

Quercetin – An Alternative to Hydroxychloroquine, and More

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✓ Fact Checked

STORY AT-A-GLANCE

- › Quercetin works much like hydroxychloroquine, a drug found to be effective against SARS-CoV-2 when used early enough. Both are zinc ionophores, meaning they shuttle antiviral zinc into your cells
- › The Front Line Critical COVID-19 Care Alliance's early treatment protocol includes quercetin at a dose of 250 milligrams twice a day, in combination with 100 mg elemental zinc and 500 mg to 1,000 mg of vitamin C twice a day
- › Quercetin also has other mechanisms of action that make it useful in the fight against COVID-19. For example, it may inhibit SARS-CoV-2 spike protein to ACE2 receptor docking. By binding to the ACE2 receptor and the spike protein interface, quercetin inhibits viral attachment and entry into the cell
- › Quercetin also modulates NLRP3 inflammasome, an immune system component involved in the uncontrolled release of proinflammatory cytokines that occurs during a cytokine storm
- › Quercetin-rich foods include onions and shallots, apples, broccoli, asparagus, green peppers, tomatoes, red leaf lettuce, strawberries, raspberries, blueberries, cranberries, black currants and green tea

The Substack Modern Discontent recently posted an anthology series on the benefits of quercetin,¹ including the finding that it works like hydroxychloroquine, a drug found to be

effective against SARS-CoV-2 when used early enough.

Part 1² begins with a brief overview of what quercetin is and its basic mechanisms of action. Quercetin is a flavonoid found in a variety of fruits and vegetables, such as onions and shallots, apples, broccoli, asparagus, green peppers, tomatoes, red leaf lettuce, strawberries, raspberries, blueberries, cranberries, black currants and green tea.

The quercetin content in any given food is largely dependent on light exposure, though, so depending on the country you're in, different foods will top the list of most quercetin-rich. General mechanisms of action of this nutrient include:³

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| Antioxidant activity – Antioxidants help prevent oxidative damage from harmful reactive oxygen species (ROS). Quercetin acts as a free radical scavenger, and its activity can be further enhanced by vitamin C | Anti-inflammatory activity – This is in part responsible for quercetin's cardiovascular benefits |
| Inhibition of platelet aggregation | Anti-allergy activities (inhibits release of histamine and other allergic substances) |
| Immunomodulation | Anticancer activity |
| Antiviral activity – It's been found to reduce replication of many viruses, including HIV, hepatitis C, enterovirus 71, porcine epidemic diarrhea virus and SARS-CoV-2, by targeting the proteases in these viruses | Zinc ionophore – Quercetin helps zinc enter your cells. Zinc, in turn, has potent antiviral activity |

Quercetin Against SARS-CoV-2

In Part 2⁴ of the anthology, Modern Discontent reviews the evidence behind the recommendation to use quercetin against COVID-19 specifically. As mentioned, zinc has antiviral activity, and quercetin helps shuttle the zinc into the cell. But quercetin also has other mechanisms of action that make it useful in the fight against COVID-19.

“ Quercetin modulates NLRP3 inflammasome, an immune system component involved in the uncontrolled release of proinflammatory cytokines that occurs during a cytokine storm. ”

For example, quercetin has been shown to:

Inhibit SARS-CoV-2 spike protein to ACE2 receptor docking.^{5,6,7} Computational modeling studies have shown quercetin can bind to the ACE2 receptor and the spike protein interface, thereby inhibiting the two from binding together. By preventing viral attachment, it helps prevent viral entry into the cell. Commenting on one of these studies, Modern Discontent notes:⁸

“Although [a] computer modeled study,⁹ the evidence here suggests that quercetin’s binding activity to ACE2 is comparable to other standard of care drugs used to treat SARS-CoV-2 (eg. Remdesivir, Lopinavir, Ritonavir).”

