



Quercetin: Sweet Allergy Relief

Quercetin: ubiquitous in the world of botanicals and the most abundant of polyphenolic flavonoids, this vibrantly colored substance is making quite the name for itself in health circles. With the benefits of being an anti-inflammatory, anti-proliferative, anti-oxidant, anti-bacterial, anti-atherogenic, anti-hypertensive, and of course anti-allergenic¹⁻⁵ it's lucky for us that 70% of flavonoid consumption in the diet is actually quercetin.⁶ Apples and onions are the most well known sources of quercetin but there are also healthy doses of this flavonoid favorite in kale, broccoli, green and black teas, berries, and even red wine.⁷⁻⁹

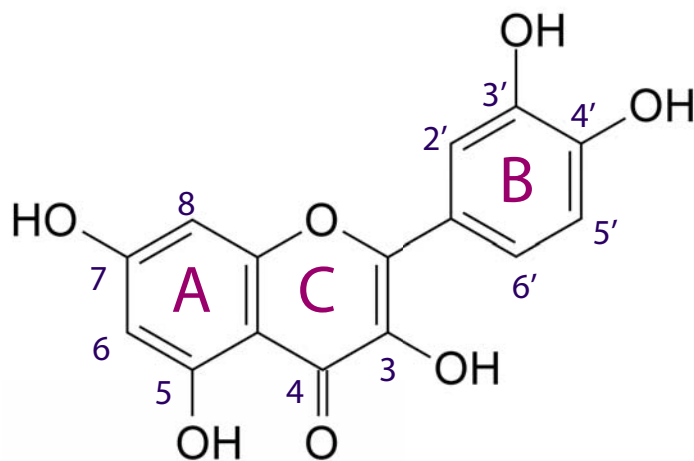


Figure 1: The Chemical Structure of Quercetin

Of the 5000 different flavonoids discovered, with more being added to this count everyday, quercetin is stealing the show as studies are demonstrating again and again how it is one of the most potent and effective of the polyphenolic flavonoids.¹ Flavonoids in

general are composed of a three-ringed structure that allows for the antioxidant and anti-inflammatory actions they are famous for. Quercetin in particular contains a catechol group (B ring) and a strategically placed hydroxy group (at position 3) that contribute to its more potent antioxidative actions, allowing it to scavenge free radicals more efficiently.¹⁰

The antioxidant action of quercetin, that is its ability to scavenge reactive oxygen species (ROS), is hypothesized to be the source of its beneficial effects, and particularly its anti-inflammatory properties.¹ This is mediated through the actions of a regulatory molecule called Nuclear factor kappa beta (NF-kB) which, when stimulated, promotes production of inflammatory molecules including tumour necrosis factor (TNF)-alpha and others.¹¹ ROS increase NF-kB stimulation, which through TNF-alpha leads to inflammatory cytokines, which leads to the production of ROS and the cycle continues.¹² Quercetin acts to both inhibit NF-kB¹³ and neutralize the ROS produced¹⁴, thus breaking the cycle of oxidative stress and down regulating the progression of disease processes.

This effect leads to the many benefits associated with this flavonoid powerhouse. Quercetin is used in the management of pain and inflammation as it works to block the action of lipoxygenases and cyclooxygenases, enzymes that produce proinflammatory, and thus pain producing, mediators.^{15,16} Quercetin inhibits aldose reductase, an enzyme that promotes the formation of fructose and sorbitol from circulating glucose, suggesting a use in diabetes related conditions such as cataracts, glaucoma, nephropathy and neuropathy.¹⁷ Quercetin is also showing great promise in cardiovascular health, including a recent double-blind placebo controlled trial, which demonstrated that quercetin supplementation at 730mg/day for 28 days

was effective in reducing blood pressure in stage I hypertensive patients.¹⁸ Due to its free-radical scavenging structure quercetin also has a role in cancer prevention and treatment, particularly colon and lung cancers.¹⁹ Interestingly, quercetin has also shown benefit in the treatment of chronic prostatitis specifically in treating the associated pelvic pain, which can be attributed to the anti-inflammatory and analgesic properties of quercetin.²⁰

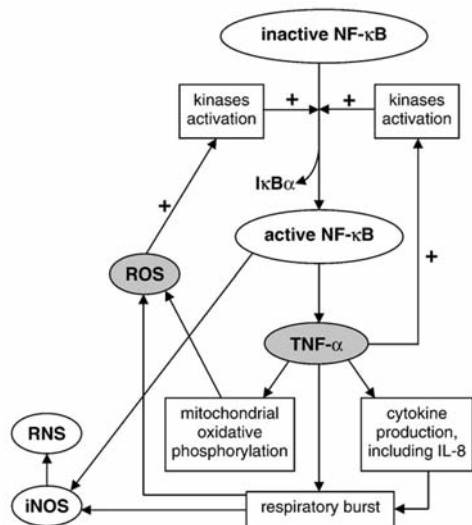


Figure 2: The antioxidant and anti-inflammatory actions of quercetin

The list of benefits goes on, but the topic of interest this season is, of course, quercetin's ability to ease the woes of allergy sufferers. Both seasonal and chronic allergies are associated with debilitating symptoms such as itchy, watery eyes, nasal congestion, hives, atopic dermatitis, asthma and in severe cases of allergen exposure, anaphylaxis. Fortunately for those afflicted, one of quercetin's most well known effects is that of allergy relief. Since the early 1980's quercetin has been studied for its effects on allergy related immune cells in the body.²¹ These immune cells, most notably basophils, mast cells, eosinophils, and T-helper cells, are part of the intricate network in the body that works to prevent invasion by infectious offenders, however they can become part of an overactive response leading to allergic reactions, autoimmunity and inflammation.²²

