

### **Attacks the Flu, Commonly Found in Onion Skins**

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May 07, 2022

#### **STORY AT-A-GLANCE**

- > Quercetin packs a powerful antiviral punch, inhibiting several strains of influenza, hepatitis B and C and other viruses
- > It also combats inflammation and has been shown to lower blood pressure in those with Stage 1 high blood pressure and may help regress tumors
- > Quercetin reduces your risk of cold or flu and boosts mental performance following extreme physical stress, which might otherwise undermine your immune function and render you more susceptible to infections
- > Quercetin stabilizes mast cells, has cytoprotective activity in the gastrointestinal tract, and has a direct regulatory effect on the basic functional properties of immune cells
- > In supplement form, quercetin has been used to ameliorate obesity, Type 2 diabetes, circulatory dysfunction, chronic inflammation, hay fever and mood disorders

This article was previously published September 9, 2019, and has been updated with new information.

Your immune system is your first-line defense against bacterial and viral infections, so the most effective way to prevent infectious illness is maintaining robust immune function. Your diet and other lifestyle factors are foundational for this, but certain supplements can also be helpful.

One such supplement is quercetin,1 an antioxidant flavonol found naturally in apples, plums, red grapes, green tea, elder flower and onions, just to name a few.<sup>2</sup>

Quercetin is one of those compounds with a wide range of benefits, making it useful for a variety of different conditions. That said, it's perhaps most known for its strong antioxidant<sup>3</sup> and antiviral<sup>4</sup> activity. Elderflower extract, which is rich in quercetin, is also a traditional tonic used to boost immunity.

In supplement form, quercetin has been used to ameliorate obesity, Type 2 diabetes,<sup>5</sup> circulatory dysfunction, chronic inflammation, hay fever and mood disorders.<sup>6</sup> Several studies have also highlighted quercetin's ability to prevent and treat the common cold and influenza.<sup>7</sup>

In fact, its antiviral capacity appears to be the primary focus of many studies looking at quercetin's benefits. But there are also other, less known uses for this supplement, including blood pressure control and tumor regression.

## **Quercetin May Lower Blood Pressure**

For example, there's evidence to suggest quercetin benefits the heart, and can help lower blood pressure in patients with Stage 1 high blood pressure. As noted in one 2007 study:8

"Epidemiological studies report that quercetin ... is associated with reduced risk of coronary heart disease and stroke ... Men and women with prehypertension and stage 1 hypertension were enrolled in a randomized, double-blind, placebocontrolled, crossover study to test the efficacy of 730 mg quercetin/d for 28 d[ays] vs. placebo.

Blood pressure at enrollment was ... 148 +/- 2/96 +/- 1 in stage 1 hypertensive subjects ... [R]eductions in systolic (-7 +/- 2 mm Hg), diastolic (-5 +/- 2 mm Hg), and mean arterial pressures (-5 +/- 2 mm Hg) were observed in stage 1 hypertensive patients after quercetin treatment ... These data are the first to our

knowledge to show that quercetin supplementation reduces blood pressure in hypertensive subjects."

### **Quercetin May Regress Tumors**

Another study,<sup>9</sup> published in Scientific Reports in 2016, found quercetin has the ability to trigger tumor regression by interacting with your DNA and activating the mitochondrial pathway of apoptosis, which is the programmed cell death of damaged cells. As noted in the abstract of this study:

"... quercetin induced cytotoxicity in leukemic cells in a dose-dependent manner ... Besides leukemic cells, quercetin also induced cytotoxicity in breast cancer cells, however, its effect on normal cells was limited or none.

Further, quercetin caused S phase arrest during cell cycle progression in tested cancer cells ... Importantly, administration of quercetin lead to ~5 fold increase in the life span in tumor bearing mice compared to that of untreated controls.

Further, we found that quercetin interacts with DNA directly, and could be one of the mechanisms for inducing apoptosis in both cancer cell lines and tumor tissues by activating the intrinsic pathway. Thus, our data suggests that quercetin can be further explored for its potential to be used in cancer therapeutics and combination therapy."

