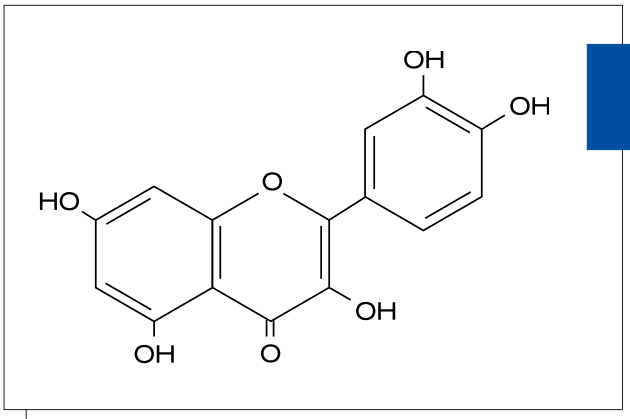

Monograph

Quercetin

Description

Quercetin is widely distributed in the plant kingdom and is the most abundant of the flavonoid molecules. It is found in many often-consumed foods, including apple, onion, tea, berries, and brassica vegetables, as well as many seeds, nuts, flowers, barks, and leaves. It is also found in medicinal botanicals, including *Ginkgo biloba*, *Hypericum perforatum* (St. John's Wort), *Sambucus canadensis* (Elder), and many others. It is often a major component of the medicinal activity of the plant, and has been shown in experimental studies to have numerous effects on the body.

All flavonoids have the same basic chemical structure, a three-ringed molecule with hydroxyl (OH) groups attached (see Figure). A multitude of other substitutions can occur, giving rise to the many types of flavonoids. Flavonoids often occur in foods as a glycoside, meaning they have a sugar molecule (rhamnose, glucose, galactose, etc.) attached to the center (C) ring. Quercetin is the aglycone (meaning minus the sugar molecule) of a number of other flavonoids, including rutin, quercetrin, isoquercetin, and hyperoside. These molecules have the same structure as quercetin except they have a specific sugar molecule in place of one of quercetin's hydroxyl groups on the C ring, which dramatically changes the activity of the molecule. Activity comparison studies have identified other flavonoids as often having similar effects as quercetin; but quercetin usually has the greatest activity.

Quercetin appears to have many beneficial effects on human health, including cardiovascular protection, anti-cancer activity, anti-ulcer effects, anti-allergy activity, cataract prevention, antiviral activity, and anti-inflammatory effects.

Mechanisms of Action

Flavonoids, as a rule, are antioxidants, and a number of quercetin's effects appear to be due to its antioxidant activity. Quercetin scavenges oxygen radicals,[1,2] inhibits xanthine oxidase,[3] and inhibits lipid peroxidation *in vitro*.[4] As another indicator of its antioxidant effects, quercetin inhibits oxidation of LDL cholesterol *in vitro*, probably by inhibiting LDL oxidation itself, by protecting vitamin E in LDL from being oxidized or by regenerating oxidized vitamin E.[5] By itself, and paired with ascorbic acid, quercetin reduced the incidence of oxidative damage to neurovasculature structures in skin, and inhibited damage to neurons caused by experimental glutathione depletion.[6]

Quercetin's anti-inflammatory activity appears to be due to its antioxidant and inhibitory effects on inflammation-producing enzymes (cyclooxygenase, lipoxygenase) and the subsequent inhibition of inflammatory mediators, including leukotrienes and prostaglandins.[7,8] Inhibition of histamine release by mast cells and basophils[9,10] also contributes to quercetin's anti-inflammatory activity.