Inhibit lipopolysaccharide (LPS)-induced tumor necrosis factor α (TNF- α) production in macrophages.¹⁰ (TNF- α is a cytokine involved in systemic inflammation, secreted by activated macrophages, a type of immune cell that digests foreign substances, microbes and other harmful or damaged components.)

Inhibit the release of proinflammatory cytokines and histamine by modulating calcium influx into the cell.¹¹

Stabilize mast cells and regulate the basic functional properties of immune cells,

thereby allowing it to inhibit “a huge panoply of molecular targets in the micromolar concentration range, either by down-regulating or suppressing many inflammatory pathways and functions.”¹²

Act as a zinc ionophore, i.e., a compound that shuttles zinc into your cells.¹³ This is one of the mechanisms that can account for the effectiveness seen with hydroxychloroquine, which is also a zinc ionophore.

Boost interferon response to viruses, including SARS-CoV-2, by inhibiting the expression of casein kinase II (CK2)¹⁴ – CK2 is an enzyme that is fundamental to controlling homeostasis at the cellular level. There is evidence that it down-regulates the ability a cell has to generate Type 1 interferon when attacked by a virus.

It does this by inhibiting retinoic acid-inducible gene I (RIG-I),¹⁵ which has protein sensors that signal genetic expression of type 1 interferon by identifying the replication of RNA viruses, such as SARS-CoV-2. Quercetin inhibits the expression of CK2, which slows the replication of RNA viruses.¹⁶

Interferons are a subset of cytokines discovered in 1957.¹⁷ These cells are often the initial defense against viruses. There are two types and three forms of interferon. Within Type 1 interferon, there are alpha and beta. Type 2 interferon has the gamma form.¹⁸

The different types are based on the function of the cytokine. Type 1 interferons help cells resist viruses. Type 2 aids in responding to infections and cancer growth. The name "interferon" came from the ability of Type 1 to interfere with the virus's ability to duplicate. A cell secretes interferons when a foreign substance, like a virus, is detected.

However, the interferon does not function by attacking the virus. Instead, it tells the infected cell and the cells that surround the infected cell to make proteins that stop viral replication. In a nutshell, quercetin stops CK2 from interfering with the action of Type 1 interferon so cells receive the signal to stop viral replication.

Modulate NLRP3 inflammasome, an immune system component involved in the uncontrolled release of proinflammatory cytokines that occurs during a cytokine storm.¹⁹

Exert a direct antiviral activity against SARS-CoV^{20,21,22} — Quercetin's general antiviral capacity has been attributed to three primary mechanisms of action:

1. Binding to the spike protein, thereby inhibiting its ability to infect host cells²³
 2. Inhibiting replication of already infected cells
 3. Reducing infected cells' resistance to treatment with antiviral medication
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Inhibit the SARS-CoV-2 main protease.²⁴

The Front Line Critical COVID-19 Care Alliance (FLCCC) early treatment protocol²⁵ includes quercetin at a dose of 250 milligrams twice a day, in combination with 100 mg elemental zinc and 500 mg to 1,000 mg of vitamin C twice a day.

Quercetin in COVID-19 Medical Literature

In Part 3,²⁶ Modern Discontent reviews some of the clinical trials that have taken place. One COVID-19-specific study²⁷ found that people who took zinc and two zinc ionophores — quinine drops and quercetin — had lower incidence of COVID-19 than the control group. Over the course of the study (20 weeks), only two of the 53 test subjects became symptomatic, compared to 12 of the 60 controls. As noted by Modern Discontent:²⁸

“Although this didn't test quercetin in isolation, the study does suggest that over-the-counter, easily accessible compounds may be extremely beneficial in fighting against COVID, especially when taken as a prophylactic.”

In another trial,²⁹ 76 outpatients who tested positive but had only mild symptoms were given 1,000 mg of Quercetin Phytosome® (quercetin in sunflower phospholipids that increase oral absorption 20-fold) per day for 30 days, in addition to standard care

(analgesics, oral steroids and antibiotics). Another 76 patients were given standard of care only.