### **How Quercetin Combats Inflammation and Boosts Immunity**

As mentioned, quercetin is most known for boosting immunity and combating inflammation. As noted in a 2016 study<sup>10</sup> in the journal Nutrients, mechanisms of action include (but is not limited to) the inhibition of:<sup>11</sup>

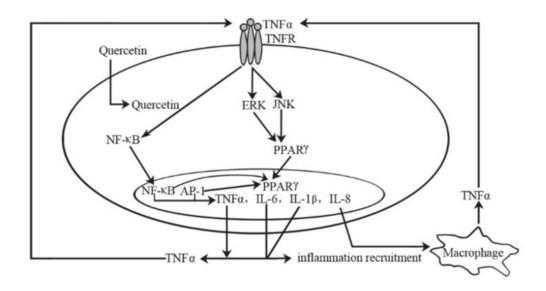
• Lipopolysaccharide (LPS)-induced tumor necrosis factor  $\alpha$  (TNF- $\alpha$ ) production in macrophages (TNF- $\alpha$  is a cytokine involved in systemic inflammation, secreted by

activated macrophages, a type of immune cell that digests foreign substances, microbes and other harmful or damaged components)

- LPS-induced mRNA levels of TNF- $\alpha$  and interleukin (IL)-1 $\alpha$  in glial cells, which results in "diminished apoptotic neuronal cell death"
- The production of inflammation-producing enzymes
- · Calcium influx into the cell, which in turn inhibits:
  - Pro-inflammatory cytokine release
  - Histamine and serotonin release from intestinal mast cells release<sup>12</sup>

According to this paper, quercetin also stabilizes mast cells, has cytoprotective activity in the gastrointestinal tract, and "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."

The following figure from the journal Nutrients<sup>14</sup> shows the many possible pathways by which quercetin inhibits inflammation and boosts immune function. Table 1 in this study also summarizes the primary effects of quercetin on inflammation and immune function depending on the specific cell line used in the investigation.



### **Demonstrated Health Benefits of Quercetin**

In animal models, quercetin has been shown to:15

- Ameliorate the inflammatory response induced by carrageenan,<sup>16</sup> a common food additive
- Reduce the production of TNF- $\alpha$  in visceral adipose tissue (intra-abdominal fat that raises your risk of health complications such as Type 2 diabetes and heart disease)
- · Reduce clinical signs of arthritis
- Improve recovery of motor function after spinal cord injury (according to this paper,
  "Intraperitoneal doses of 5-100 micromoles quercetin/kg body weight resulted in
  half or more of the animals walking ... This ability to promote recovery from spinal
  cord injury appears to be highly dependent on the dose and frequency of dosing"

In human studies, quercetin has been shown to:17

- Reduce total sick days and symptom severity associated with upper-respiratory tract infection (URTI) in physically fit individuals over the age of 40 (dosage: 500 or 1000 mg/day for 12 weeks)
- Significantly reduce risk of illness, inflammation and oxidative stress after intense exercise
- Augment innate immune function in exercise-stressed athletes
- Reduce viral illness and boost mental performance after extreme physical stress
  that might otherwise undermine your immune function (in one study,<sup>18</sup> 45% in the
  placebo group got sick with a cold or influenza after a strenuous three-day exercise
  routine, compared to just 5% in the treatment group, which received 1,000
  milligrams quercetin combined with vitamin C and niacin to improve absorption)
- Protect against abroad spectrum of pathogens, including rhinoviruses, adenoviruses and coronaviruses

# **Quercetin Is a Potent Antiviral Remedy**

Indeed, several studies have confirmed quercetin's effectiveness against a range of viral infections. Below, I list some of them. In summary, quercetin's powerful antiviral effects can be 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

A 1985 study found quercetin inhibits infectivity and replication of herpes simplex virus type 1, polio-virus type 1, parainfluenza virus type 3 and respiratory syncytial virus.<sup>19</sup>

A 2010 animal study<sup>20</sup> found quercetin inhibits influenza A and B viruses. Two other important discoveries were made:

- 1. The viruses were unable to develop resistance to quercetin
- 2. When used concomitant with antiviral drugs (amantadine or oseltamivir), the effect was significantly amplified and it prevented drug-resistance from developing

A 2004 animal study investigating quercetin's effect on influenza used a strain of the H3N2 virus. According to the authors:<sup>21</sup>

"In the mice, instillation of influenza virus A/Udorn/317/72(H3N2) intranasally resulted in a significant decrease in the pulmonary concentrations of catalase, reduced glutathione and superoxide dismutase ... These effects were observed on the 5th day after viral instillation.

