

Quercetin and Vitamin D – Allies Against Coronavirus?

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STORY AT-A-GLANCE

- › As the outbreak of COVID-19 continues to spread around the world, more than 80 clinical trials are underway testing remedies ranging from intravenous vitamin C and stem cells to HIV drugs and malaria medication
- › A derivative of quercetin has been shown to provide broad-spectrum protection against a wide range of viruses, including SARS. Canadian and Chinese researchers are now collaborating on a study to assess the effectiveness of quercetin against COVID-19 infection
- › Quercetin is a powerful immune booster and broad-spectrum antiviral. It also inhibits the release of pro-inflammatory cytokines, which may be beneficial since serious COVID-19 infection and subsequent death appears to be due to cytokine storm activity
- › There are plenty of data showing it's an important component in the prevention and treatment of influenza and upper respiratory tract infections
- › Other nutraceuticals thought to be useful in the prevention of coronavirus infection include NAC, spirulina, beta-glucan, glucosamine, selenium, zinc, lipoic acid and sulforaphane

As the outbreak of novel coronavirus, COVID-19,¹ continues into its third year around the world,² researchers are still feverishly searching for effective remedies, for both the original virus and its substrates. According to a February 15, 2020, Nature article,³ more than 80 clinical trials were already underway testing remedies ranging from intravenous **vitamin C** and stem cells from menstrual blood to HIV drugs and malaria medication.

There's also a study looking at serum obtained from patients who recovered from laboratory confirmed COVID-19 infection – the idea being that it will contain antibodies a freshly-infected patient would need to fight off the infection more effectively.

Two other potential remedies vying for attention are quercetin and vitamin D. Not only are both known for their immune-boosting and antiviral benefits, they're also inexpensive and widely available.

Can Quercetin Quell COVID-19 Infection?

As reported by Maclean's,⁴ Canadian researchers Michel Chrétien and Majambu Mbikay began investigating quercetin in the aftermath of the SARS epidemic that broke out across 26 countries in 2003. They discovered a derivative of quercetin provided broad-spectrum protection against a wide range of viruses, including SARS.^{5,6}

The Ebola outbreak in 2014 offered another chance to investigate quercetin's antiviral powers and, here too, they found it effectively prevented infection in mice, "even when administered only minutes before infection."

So, when the COVID-19 outbreak was announced in Wuhan City, China, in late December 2019, Chrétien contacted colleagues in China with an offer to help. In February 2020, Chrétien and his team received an official invitation to begin clinical trials. Maclean reports:⁷

"The Canadian and Chinese scientists would collaborate on the trials, which would include about 1,000 test patients. Chrétien and Mbikay plan to join colleagues from the non-profit International Consortium of Antivirals – which Chrétien co-founded with Jeremy Carver in 2004 as a response to the SARS epidemic – in manning a 24/7 communications centre as soon as clinical trials go ahead.

The U.S.-based Food and Drug Administration has already approved quercetin as safe for human consumption, which means the researchers can skip testing

on animals. If the treatment works, it'll be readily available ... Chrétien's team says their treatment would cost only \$2 a day."

Quercetin Is a Powerful Immune Booster

Research has already demonstrated that quercetin is a powerful immune booster and broad-spectrum antiviral. As such, it may be useful for both prevention and treatment of COVID-19 infection.

As noted in a 2016 study⁸ in the journal *Nutrients*, quercetin's mechanisms of action include the inhibition of lipopolysaccharide (LPS)-induced tumor necrosis factor α (TNF- α) production in macrophages.

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. Quercetin also inhibits the release of pro-inflammatory cytokines and histamine by modulating calcium influx into the cell.⁹

According to this paper, quercetin also stabilizes mast cells and has "a direct regulatory effect on basic functional properties of immune cells," which allows 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."¹⁰

How Quercetin Inhibits Viral Infection

One of the most well-studied attributes of quercetin, however, is its antiviral capacity, which has been attributed to three main mechanisms of action:

1. Inhibiting the virus' ability to infect cells
2. Inhibiting replication of already infected cells
3. Reducing infected cells' resistance to treatment with antiviral medication

Research¹¹ funded by the U.S. Department of Defense, published in 2007, found it lowers your risk of viral illness following extreme physical stress, which might otherwise undermine your immune function and render you more susceptible to infections.