In the quercetin group, only 9.2% of participants went on to require hospitalization, compared to 28.9% of patients who received standard of care only. According to the authors:³⁰

“The results revealed a reduction in frequency and length of hospitalization, in need of non-invasive oxygen therapy, in progression to intensive care units and in number of deaths.

The results also confirmed the very high safety profile of quercetin and suggested possible anti-fatigue and pro-appetite properties. QP [Quercetin Phytosome®] is a safe agent and in combination with standard care, when used in early stage of viral infection, could aid in improving the early symptoms and help in preventing the severity of COVID-19 disease.”

Quercetin was also featured in two scientific reviews published in 2020.³¹ The first, published in the Integrative Medicine journal in May 2020,³² highlighted quercetin’s promotion of SIRT2, which inhibits NLRP3 inflammasome.

The second review article,³³ published in the June 19, 2020, issue of Frontiers in Immunology, highlighted quercetin’s usefulness as a COVID-19 treatment when used in conjunction with vitamin C. The vitamin C recycles oxidized quercetin, producing a synergistic effect. It also enhances quercetin’s antiviral capacity.

Food as Medicine

With the advent of processed foods, many important nutrients have been lost or minimized in the average person’s diet. Quercetin, being found in fresh fruits, vegetables and berries is one of them. Unfortunately, while essential vitamins and minerals are generally recognized for their importance, antioxidants such as quercetin are often overlooked, and sometimes labeled as “pseudoscience” or “fad” supplements. As noted by Modern Discontent:

“The great number of benefits that these compounds contribute to humans cannot be overstated ... An argument can be made that not only could quercetin prove beneficial to our health, but an absence of it may prove detrimental in the long term.”

If COVID-19 has taught us anything, it's the importance of basic health and a healthy immune function. In this regard, a diet high in fresh fruits and vegetables can go a long way. Nutritional supplements also have their place, especially in situations like a pandemic.

Summary

In conclusion, Modern Discontent provides the following summary of findings:³⁴

- ***“There’s evidence that quercetin may work similarly to hydroxychloroquine – It seems that quercetin may operate as both an immunomodulator and a zinc ionophore. Its use as an over-the-counter anti-allergic supplement as well as its use for asthma indicates an ability to affect the production of histamine and cytokines ...***
- ***Quercetin has plenty of other benefits – ... Antioxidants ... are some of the most well studied compounds, with possible anti-cancer, pro-heart and pro-organ benefits. Add on possible antimicrobial properties and it becomes hard to argue that this is nothing more than a possible fad supplement.***
- ***Although limited, there is some evidence that quercetin may be effective against SARS-CoV2 – Computer models and in vitro studies suggest that ACE2 receptors and the main protease of SARS-CoV2 may be good target candidates for quercetin ... the limited number of studies suggest quercetin may be effective, especially if used early on or as a prophylactic.***
- ***Dietary quercetin is the main source of quercetin, and its deficiency in modern diets may be contributing to our health problems – Quercetin is primarily sourced from colorful fruits, vegetables, teas ... all foods that many of our ancestors would have consumed on a regular basis ... Modern ‘enriched’ foods tend to supplement with***

additional vitamins and minerals, but may miss out on other plant-derived compounds that have played a substantial role in our diet.

Similar to reduced sunlight exposure and the need for increased vitamin D supplementation, we may need to look at possible supplementation of overlooked compounds such as polyphenols. Sourcing these compounds from real foods would prove the most beneficial, but in groups of people who may not have access to fresh fruits and vegetables, quercetin and polyphenol supplementation may be useful.

This would include people with alternative diets such as keto, who may avoid high carb fruits, and thus may be missing a key nutrient in their diets.

Quercetin has plenty of benefits, and for those who may be missing out on it in their diet they may want to look into sourcing it with supplementation. Don't take this as a prescription or recommendation, but an argument to examine your own health and see what you may be lacking ..."

Sources and References

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