such as remdesivir or convalescent plasma [23].

with prevention aim. \$: All studies are ongoing. \* Both sexes were recruited.

 $<sup>^{\</sup>dagger}$  IG = intervention group; CG = control group.  $^{\dagger}$  The trial is being carried out on elderly participants.  $^{\dagger}$  Studies

#### VITAMIN D

Sunlight is the best way to obtain optimal vitamin D levels, but optimal skin conversion will only occur during the summer months. Vitamin D is found naturally in only a few foods, so supplementation is often needed, it has too many immune benefits. Vitamin D has been called a "pro-survival molecule", it helps innate cells to kill viruses. Vitamin D3 supplementation could be an essential pandemic support protocol for optimal immune support system. Studies have shown that people supplemented with adequate levels of vitamin D3 during the cold and flu season had significantly lower rates of infection. Vitamin D3 increases our body's production of cathelicidin, an antimicrobial compound, to help fight viral and bacterial infections [24].

A recent study of genomics-guided tracing of SARS-CoV-2 targets in human cells identified quercetin and vitamin D as mitigation combination effects the gene expression signatures of potential coronavirus infection [25]. In the meta-analysis, vitamin D supplementation has been shown as safe and effective against acute respiratory tract infections [26].

#### ZINC

Zinc deficiency is known to increase susceptibility to many infections [26]. Zinc and zinc-ionophores (compounds that increase zinc uptake into cells) have been found to inhibit SARS-CoV replication in vitro – that means that it has the potential to prevent the virus from multiplying and wreaking havoc in our bodies [27]. Zinc is essential to preserve natural tissue barriers such as the respiratory epithelium, preventing pathogen entry, for a balanced function of the immune system and the redox system. Zinc supplementation improves the mucociliary clearance, strengthens the integrity of the epithelium, decreases viral replication, preserves antiviral immunity, attenuates the risk of hyper-inflammation, supports anti-oxidative effects and thus reduces lung damage and minimized secondary infections [28].

Administration of Zn supplement has a potential to enhance antiviral immunity, both innate and humoral, and to restore depleted immune cell function or to improve normal immune cell function, in particular in immunocompromised or elderly patients [29]. It may be of benefit for prophylaxis and treatment of COVID-19 [30].Zn2+ prevents Coronavirus replication through the inhibition of RNA Polymerase Activity.

# VITAMIN C VITAMIN D ZINC Essential nutrients in normal immune function Enhance immunity in Viral infections Combination with complimentary and synergistic effects Ameliorate symptoms of Respiratory infections

#### **COMPOSITION**

Ingredient	Strength	
Quercetin	500 mg	
Zinc Oxide	25 mg	
Vitamin C	250 mg	
Vitamin D3	2000 I.U.	



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