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REVIEW ON QUERCETIN AND THEIR BENEFICIAL PROPERTIES

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ABSTRACT

Quercetin (3,3',4',5,7-pentahydroxyflavone) is a type of flavonoid which is present commonly in various foods including fruits, and vegetable. Quercetin provides many health promoting benefits, including improvement of cardiovascular health, anti- cancer, allergic disorders, arthritis, anti- inflammatory etc. The main aim of this review to understanding of physiochemical behavior of quercetin and their pharmacokinetic and biosynthesis mechanism and also quercetin have clinical application.

KEYWORDS: Quercetin; ADME of quercetin; anti- inflammatory; anti- cancer.

INTRODUCTION

Quercetin (3,3',4',5,7-pentahydroxyflavone) is a type of flavonoid which is present commonly in various foods including fruits, and vegetable.[1] Quercetin is the richest of the flavonoids. Flavonoids is regular elements for the diet, were first known as vitamin P, and, along with vitamin C were found to be important in the maintenance of capillary wall integrity and capillary resistance.[2] Quercetum, meaning oak forest or quercus oak, come from the Latin. They contain of 3 ring and 5 hydroxyl group. Quercetin is naturally found in plants as glycone or carbohydrate conjugates.[3] 4000 naturally phenolic plant are available.

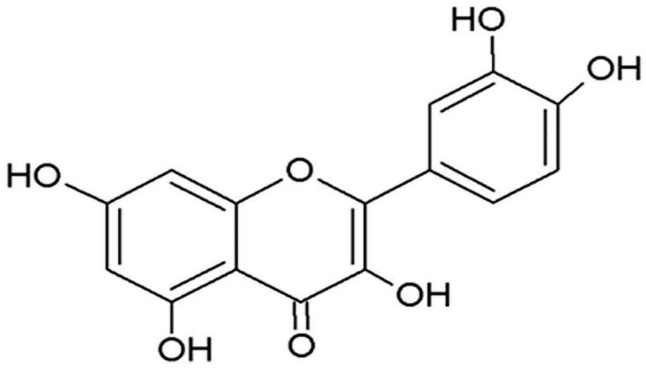

Figure 1: Structure of quercetin.

For quercetin, That 1st isolation and identification by Szent-Gyor- gyi in 1936.[4] It is established to show the antiviral, antibacterial, anticarcinogenic and anti-inflammatory effect.[5] The anticarcinogenic properties of quercetin effect important impact on an increase in the apoptosis of mutated cell, inhibition of cancerous cell growth, inhibition of DNA synthesis, decrease and modification of cellular signal transduction pathways.[6]

General occurrence of quercetin

Quercetin is a yellow, crystalline solid which is bitter in taste, which is insoluble in water, and soluble in glacial acetic, slightly soluble in alcohol acid and aqueous alkaline solutions.[1] A molecule of quercetin (Figure 1), which consists of five hydroxyl groups, whose presence determines the potential activity of biological activity and derivatives of the premises. The main groups of quercetin derivatives are glycosides and ether, as well as the less frequently sulfate and phenyl substituent. Animals are unable to produce the flavones nucleus; thus, flavonoids are found completely in the plant kingdom. Quercetin is found in various food products and plants, including seeds, fruits, tea, coffee, vegetables, bracken fern, and natural dyes. Quercetin is usually found from the rutin (quercetin-3rutinoside).[7]

Amount of quercetin in selected foods.[32]

S.n.	Food source	Quercetin content (mg/100g)
1.	Capers	233.00
2.	Onions	22.00
3.	Cranberries	14.00
4.	Cocoa powder	20.00
5.	Lingonberries	7.40
6.	Asparagus, cooked	7.61
7.	Blueberries	5.05
8.	Apple, Red Delicious	4.70
9.	Cherries	2.64
10.	Broccoli, raw	2.51

11.	Apple, Fuji	2.02
12.	Green tea	2.69
14.	Black tea	1.99
15.	Red grapes	1.38

Biosynthesis of quercetin[8]

Phenylpropanoid pathway

Phenylalanine

↓ phenylalanine ammonia-lyase, cinnamate-4-hydroxylase, and 4-coumaroyl-CoA-ligase.

One molecule of 4-coumaroyl-CoA

+

Three molecules of malonyl-CoA

↓ 7,2′-dihydroxy-4′-methoxyisoflavanol synthase

trahydroxychalcone

↓ chalcone isomerase

naringenin

↓ flavanoid 3′-hydroxylas

eriodictyol

↓ flavanoid 3-hydroxylas

dihydroquercetin quercetin using

↓ flavonol synthase

Quercetin

Absorption, metabolism, distribution and excretion

Quercetin aglycone and glycosides are absorbed from the gastrointestinal tract to a different range, as well absorption of quercetin glycosides depends on the site and nature of sugar replacements. The stomach can be easily absorbed lipophilic quercetin molecule and then secreted in the bile. The absorption of quercetin glycosides is not dependent on pH condition of the stomach and they pass through the small intestine and absorbed by deglycosylated. There are two mechanism enabling intestinal absorption of quercetin glycosides. In the first, they are a potential substrate for lactose polarizing hydrolase (LPH) in the brush border membrane. The second mechanism allowing intestinal absorption of quercetin glycosides assumes the possibility of interacting with sodium-dependent glucose transporter SGLT1.[9,10]

