

# **More Health Benefits of Quercetin Revealed**

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✓ Fact Checked

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

- > Quercetin has been shown to combat inflammation and acts as a natural antihistamine.
  Several studies have highlighted quercetin's ability to prevent and treat both the common cold and influenza
- > Another, less known benefit and use for quercetin includes the prevention and/or treatment of high blood pressure, cardiovascular disease, metabolic syndrome, certain cancers, gout, arthritis and mood disorders
- > A review of quercetin's effect on metabolic syndrome found it significantly reduced fasting plasma glucose when taken for at least eight weeks at a dosage of 500 milligrams per day or more
- > Other recent research found quercetin has a beneficial impact on nonalcoholic fatty liver disease by ameliorating inflammation, oxidative stress and lipid metabolism
- Quercetin also has the ability to trigger tumor regression by interacting with your DNA and activating the mitochondrial pathway of apoptosis (the programmed cell death of damaged cells)

Quercetin<sup>1</sup> is an antioxidant flavonol found naturally in foods such as **apples**, plums, red grapes, green tea, elder flower and **onions**, just to name a few.<sup>2</sup> According to a 2022 LinkedIn report,<sup>3</sup> the quercetin market is growing rapidly as its health benefits are becoming more widely known, with a projected global market of \$406 million by 2027.

Quercetin has been shown to combat inflammation and acts as a natural antihistamine. In fact, its antiviral capacity appears to be the primary focus of many studies looking at quercetin's benefits, and a number of studies have highlighted quercetin's ability to prevent and treat both the common cold and influenza.<sup>4,5,6</sup>

But there are also other, less known benefits and uses for this supplement, including the prevention and/or treatment of:<sup>7</sup>

High blood pressure <sup>8</sup>	Cardiovascular disease9
Metabolic syndrome <sup>10</sup>	Certain kinds of cancer <sup>11</sup>
Nonalcoholic fatty liver disease (NAFLD) <sup>12</sup>	Gout <sup>13</sup>
Arthritis <sup>14</sup>	Mood disorders <sup>15</sup>
Longevity, thanks to its senolytic benefits (clearing out damaged and worn-out cells) <sup>16,17</sup>	

Additionally, quercetin is also helpful for aluminum-induced neurodegenerative changes, such as those seen in Alzheimer's, Parkinson's and amyotrophic lateral sclerosis (ALS). As noted in a 2016 study:<sup>18</sup>

"Administration of quercetin (10 mg/kg body wt/day) reduced aluminum (10 mg/kg body wt/day)-induced oxidative stress (decreased ROS production, increased mitochondrial superoxide dismutase (MnSOD) activity).

In addition, quercetin also prevents aluminum-induced translocation of cyt-c, and up-regulates Bcl-2, down-regulates Bax, p53, caspase-3 activation and reduces DNA fragmentation ... Further electron microscopic studies revealed that quercetin attenuates aluminum-induced mitochondrial swelling, loss of cristae and chromatin condensation. These results indicate that treatment with quercetin may represent a therapeutic strategy to attenuate the neuronal death against aluminum-induced neurodegeneration."

### **Quercetin Improves Metabolic Syndrome Traits**

Among the most recent papers on this powerful antioxidant is a review<sup>19</sup> published in the March 2019 issue of Phytotherapy Research, which looked at nine randomized controlled trials investigating quercetin's effect on metabolic syndrome.

Metabolic syndrome refers to a cluster of conditions (including high blood pressure, high blood sugar, high triglyceride levels and fat accumulation around the waist) that raise your risk for Type 2 diabetes, heart disease and stroke.

While pooled findings found no effect on fasting plasma glucose, insulin resistance or hemoglobin A1c levels, further subgroup analyses revealed quercetin supplementation "significantly reduced" fasting plasma glucose in studies lasting at least eight weeks and in which dosages of at least 500 milligrams (mg) per day were used.

In studies that included people over the age of 45, "significant" reductions in insulin were also found when using a dosage of 500 mg per day or more. An earlier study,<sup>20</sup> published in 2011, looked at quercetin's effects on certain traits of metabolic syndrome.

This study focused specifically atherosclerosis and inflammation in men with the APOE genotype 3/3, 3/4 and 4/4, and found quercetin significantly decreased waist circumference, postprandial systolic blood pressure, postprandial triacylglycerol, and increased HDL-cholesterol compared to placebo. Here, participants were given 150 mg of quercetin per day for eight weeks.

Research<sup>21</sup> on obese rats published in 2008 also found that quercetin supplementation at doses of 2 mg per kilo or 10 mg/kg of body weight for 10 weeks improved systolic

blood pressure, triglyceride, total cholesterol and free fatty acid levels. The 10 mg/kg dose also improved the animals' inflammation status. As noted by the authors:

"In conclusion, both doses of quercetin improved dyslipidemia, hypertension, and hyperinsulinemia in obese Zucker rats, but only the high dose produced antiinflammatory effects in VAT together with a reduction in body weight gain."

One of the first studies<sup>22</sup> to demonstrate quercetin's beneficial effects on blood pressure was published in 2007. As reported by the authors:

"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 ... Reductions 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."

Similarly, a January 2020 systematic review<sup>23</sup> of 17 studies concluded quercetin "significantly decreased" blood pressure in human subjects. Those who took it for eight weeks or more also had "significantly" improved high-density lipoprotein cholesterol and triglycerides.