Cyclists who received a daily dose of 1,000 mg of quercetin in combination with vitamin C (which enhances plasma quercetin levels^{12,13}) and niacin (to improve absorption) for five weeks were significantly less likely to contract a viral illness after bicycling three hours a day for three consecutive days, compared to untreated controls. While 45% of the placebo group got sick, only 5% of the treatment group did.

In another study¹⁴ funded by the U.S. Defense Advanced Research Projects Agency (DARPA), published in 2008, animals treated with quercetin were challenged with a highly pathogenic H1N1 influenza virus. Again, the treatment group had significantly lower morbidity and mortality than the placebo group.

Quercetin Effectively Treats a Broad Range of Viruses

Other studies have also confirmed quercetin's effectiveness against a broad range of viruses. Among them:

A 1985 study, which found quercetin inhibits infectivity and replication of herpes simplex virus type 1, polio-virus type 1, parainfluenza virus type 3 and respiratory syncytial virus.¹⁵

A 2010 animal study found that quercetin inhibits both influenza A and B viruses. Two other important discoveries were made. Firstly, the viruses were unable to develop resistance to quercetin and, secondly, when used concomitantly with antiviral drugs (amantadine or oseltamivir), the effect was significantly amplified – and it prevented drug-resistance from developing.¹⁶

A 2004 animal study investigating quercetin's effect on influenza used a strain of the H3N2 virus. According to the authors:¹⁷

"During influenza virus infection, there is 'oxidative stress.' Because quercetin restored the concentrations of many antioxidants, it is proposed that it may be useful as a drug in protecting the lung from the deleterious effects of oxygen derived free radicals released during influenza virus infection."

Another 2016 study found quercetin offered protection against influenza A virus H1N1 by modulating protein expression. More specifically, the regulation of heat shock proteins, fibronectin 1 and prohibitin was instrumental in reducing viral replication.¹⁸

A third study published in 2016 found quercetin inhibited a wide spectrum of influenza strains, including H1N1, H3N2 and H5N1. According to the authors, "This study indicates that quercetin showing inhibitory activity in the early stage of influenza infection provides a future therapeutic option to develop effective, safe and affordable natural products for the treatment and prophylaxis of [influenza A viruses] infections."¹⁹

In 2014, researchers noted that quercetin appears to be "a promising treatment for the common cold," caused by the rhinovirus, adding that "Quercetin has been shown to reduce viral internalization and replication in vitro, and viral load, lung inflammation and airways hyper-responsiveness in vivo."²⁰

By attenuating oxidative damage, it also lowers your risk of secondary bacterial infections, which is actually the **primary cause of influenza-related deaths**. Importantly, quercetin increases mitochondrial biogenesis in skeletal muscle, which suggests part of its antiviral effects are due to enhanced mitochondrial antiviral signaling.

A 2016 animal study²¹ found quercetin inhibited mouse dengue virus and hepatitis virus. Other studies have confirmed quercetin's power to inhibit both hepatitis B²² and C²³ infection.

Most recently, a March 2020 study²⁴ in the *Microbial Pathogenesis* journal found quercetin "provides comprehensive protection against *Streptococcus pneumoniae* infection," both in vitro and in vivo, primarily by neutralizing pneumolysin (PLY),²⁵ one of the toxins released from pneumococci that encourages *S. pneumoniae* infection to blossom in the first place. As reported by the authors in *Microbial Pathogenesis*:

"The results indicated that quercetin significantly reduced PLY-induced hemolytic activity and cytotoxicity via repressing the formation of oligomers.