Oral supplementation with quercetin simultaneous with viral instillation produced significant increases in the pulmonary concentrations of catalase, reduced glutathione and superoxide dismutase ...

It is concluded that 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."

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."<sup>22</sup>

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. According to the authors:

"... [I]n vitro studies have demonstrated that quercetin acts as a potent antiviral agent by inhibiting viral replication of several respiratory viruses, including influenza virus, parainfluenza virus, respiratory syncytial virus, adenovirus and rhinovirus. Although the quercetin's antiviral mechanisms are not well understood, a number of possibilities have been proposed and is summarized in Figure 1."

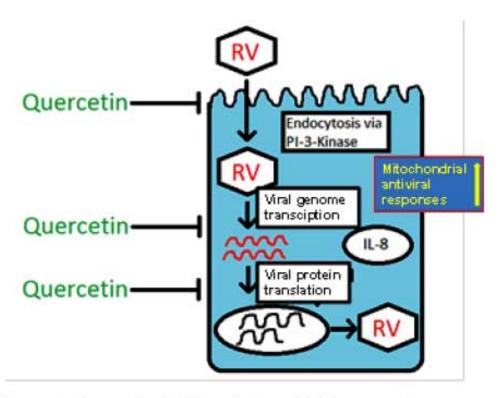


Figure 1: Quercetin inhibits viral replication at various stages: blocks endocytosis via inhibition of PI-3 kinase, transcription of viral genome by inhibiting RNA polymerase 3D POL and viral protein translation by promoting cleavage of eIF4G. At the same time quercetin also increases viral clearance by enhancing mitochondrial antiviral responses. All these events together lead to reduced pro-inflammatory responses.

Source: Journal of Infectious Diseases and Preventive Medicine May 24, 2014; 2: 111

Research<sup>23</sup> published in 2015 found quercetin inhibited hepatitis B virus replication in human liver cells, protecting cells from infection and limiting the spread of infection in already infected samples. What's more, when combined with antiviral drugs (lamivudine, entecavir or adefovir), the antiviral effect was greatly enhanced.

According to the authors, "The results indicate that quercetin inhibited HBV [hepatitis B virus] antigen secretion and genome replication in human hepatoma cell lines, which suggests that quercetin may be a potentially effective anti-HBV agent." Other studies<sup>24,25</sup> show quercetin can inhibit hepatitis C infection as well.

A 2016 animal study found quercetin inhibited mouse hepatitis virus and the dengue virus.<sup>26</sup>

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.<sup>27</sup>

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."<sup>28</sup>

### **Quercetin Is a Far Safer Alternative to Antiviral Drugs**

Considering the powerful antiviral effects of quercetin, it would be sensible to make use of it first, before resorting to antiviral drugs such as Tamiflu. Not only has Tamiflu been shown to shorten the duration of flu symptoms by less than 17 hours,<sup>29,30</sup> it also does not reduce viral transmission and does not lower your risk of complications from the flu, such as pneumonia.<sup>31,32</sup>

Scientists have also warned that the risks of Tamiflu far outweigh the benefits.<sup>33</sup> These risks include convulsions, brain infections, psychosis and other neuropsychiatric problems,<sup>34</sup> including mood swings, suicidal feelings, auditory hallucinations, memory deterioration and insomnia.<sup>35</sup>

The drug is particularly risky for children, and more than half of all children taking Tamiflu suffer side effects from the drug.<sup>36,37</sup> Considering its risks, and its limited effectiveness, quercetin appears to be a far safer and more effective alternative. Studies have repeatedly found quercetin to be nontoxic, with no adverse side effects.

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