Quercetin's Powerful Influence: Cytoprotective, Antioxidant, and Immunomodulatory

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Discussion

Quercetin is a prominent member of the vast polyphenol family. These naturally-occurring biochemical compounds are produced by plants as part of their defense system. Vegetables, fruits, whole grains, and herbs provide an abundance of these complex and diverse plant micronutrients. Of over 10,000 known polyphenolic compounds, almost half are flavonoids. First discovered in 1930 by the Nobel Prize laureate Albert Szent-Gyorgyi, flavonoids are readily bioavailable and promote health in numerous ways.[1,2] Diets high in plant polyphenols are found to correlate with increased health and decreased incidence of chronic degenerative disease.[1-6]

The flavonol quercetin is ubiquitous in the plant kingdom. The highest levels occur in onions, broccoli, curly kale, leeks, apples, asparagus, red leaf lettuce, cherries, black currants, buckwheat, wild greens, and *Camellia sinensis*.[1,3,6-8] A diet that includes an abundance of fresh fruits and vegetables can provide as much as 200 mg/day of quercetin.[6]

QUERCETIN: DIVERSE BIOLOGICAL INFLUENCE

Quercetin offers a diverse range of biological influence and is best known for its potent antioxidant and anti-inflammatory activity. It is also known to offer immunomodulatory benefits.[1,2,7-9] Largely because of these actions, quercetin is notable for its cytoprotective and neuroprotective influence.[1,7-11]

Quercetin is found to act as a vasodilator, to benefit cardiovascular health, and to reduce hypertension. It is also found to be beneficial in the prevention and treatment of cancer and cardiovascular disease. Quercetin is noted for its ability to promote overall health and is widely used to treat and prevent allergies and both bacterial and viral infections.[1,7,8,12]

Cytoprotective

Flavonoids are known for their cytoprotective influence. Quercetin is found to protect cells directly through its antioxidant activity and indirectly through other mechanisms.

Quercetin protects cellular health through its ability to chelate metal ions, including iron, and to inhibit superoxide production (O2-). Both these activities help prevent the formation of ROS. Chelation of metal ions helps reduce the concentration of ions such as iron, cadmium, and other metals that generate ROS which damage the cellular membrane and cellular components.[7,13]

As a powerful antioxidant, quercetin inhibits free-radical damage, scavenges free radicals, and increases glutathione concentrations. It is found to strongly inhibit lipid peroxidation. These actions contribute to quercetin's ability to protect DNA, the cellular mitochondria, and the cellular membrane from oxidative damage.[2,7,14]

Neuroprotective

Like many polyphenolic compounds, quercetin is found to be neuroprotective in all stages of human development from infancy through old age.[15-17] Studies *in vivo* and *in vitro* show that quercetin is protective against neurotoxic chemicals, neuronal injury, and in neurodegenerative disease. While this influence is partially explained by its antioxidant and anti-inflammatory activity, the exact mechanisms have yet to be clearly elucidated.[6] Studies find that quercetin does indeed pass through the blood-brain barrier.[6]

Anticancer Influence

Quercetin benefits cellular health and is widely researched for its ability to inhibit abnormal cell growth. It is reported to

be antiangiogenic and able to induce normal apoptosis.[18-24] Quercetin is known to promote apoptosis of cancer cells, which is a property of many flavonoids. It is found to act as an anticarcinogenic and antiproliferative.[7,12,25] Studies report that quercetin exerts direct anticancer influence. Diets high in quercetin are correlated with lower incidence of certain types of cancers in a number of studies.[7]

Quercetin exhibits both antioxidative and anti-inflammatory activity. It inhibits NF-kB (nuclear factor k-B), downregulates production of pro-inflammatory cytokines, and modulates other inflammatory pathways.[7] Many flavonoids, including quercetin, are well-known for their ability to modulate cell signaling.[12] Quercetin is known as a phytoestrogen that interfaces with estrogen-responsive receptors. It is found to interact with the cannabinoid CBI receptor, which exerts an inhibitory effect on cell growth.[7]

Quercetin is found to inhibit transcription of heat shock protein and other factors that influence cellular oxygen status in oncogenesis. Quercetin is also found to inhibit tumor invasion and metastasis through influencing various MMPs (matrix metalloproteinases) and other pathways.[7]

Studies indicate that quercetin may be helpful to resensitize cancer cells to chemotherapy and to help reduce or reverse multi-drug resistance. It is suggested that quercetin helps potentiate the beneficial actions of some chemotherapeutic agents.[7]

Immunomodulatory

Quercetin modulates inflammatory pathways including the NF-kB, COX (cyclooxygenase) and LOX (lipoxygenase).[27-30] Studies find it down-regulates NF-kB and EGF (epidermal growth factor) expression and improves cell signaling.[30-34] It mediates TLR (toll-like receptor) expression and influence. TLRs play key roles in innate and adaptive immune response systems. They comprise the recognition and signaling aspect of the immune response.[26]

Allergy Relief and Antimicrobial Activity

Quercetin benefits those suffering from allergies primarily due to its antihistamine activity.[35] It inhibits formation of the mast cells which play a key role in allergic reactions. Quercetin influences mast cells through modulation of multiple factors and pathways that influence their activation and inhibition.[7]