Aldose reductase, the enzyme which catalyzes the conversion of glucose to sorbitol, is especially important in the eye, and plays a part in the formation of diabetic cataracts. Quercetin is a strong inhibitor of human lens aldose reductase.[11]

Quercetin exerts antiviral activity against reverse transcriptase of HIV and other retroviruses, and was shown to reduce the infectivity and cellular replication of Herpes simplex virus type 1, polio-virus type 1, parainfluenza virus type 3, and respiratory syncytial virus (RSV).[12]

Early studies on quercetin reported that administration to rats caused an increased incidence of urinary bladder tumors. Subsequent studies on rats, mice, and hamsters were unable to confirm the potential carcinogenicity of this molecule.[13,14] In fact, much of the recent research on quercetin has shown it to be an anticarcinogen to numerous cancer cell types, including breast,[15-17] leukemia,[18,19] colon,[20] ovary,[21,22] squamous cell,[23] endometrial,[21] gastric,[24] and non-small-cell lung.[25]

Clinical Indications

Allergies: Quercetin's mast-cell-stabilizing effects make it an obvious choice for use in preventing histamine release in allergy cases, similar to the synthetic flavonoid analogue cromolyn sodium. Absorption of the pure aglycone quercetin is poor (see below); however, much of quercetin's anti-allergy effects may be due to anti-inflammatory and anti-histaminic effects in the gut.

Cardiovascular Disease Prevention: Quercetin's cardiovascular effects center on its antioxidant and anti-inflammatory activity, and its ability to inhibit platelet aggregation *ex vivo*.[26]The Zutphen Elderly Study investigated dietary flavonoid intake and risk of coronary heart disease. The risk of heart disease mortality decreased significantly as flavonoid intake increased. Individuals in the upper 25 percent of flavonoid intake had a relative risk of 0.42 compared to the lowest 25 percent in this 5-year follow-up study of men ages 65-84. Interestingly, the flavonoid-containing foods most commonly eaten in this study contain a high amount of quercetin (tea, onions, apples).[27] In a cohort of the same study, dietary flavonoids (mainly quercetin) were inversely associated with stroke incidence.[28]

Inflammation: Quercetin is indicated in any inflammatory condition, as it inhibits the formation of the inflammatory mediators prostaglandins and leukotrienes, as well as histamine release. This may be especially helpful in asthma, as leukotriene B4 is a potent bronchial constrictor. Quercetin's inhibition of xanthine oxidase decreases the formation of uric acid, and thus it may be of value in the treatment of gout.

Anti-ulcer/Gastroprotective effects: Animal studies have shown quercetin to be protective of gastric ulceration caused by ethanol, probably by inhibiting lipid peroxidation of gastric cells[29,30] and/or by inhibition of gastric acid secretion.[31] An interesting aspect of quercetin's anti-ulcer effect is that it has been shown to inhibit growth of *Helicobacter pylori* in a dose-dependent manner *in vitro*.[31]

Cancer: As mentioned above, quercetin has been investigated in a number of animal models and human cancer cell lines, and has been found to have antiproliferative effects. It may also increase the effectiveness of chemotherapeutic agents.[21,22] More clinically-oriented research needs to be done in this area to discover effective dosage ranges and protocols.

Diabetic Complications: Quercetin's aldose reductase-inhibiting properties make it a useful addition to diabetic nutritional supplementation, to prevent cataract and neurovascular complications.

Viral Infections: Quercetin may be useful in viral infections; however, none of the research so far is clinically-based. Even so, concentration on ingesting quercetin-rich foods or supplementation with the pure substance may be helpful during viral illnesses.

Pharmacokinetics

Few human quercetin absorption studies exist. It appears that only a small percentage of quercetin is absorbed after an oral dose, possibly only two percent, according to one study.[32] A recent study of absorption in "healthy" ileostomy patients revealed an absorption of 24 percent of the pure aglycone and 52 percent of quercetin glycosides from onions.[33] However, no intestinal permeability values were obtained in this group, and thus the results might not be reliable. Quercetin undergoes bacterial metabolism in the intestinal tract, and is converted into phenolic acids. Absorbed quercetin is transported to the liver bound to albumin, where some may be converted via methylation, hydroxylation, or conjugation.[34]

Dosage

An oral dose of 400-500 mg three times per day is typically used in clinical practice. Since solubility is an issue in quercetin absorption,[34] a new, water-soluble quercetin molecule, quercetin chalcone, might be used in smaller doses, typically 250 mg three times per day.

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