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Quercetin – A Flavonoid :A Systematic Review

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Abstract
Quercetin which belongs to a group of plant pigments called flavonoids which help give many fruits, flowers and vegetables their colours. Such flavonoids, such as Quercetin also act as anti-oxidants. They hunt and neutralise the free radicals which damage cell membranes, change the DNA structure and also cause cell death. Quercetin is also believed to help protection against several degenerative diseases by preventing lipid peroxidation. However, the degree and method of Quercetin's in vivo absorption s yet to be determined. This review provides a survey of literature regarding flavonoids in general, but more specifically on Quercetin.
Keywords : Quercetin, Flavonoid, Antioxidant, Metabolism

INTRODUCTION

Flavonoids are a group of plant metabolites thought to provide health benefits through cell signalling pathways and antioxidant effects. These molecules are found in a variety of fruits and vegetables.[1]
Flavonoids are polyphenolic molecules containing 15 carbon atoms and are soluble in water. They consist of two benzene rings connected by a short three carbon chain. One of the carbons in this chain is connected to a carbon in one of the benzine rings, either through an oxygen bridge or directly, which gives a third middle ring. The flavonoids can be divided into six major subtypes, which include chalcones, flavones, isoflavonoids, flavanones, anthoxanthins and anthocyanins. Many of these molecules, particularly the anthoxanthins give rise to the yellow colour of some petals, while anthocyanins are often responsible for the red colour of buds and the purple-red colour of autumn leaves.[1] This review mainly focuses on Quercetin, which is bioflavonoid found.
Quercetin is a unique bioflavonoid that has been extensively studied by researchers over the past 30 years. Bioflavonoids were first discovered in the year 1930. Flavonoids belong to a group of natural substances with variable phenolic structure and are found in the fruits, vegetables, grains, bark roots, stem, flowers, tea and many more.[2]
International Union of Pure and Applied Chemistry (IUPAC)) nomenclature for quercetin is 3,3',4',5,7 –pentahydroxyflavanone (or its synonym 3,3',4',5,7-pentahydroxy-2-phenylchro- men-4-one). is means that quercetin has an OH group attached at positions 3, 5, 7, 3', and 4' the difference between quercetin and Kaempferol is that the latter lacks the OH group at position 3'. The difference between quercetin and Myricetin is that the latter has an extra OH group at position 5'.[3]
A multitude of other substitutions can occur, giving rise to more than 4,000 identified flavonoids [4]. Quercetin is an aglycone, lacking an attached sugar. It is a brilliant citron yellow colour and is entirely insoluble in cold water, poorly soluble in hot water, but quite soluble in alcohol.[3] In food, quercetin occurs mainly in a bounded form, with sugars, phenolic acids, alcohols etc. After ingestion, derivatives of quercetin are hydrolysed mostly in the gastrointestinal tract and then absorbed and metabolised. Therefore, the content and form of all quercetin derivatives in food is significant for their bioavailability as aglycone.[5] Technically, the term quercetin should be used to describe the aglycone only; however, this is not always the case in research or in the supplement industry, where quercetin is occasionally used generically to refer to quercetin-type molecules, including its glycosides. [3]

DIETARY SOURCES

Quercetin is widely available and easy to extract, isolate and detect .Commonly found in vegetables and fruits in the form of a glycoside, a quercetin is in every sense a polyphenol.[8]

Quercetin-type flavonols (primarily as quercetin glycosides), the most abundant of the flavonoid molecules, are widely distributed in the plant kingdom. They are found in a variety of foods including apples, berries, Brassica vegetables, capers, grapes, onions, shallots, tea, and tomatoes, as well as many seeds, nuts, flowers, barks, and leaves.[6,7]

METABOLISM

Once quercetin is absorbed in the gastrointestinal tract, it is processed by Phase II enzymes in the epithelial cells of the stomach and intestines. The combined metabolites are then processed further in the liver and kidney [9,10]. The

B-ring catechol structure undergoes methylation at the 3′or 4′ hydroxyl site by catechol-O-methyl transferase (COMT) to form Isorhamnetin and Tamarixetin, respectively [11]. Quercetin metabolites even seem to build up in tissues shortly after quercetin-rich vegetables are eaten [12]. In vitro studies have shown that quercetin metabolites, that are produced in enterocytes and the liver, function as antioxidants by raising the resistance of low-density lipoprotein (LDL) cholesterol to oxidation.
Cellular studies have shown that Quercetin can generate both antioxidant and pro-oxidant effects according to its concentration. Quercetin is the most powerful flavonoids for protecting the body against reactive oxygen species, produced during the normal oxygen metabolism or are induced by exogenous damage. Quercetin seems to be the most powerful flavonoids for protecting the body against reactive oxygen species, produced during the normal oxygen metabolism or are induced by exogenous damage. Because of its pro-oxidant properties, quercetin can result in oxidative damage when it reacts with different biomolecules, such as lipids, proteins and DNA.[13]