Mast cells participate in allergies, immunity, and inflammation by secreting pro-inflammatory cytokines. This includes histamine, prostaglandin D2, leukotrienes, specific cytokines, and proteolytic enzymes.[7]

Quercetin is found to inhibit histamine and some cytokine release from basophils and mast cells. It is shown to effectively prevent mast cell degranulation and histamine release. It can inhibit histamine release by 52% to 77%.[36] Quercetin is found to stabilize mast cell walls by various mechanisms. It decreases capillary fragility and inhibits pro-inflammatory processes including formation of prostaglandin PGE.[2,9,11]

Quercetin is found *in vitro* and *in vivo* to exert antibacterial and antimicrobial activity. It is found effective against various species including *Porphyromonas gingivalis* and *Helicobacter pylori*.[7] Studies report that quercetin also demonstrates antiviral influence through multiple mechanisms.[7]

Cardiovascular Health

There is a large body of research that demonstrates the benefits of quercetin for cardiovascular health. Overall, a positive correlation is seen between a high intake of dietary flavonoids and a reduction in disease and mortality from cardiovascular disease.[12]

Quercetin is found to act as a vasodilator, to exert antiplatelet influence, and to benefit endothelial function.[2,12] Because of these actions, quercetin is found to help reduce blood pressure.[7,25] In both human and animal models of systemic hypertension, quercetin is found to help reduce the adverse effects of hypertension in the vascular and cardiac systems.[7,25]

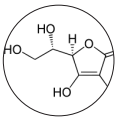
Quercetin demonstrates a significant beneficial effect in lowering blood pressure and is considered a useful adjunct in antihypertensive therapy.[2,12] Quercetin calms inflammation, benefits endothelial function, and demonstrates the ability to significantly reduce LDL-C.[2]

Metabolic and Eye Health

Some studies indicate that quercetin helps lower blood glucose and supports pancreatic beta-cell activity. It is found to be protective against internal damage caused by high glucose levels and to enhance repair of vascular and other tisuses.[2,7] Quercetin is also found to modulate various inflammatory factors that mediate inflammation and insulin resistance in human adipocyte tissue.[8]

Because of its cytoprotective, antioxidative, and other actions, quercetin is considered beneficial for use in early AMD (age-related macular degeneration). An *in vitro* study concludes that quercetin exerts a beneficial effect on the retinal pigment epithelium cells protecting them from oxidative damage, stress-induced changes, and cellular aging.[37]

Additional Ingredients that Enhance Quercetin's Multi-Actions



Vitamin C

Vitamin C is a water-soluble vitamin that is an essential cofactor in many biochemical and enzymatic reactions throughout the body. Widely known for its antioxidant capacity, it plays a key role in the redox recycling of antioxidants including vitamin E.[38]

Nettle Leaf (*Urtica dioica*)

Stinging Nettle is a time-revered herbal panacea and nutritive tonic used as a medicine, home remedy, and food for thousands of years. Nettle leaf is a traditional remedy for those suffering with allergies. As a lung tonic, Nettle is traditionally used for asthma, mucus conditions of the lungs, and chronic coughs. Nettle tincture is also valued to alleviate flus, colds, bronchitis, and pneumonia.[39]

Nutrient-dense Nettle leaf offers a wide spectrum of bioavailable minerals including iron, potassium, calcium, and silica. High in chlorophyll, Nettle leaf provides a rich source of carotenoids along with vitamins C, K, and B. Nettle also contains high levels of protein (about 10%). Stinging Nettle is well-known for its ability to enhance healthy immune response and overall health.[39] The stinging hairs of Nettle leaf are found to contain histamine, betaine, choline, acetylcholine, serotonin, and formic acid.[40]

Organic freeze-dried Nettle maintains some of the activity of the fresh plant and is found to exert an antihistamine-like effect, while tonifying and firming inflamed tissues. In the late 1980s, scientists studying the differences between dried and freeze-dried herbs discovered that freeze-dried Nettle leaf alleviated one of the researcher's hay fever. Subsequently, a randomized double-blind study showed that 58% of hay fever sufferers given freeze-dried Nettle rated it moderately to highly effective.[40]

An *in vitro* study found that Nettle leaf extract inhibits inflammatory processes involved with seasonal allergies. It inhibits histamine response and helps prevent mast cell degranulation and subsequent release of pro-inflammatory mediators. Nettle extract is found to inhibit prostaglandin formation through several pathways including inhibition of COX-1 and COX-2 pathways.[41]

Bromelain (*Ananas comosus*)

Bromelain, a proteolytic enzyme, is a component of pineapple commonly used as a digestive aid. It demonstrates anti-edematous, anti-inflammatory, and fibrinolytic activities. Bromelain exerts immunomodulatory influence and is found to modulate cytokines.[42,43] The therapeutic effects of bromelain are enhanced at higher doses.[44]

For more information on any of the ingredients listed here, including extensive research or individual monographs compiled by Donnie Yance, please email info@naturaedu.com.

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