*In addition, treatment with quercetin can reduce PLY-mediated cell injury, improve the survival rate of mice infected with a lethal dose of *S. pneumoniae*, alleviate the pathological damage of lung tissue and inhibit the release of cytokines (IL-1 β and TNF- α) in bronchoalveolar lavage fluid.*

*Considering the importance of these events in antimicrobial resistant *S. pneumoniae* pathogenesis, our results indicated that quercetin may be a novel potential drug candidate for the treatment of clinical pneumococcal infections."*

The Importance of Vitamin D

In the featured MedCram video, pulmonologist Dr. Roger Seheult discusses the importance of vitamin D for the prevention of COVID-19. While there are no clinical trials investigating vitamin D for coronavirus specifically, there are plenty of data showing it's an important component in the prevention and treatment of influenza²⁶ and upper respiratory tract infections.²⁷

As noted by Seheult, while vitamin D does not appear to have a direct effect on the virus itself, it strengthens immune function, thus allowing the host body to combat the virus more effectively.²⁸ It also suppresses inflammatory processes. Taken together, this might make vitamin D quite useful against COVID-19.

As explained by Seheult, robust immune function is required for your body to combat the virus, but an overactivated immune system is also responsible for the cytokine storm we see in COVID-19 infection that can lead to death.

"What we want is a smart immune system," Seheult says, "An immune system that takes care of the virus but doesn't put us into an inflammatory condition that could put us on a ventilator."

Vitamin D Supplementation Cuts Respiratory Infection Rates

He goes on to cite research²⁹ published in 2017 – a meta-analysis of 25 randomized controlled trials – which confirmed that vitamin D supplementation helps protect against acute respiratory infections. Studies have also shown there's an apparent association between low vitamin D levels and susceptibility to viral infections such as influenza.

Living at northerly latitudes means you get the least amount of sunlight during winter months, resulting in lower vitamin D levels, and one hypothesis is that the seasonality of the flu is related to the fact that most people have lower vitamin D levels in the winter than in the summer.

For example, research³⁰ published in 2009 pointed suggests fatality rates during the 1918-1919 influenza pandemic were influenced by season, with greater numbers of people dying during the winter than the summer.

It remains to be seen whether this seasonality applies to COVID-19 as well. If it does, it could well be that higher vitamin D levels strengthen immune function enough to where the virus cannot overtake the system.

The 2017 meta-analysis³¹ also made another important discovery. When they dug deeper into the data from each of the more than 11,000 participants, they found that it was the daily or weekly supplementation of vitamin D that had the greatest protective effect in those with the lowest vitamin D levels.³²

Those with severe vitamin D deficiency who took a daily or weekly supplement cut their respiratory infection risk in half. Those with higher baseline levels also lowered their risk, albeit to a lesser extent. The acute administration of high bolus doses of vitamin D, on the other hand, had no significant impact on infection risk.

This supports the recommendation to maintain an optimal vitamin D level year-round. According to data from GrassrootsHealth's D*Action studies, the optimal level for health and disease prevention appears to be between 60 nanograms per milliliter (ng/mL) and 80 ng/mL, while the cutoff for sufficiency appears to be around 40 ng/mL.

In one GrassrootsHealth analysis,³³ those with a vitamin D level of at least 40 ng/mL reduced their risk of colds by 15% and flu by 41%, compared to those with a level below 20 ng/mL.

Other Potentially Beneficial Nutrients

An article³⁴ in *Progress in Cardiovascular Diseases* by Mark McCarty of the Catalytic Longevity Foundation and James DiNicolantonio, PharmD, a cardiovascular research scientist at Saint Luke's Mid America Heart Institute, highlights several other supplemental nutrients that could help bolster your immune function and lower your risk of COVID-19 infection. As reported in a February 24, 2020, press release:^{35,36}

"COVID-19 is around 30 to 60 times more lethal than the typical annual flu. Both influenza and coronavirus cause an inflammatory storm in the lungs and it is this inflammatory storm that leads to acute respiratory distress, organ failure, and death.

Certain nutraceuticals may help to reduce the inflammation in the lungs from RNA viruses and others may also help boost type 1 interferon response to these viruses, which is the body's primary way to help create antiviral antibodies to fight off viral infections."

A summary of the nutraceuticals recommended by McCarty and DiNicolantonio include the following. (For more details about each, see the full-text paper³⁷ published in

Progress in Cardiovascular Diseases.)