#### **Quercetin Improves Diabetes-Induced NAFLD**

Other recent research<sup>24</sup> published in the August 2019 issue of Phytotherapy Research concluded quercetin has a beneficial impact on NAFLD "by ameliorating inflammation, oxidative stress and lipid metabolism."

Diabetes can play a role in NAFLD as well, showing just how influential insulin resistance is in the development of chronic diseases of all kinds. As explained in the abstract:

"Multiphase pathological processes involve in Type 2 diabetes (T2DM)-induced nonalcoholic fatty liver disease (NAFLD). However, the therapies are quite limited. In the present study, the hepatoprotective effects and underlying mechanisms of quercetin in T2DM-induced NAFLD were investigated ...

The results revealed that quercetin alleviated serum transaminase levels and markedly reduced T2DM-induced histological alterations of livers. Additionally, quercetin restored superoxide dismutase, catalase, and glutathione content in livers.

Not only that, quercetin markedly attenuated T2DM-induced production of interleukin 1 beta, interleukin 6, and TNF- $\alpha$ . Accompanied by the restoration of the increased serum total bile acid and the decreased liver total bile acid, quercetin could reduce lipid accumulation in the liver ... These findings suggested that quercetin might be a potentially effective drug for the treatment of T2DM-induced NAFLD."

#### **Quercetin Helps Modulate Gene Expression**

According to research<sup>25</sup> published in 2016, quercetin even has the ability to trigger tumor regression by interacting with your DNA and activating the mitochondrial pathway of apoptosis (the programmed cell death of damaged cells).

Quercetin was found to induce cytotoxicity in leukemic cells, and the effect was dosedependent. Limited cytotoxic effects were also found in breast cancer cells. Overall, quercetin increased the life span in cancer-ridden mice fivefold compared to untreated controls.

The authors attributed these effects to quercetin's direct interaction with DNA and its activation of the mitochondrial pathway of apoptosis, and suggested quercetin's

potential use as a cancer therapy adjunct deserves further exploration.

More recent research<sup>26</sup> in the journal Molecules also highlights quercetin's epigenetic influence and ability to:

- Interact with cell-signaling pathways
- Modulate gene expression
- Influence the activity of transcription factors
- Modulate microRNAs

MicroRNAs used to be considered "junk" DNA. Far from being useless, research has now revealed that "junk" DNA is actually microRNA and plays a crucial role in regulating genes that make the proteins that build your body.

The microRNA function as "on/off" switches for the genes. Depending on the microRNA input, a single gene can code for any of more than 200 protein products. Quercetin's ability to module microRNA may also help explain its cytotoxic effects, and why it appears to improve cancer survival (at least in mice).

## **Quercetin Is a Powerful Antiviral**

As mentioned, one of the most well-studied attributes of quercetin is its antiviral capacity, which have 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

For example, research<sup>27</sup> published in 2007 found it lowered cyclists' risk of upper respiratory track infections following intensified exercise.

Here, cyclists who received a daily dose of 1,000 mg of quercetin in combination with vitamin C (which enhances plasma quercetin levels<sup>28,29</sup>) 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 study<sup>30</sup> 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. A number of other studies have also confirmed quercetin's effectiveness against a variety of viruses, including the following:

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>31</sup>

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 concomitant with antiviral drugs (amantadine or oseltamivir), the effect was significantly amplified – and it prevented drug-resistance from developing.<sup>32</sup>

A 2004 animal study investigating quercetin's effect on influenza used a strain of the H3N2 virus. According to the authors:<sup>33</sup>

"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.<sup>34</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>35</sup>

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>36</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.

A 2016 animal study<sup>37</sup> found quercetin inhibited mouse dengue virus and hepatitis virus. Other studies have confirmed quercetin's power to inhibit both hepatitis B<sup>38</sup> and C<sup>39</sup> infection.

Most recently, a March 2020 study<sup>40</sup> 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),<sup>41</sup> 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 $\beta$  and TNF- $\alpha$ ) 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."

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

Aside from its antiviral activity, quercetin is also known for boosting immunity and combating inflammation. As noted in a 2016 study<sup>42</sup> in the journal Nutrients, mechanisms of action include (but is not limited to) the inhibition of:<sup>43</sup>

- 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
- 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>44</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."<sup>45</sup>

## **Quercetin May Be a Useful Supplement for Many**

Considering its wide-ranging benefits, quercetin may be a useful supplement for many, either acutely or more long-term. It's one of the supplements I recommend keeping in your medicine chest for times when you feel you're "coming down" with something, be it the common cold or influenza.

If you're prone to colds and flu, you could consider taking it for a couple of months before cold and flu season hits to boost your immune system. More long-term, it appears useful for those with metabolic syndrome, although it would be foolish to rely on any given supplement without also addressing more fundamental strategies such as diet and exercise.

As explained in my 2015 interview with Dr. Robert Lustig, sugar has been shown to be a causative factor in insulin resistance, which is a hallmark of metabolic syndrome and a risk factor for virtually all chronic disease.

If you have one or more of the conditions that make up metabolic syndrome, you'd be wise to limit your total sugar consumption to 15 grams per day. If you're healthy, and want to stay that way, your daily sugar limit would be around 25 grams.

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