Mast Cell Stabilizer

Mast cells and basophils are at the root of allergic symptoms. Found in numerous tissue locations throughout the body, they house inflammatory mediators such as histamine as well as pro-inflammatory cytokines like TNF-alpha, tryptase and

several Interleukin (IL) molecules: IL-6, IL-8, and IL-13.^{20,23} It's these contents that, once released when mast cells 'degranulate', lead to the symptoms seen in allergies. The antibody IgE is an important player in mast cell degranulation, and is found in higher amounts in allergy sufferers.²⁰ Quercetin's claim to allergy fame is indeed its ability to stabilize these mast cells, leading to less degranulation episodes and subsequently, lower occurrence of allergy symptoms. Studies show that quercetin inhibits IgE mediated histamine release from mast cells to have an overall effect of down-regulating mast cell activation.²¹ Mast cell activation doesn't only result in degranulation, but also results in the production of more inflammatory cytokines through the action of NF-kB, thereby perpetuating the allergic cycle.^{24,25} Quercetin not only works to stabilize the mast cells and inhibit NF-kB, but also down-regulates the production of inflammatory mediators such as tryptase, IL-6, histidine decarboxylase, and TNF-alpha.^{26,27}



Figure 3. Quercetin is a flavonoid found in many common foods including apples and onions

Th-1/Th-2 Balance

In light of this it may be tempting to see the mast cell as an immune enemy, however they are important inflammatory cells of the immune system that respond to danger signals; it is the moderation of their action that is of concern. This is where the T-helper (Th) cells play an important role in what is called the Th-1/Th-2 balance. Th-2 immune cells are associated with cytokines that encourage the development of mast cells, basophils and eosinophils, all of which are implicated in allergies.²⁸ Allergy sufferers are thought to have a dominance of Th-2 to Th-1 immune cells. Thankfully quercetin acts on this level as well to moderate the actions of the immune system, lessening the effects of allergic symptoms. Quercetin has been shown *in vitro* to reduce the expression of Th-2 derived

cytokine IL-4 and increase the expression and production of the Th-1 derived cytokine Interferon (IFN)- γ .²⁹ In an animal model of allergic asthma, quercetin was also shown to modulate the Th1/Th2 balance through this decrease in IL-4 and increase in IFN- γ : The result was a decrease in allergic airway constriction and airway hyper responsiveness, as seen in allergic asthma.³⁰

Another group of allergy associated immune cells, eosinophils, are found in the blood of allergy and allergic asthma sufferers.³¹ Eosinophils are a source of cytokines and chemokines and are known to produce leukotrienes, inflammatory products that cause bronchoconstriction, and mucus hypersecretion associated with allergic asthma.³²⁻³⁵ Quercetin has been shown in animal models of asthma to decrease eosinophils in lung tissue thereby reducing asthmatic symptoms. This effect was demonstrated both with oral supplementation and with an inhaled application of quercetin.^{29,36,37} Once again, researchers are looking at quercetin's ability to inhibit NF-kB in order to explain this decrease in eosinophil levels, since it is known that NF-kB is associated with eosinophil recruitment to allergy sites.³⁸

Many of these studies are test tube or animal model studies, and although these have shown promising results, the need for more human studies is apparent. However, research is surfacing in human trials. A very recent double-blind randomized placebo controlled trial looked at the effect of an enzymatically modified quercetin glycoside on symptoms of cedar pollinosis common in Japan.³⁹ 20 subjects positive for Japanese cedar pollen IgE were assigned either 100mg twice daily of the quercetin glycoside or placebo for 8 weeks in the pollen season.³⁷ The effect was a significant reduction in ocular symptoms, that is a decrease in the symptoms of itchy watery eyes associated with seasonal pollen allergies.³⁷

With the research results so far it's no wonder quercetin is gaining a name in anti-allergy treatment, not to mention the plethora of benefits being shown to result from its consumption. Of course eating a diet high in flavonoids will benefit overall health, but often the body needs an extra kick of flavonoid action to support the immune system against an oncoming allergy season. And with quercetin in the allergy arsenal, this pollen season just got better.



Bioavailability of Quercetin

Quercetin is most commonly found in nature as a glycoside, meaning that there is a sugar group in place of one of the OH (hydroxy) groups. Quercetin glycosides include rutin, quercitrin, isoquercitrin and hyperoside. Due to its structure, the aglycone form of quercetin is the most effective antioxidant and anti-inflammatory.

Quercetin was previously thought to have a very low bioavailability, and its absorption in the intestines was questioned. In addition to this, because quercetin is bound by albumin (a blood protein) in the body, some thought this

made it less available for use in the body.⁴⁰ This led to the belief that supplementation with a digestive enzyme such as bromelain would result in better availability of quercetin both intestinally and in the serum.

However, research is lacking to support this claim. The aglycone has actually been shown to have an absorption rate of 24%, and the glycosidic forms (those with a sugar molecule attached) have an absorption rate of 52%.⁴¹ It is also now understood that quercetin is converted by enzymes in the intestinal tract to glycosidic forms to be absorbed,^{42,43} suggesting an even higher absorption rate. In addition to this, quercetin has a relatively long half-life, and on repeated supplementation of the pure aglycone, quercetin blood levels increase significantly.⁴⁴ This suggests that concurrent supplementation with digestive enzymes is unnecessary to absorb and utilize the quercetin aglycone.

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