N-acetylcysteine – Encourages glutathione production, thins mucus, lowers your chances of influenza infection and reduces your risk of developing severe bronchitis

Elderberry extract – Known to shorten influenza duration by two to four days and reduce the severity of the flu. According to the authors:³⁸

"Given that elderberry is a very rich source of anthocyanins, there is reason to suspect that its impact on viruses might be mediated, at least in part, by ferulic acid, a prominent metabolite that appears in plasma following anthocyanin ingestion."

Spirulina – Reduces severity of influenza infection severity and lowers influenza mortality in animal studies. In a human trial, spirulina significantly lowered the viral load in patients with HIV infection

Beta-glucan – Reduces severity of influenza infection severity and lowers influenza mortality in animal studies

Glucosamine – Upregulates mitochondrial antiviral-signaling protein (MAVS), reduces severity of influenza infection severity and lowers influenza mortality in animal studies

Selenium – "Since selenium is an essential cofactor for certain peroxidases, and selenium deficiency has been endemic in certain regions of China and other parts of the world, insuring adequacy of selenium nutrition might also be appropriate in this context," McCarty and DiNicolantonio note, adding:³⁹

"Selenium deficiency also increases the rate at which viruses can mutate, promoting the evolution of strains that are more pathogenic and capable of evading immune surveillance."

Zinc – Zinc has been shown to inhibit coronavirus in vitro and block coronavirus replication in cell culture.⁴⁰ In the MedCram video below, Seheult discusses compelling evidence suggesting the malaria drug chloroquine can improve zinc absorption and how this may be useful in the treatment of coronavirus infection

Lipoic acid – Helps boost type 1 interferon response. As explained in a 2014 paper:⁴¹

"Type I interferons (IFNs) activate intracellular antimicrobial programs and influence the development of innate and adaptive immune responses ... (IFNs) are polypeptides that are secreted by infected cells and have three major functions.

First, they induce cell-intrinsic antimicrobial states in infected and neighboring cells that limit the spread of infectious agents, particularly viral pathogens. Second, they modulate innate immune responses in a balanced manner that promotes antigen presentation and natural killer cell functions while restraining pro-inflammatory pathways and cytokine production.

Third, they activate the adaptive immune system, thus promoting the development of high-affinity antigen-specific T and B cell responses and immunological memory. Type I IFNs are protective in acute viral infections but can have either protective or deleterious roles in bacterial infections and autoimmune diseases."

Sulforaphane – Helps boost type 1 interferon response

The provisional daily dosage suggestions offered by McCarty and DiNicolantonio to help control RNA viruses, including influenza and coronavirus infection, are as follows:⁴²

Nutraceutical	Daily dosage
Ferulic acid	500 to 1,000 milligrams (mg)

Nutraceutical	Daily dosage
Lipoic acid	1,200 to 1,800 mg (in place of ferulic acid)
Spirulina	15 grams
NAC	1,200 to 1,800 mg
Selenium	50 to 100 micrograms (mcg)
Glucosamine	3,000 mg or more
Zinc	30 to 50 mg
Yeast beta-glucan	250 to 500 mg
Elderberry extract	600 to 1,500 mg

Coconut Oil May Also Be Useful

Integrated Chemists of the Philippines also published information about a proposed study by Dr. Mary Newport on lauric acid and its derivative, monolaurin. As noted in this post:⁴³

"Lauric acid is a medium-chain fatty acid which makes up about 50% of coconut oil; monolaurin is a metabolite that is naturally produced by the body's own enzymes upon ingestion of coconut oil and is also available in pure form as a supplement ...

Several in vitro, animal, and human studies support the potential of coconut oil, lauric acid and its derivatives as effective and safe agents against a virus like

nCoV-2019. Mechanistic studies on other viruses show that at least three mechanisms may be operating.

Given the considerable scientific evidence for the antiviral activity of coconut oil, lauric acid and its derivatives and their general safety, and the absence of a cure for nCoV-2019, we urge that clinical studies be conducted among patients who have been infected with nCoV-2019 ...

This treatment is affordable and virtually risk-free, and the potential benefits are enormous. On the other hand, given the safety and broad availability of virgin coconut oil (VCO), we recommend that VCO be considered as a general prophylactic against viral and microbial infection."

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