Clinical Manifestations

1. Antioxidant :

The best described property of Quercetin is its ability to act as antioxidant. Quercetin seems to be the most powerful flavonoids for protecting the body against reactive oxygen species, produced during the normal oxygen metabolism or are induced by exogenous damage. [14,15]. Animal evidence suggests quercetin's antioxidant effects afford protection of the brain, heart, and other tissues against Ischemia-Reperfusion injury, toxic compounds, and other factors that can induce oxidative stress.[3] However, certain findings refute the antioxidant properties of Quercetin, and suggest that Quercetin also scavenges nitric oxide (NO) while producing superoxide anions according to physiological conditions such as pH, O2- concentration and superoxide anion concentration.[16,17] Quercetin has been proven to be a better scavenger of O2- than of NO under conditions of increased O2- in the smooth muscles of blood vessels. [18] Quercetin behaves as a protective agent in the corpus cavernosum of mice by increasing the bioavailability of exogenous NO by shielding it from superoxide anions. [19] Quercetin is capable of scavenging reactive oxygen species and its antioxidant potential is attributed to this free radical scavenging activity [5].

2. Cardiovascular protection :

Quercetin has been reported to play a role in reducing cardiovascular diseases and this property is attributed to its anti-inflammatory nature. During an in vitro study on isolated rat arteries, quercetin in its a-glycan form has been demonstrated to be a vasodilator.[20] Epidemiological data show a positive correlation between a diet rich in quercetin and reduction in cardiovascular problems. Several epidemiological studies have reported an inverse association between quercetin intakes and coronary heart disease. In the Zutphen Elderly Study, the risk of heart disease mortality decreased significantly as flavonoid intake increased, with the flavonoid-containing foods most commonly eaten in this study containing high amounts of quercetin compounds (e.g., tea, onions, apples). In a cohort of the same study, dietary flavonoids (mainly quercetin) were inversely associated with stroke incidence.[22] In the Finnish Mobile Clinic Health Examination Survey, low flavonoid intake was associated with higher risks of coronary disease. Intakes of onions and apples, the main dietary sources of flavonoids as well as rich sources of quercetin compounds, had similar associations. [23] In a clinical trial of quercetin supplementation in healthy subjects, a marked increase in plasma quercetin levels was seen; however, no improvements were noted in selected risk factors for cardiovascular disease or thrombogenesis.[24]

3. Inflammation, Injury, and Pain :

Quercetin is indicated in inflammatory conditions, as it inhibits formation of prostaglandins and leukotrienes, as well as histamine release. This may be especially helpful in asthma, as leukotriene B4 is a potent bronchoconstrictor. Patients suffering from chronic inflammatory conditions such as chronic prostatitis and interstitial cystitis show significant symptomatic improvement with oral quercetin supplementation (500 mg BID for one month).[25,26]

In vivo animal experiments also support an anti-inflammatory effect. Quercetin ameliorates the inflammatory response induced by carrageenan and a high-fat diet. Quercetin reduced visceral adipose tissue TNF-a and nitric oxide production and down regulated NOS expression in obese Zucker rats. In chronic rat adjuvant-induced arthritis, quercetin decreased clinical signs of arthritis compared to untreated controls. [27]

4. Cancer :

Quercetin has been investigated in a number of animal models and human cancer cell lines, and has been found to have anti-proliferative effects in numerous cancer cell types, including breast, leukaemia, colon, ovary, squamous cell, endometrial, gastric, and non-small-cell lung. It may also increase the effectiveness of chemotherapeutic agents. Phase one clinical trials show evidence of in vivo lymphocyte tyrosine kinase inhibition and anti-tumour activity of parenteral quercetin. More clinically oriented research needs to be done in this area to discover effective dosage ranges and protocols.[21]

Conclusion

Quercetin and its derivatives have been studied for their pharmacological properties in the recent years. We have discussed some of the pharmacological properties, including, antiviral, antioxidant, anticancer, antimicrobial, anti- inflammatory, neurological effects, cardiovascular, and hepatoprotective. However, research published on anti-inflammatory aspect of quercetin and its derivatives is not enough for its application in humans. Quercetin and its derivatives are versatile molecules and should be investigated more extensively for their wider applications in human health, including their therapeutic activities.

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