After absorption, quercetin is metabolized in different organs, such as the small intestine, colon, liver, and kidney.[11] In rats, quercetin did not undergo any significant phase I metabolism. In contrast, quercetin did undergo extensive phase II (conjugation) to produce metabolites that are more polar than the parent substance and hence are more rapidly excreted from the body. The meta-hydroxyl group of catechol is methylated by Catechol-O-methyl transferase. Five hydroxyl groups of quercetin are converted to glucuronidated by UDP-glucuronosyltransferase. The exception is the 5-hydroxyl group of the flavonoid ring that usually does not undergo glucuronidation. The major metabolites of orally absorbed quercetin are quercetin-3-glucuronide, quercetin-3'-sulfate, and 3'-methylquercetin-3-glucuronide.[12,13] Equal distribution of quercetin systemic absorbed across all major tissue. quercetin was observed to concentrated in serval organs- i.e. lungs kidney, thymus, testes, heart and liver. Highest concentrations of quercetin detected in the pulmonary tissue.[14] Quercetin may be eliminated by the urine or otherwise, may be secreted into the bile and excreted in the feces. The phenolic acid and unabsorbed quercetin products are eliminated in the feces.[15,16]

Properties of quercetin

Antioxidant and pro-oxidant properties of quercetin

Quercetin's most described property has the ability to act as antioxidant. Animal evidence shows that quercetin's antioxidant effect is to protect the brain, heart and other tissues against ischemia-reperfusion injury, toxic compounds, and other factors that can induce oxidative stress.[10] Quercetin protect against the free radicals in the environment i.e. smocking. That free radicals, destroy the membrane of red blood cell, which come from cigarette. According

to scientist the quercetin aglycone and its conjugate metabolites are able to prevent damage to the membranes of red blood cells due to smoking.[17] Quercetin show antioxidant behavior against the oxidative stress produced by streptozotocin-induced diabetes mellitus in rats.[12] During in vitro studies antioxidant behavior quercetin capable of inhibiting cataract formation caused by oxidative stress in rat eye lens cultured in a hydrogen peroxide environment. It has been reported that using methanolic extract of Heterotheca inuloides having quercetin. Can be efficiently reduce oxidative damage caused by an industrial compound,[18]

Anticancer activity

Quercetin has been studied in a human cancer cell lines and number of animal mode, and has been found to have anti-proliferative effects in cancer cell types, including breast, leukemia, squamous cell, colon, ovary, endometrial, and gastric cell.[19] Quercetin has been reported as an effective anticancer agent. Quercetin has essential hunting potential, thus, it is capable of preventing cancer induced by oxidative stress. Its reported to quercetin has protect against cancer, during in vitro studies in various cancer cell lines and in vivo in rodents especially mice.[20] It has been reported to enhancing immune responses against growth in breast tumors by introduce quercetin with intratumoral doxorubicin injection, quercetin has been described to prevent angiogenesis in tamoxifen-resistant cancer in breast cell.[21]

Anti-inflammatory activity

Quercetin has useful in some of the allergies such as hives, and hay fever. It inhibits the production and release of histamine and other inflammatory substances by stabilizing cell membranes of mast cells.[22] Quercetin also helpful in asthma, as leukotriene B4 is a potent Broncho constrictor. Patients suffering from chronic prostatitis and interstitial cystitis show significant symptomatic improvement with oral quercetin supplementation (500 mg BID for one month).[4,21]

Diabetic complications

Quercetin has been converting glucose to sorbitol (sugar-a sugar alcohol) in the body by inhibition of enzyme aldose reductase. His reduce glucose in blood plasma, glucose tolerance, defense of β-cell activity in the pancreas, and also protected against diabetic effect on mood and renal function.[24,25] QR-333 is a compound that comprises three active ingredients: 1. quercetin (a flavonoid with aldose reductase inhibitor effects), ascorbyl palmitate, and 3. vitamin D3. It is distributed as a hydrophilic ointment. Systemically

administered, aldose reductase inhibitors have shown established modest effects on diabetic neuropathy in studies.[26]

Cardiovascular protection

Quercetin has been play a major role for reducing cardiovascular diseases. Quercetin has proved to be a vasodilator in its A-glycone form, during an in vitro study on isolated rat arteries.[21]

From Epidemiology Studies Consistently show that fully consumed Foods like fruits and vegetables are strongly Related to reduce risk of cardiovascular Diseases.[27] In the Finnish Mobile Clinic Health Examination Survey, low flavonoid intake was connected with high risk of coronary disease. Supplementation with quercetin-containing capsules markedly improved the plasma quercetin concentration but had no effect on other cardiovascular or thrombogenic risk factors.[28]

Potential effects of quercetin on asthma:

Mast cells release several mediators including histamine, cytokines, leukotrienes and play important role in the initial and late phases of asthma. When the treatment with quercetin inhibits the release of histamine and pro-inflammatory mediators (TNF-α, IL-1β, IL-6 and IL-8) from mast cells stimulated with IgE. Thus, quercetin demonstrates the potential to modulate the early and late phases of asthma.[28,29] Quercetin can be used medically, either alone or as a supplement to other medicines used for the treatment of asthma. In addition, it can also be used as a nutraceutical. Thus, a diagnostic study should be done to evaluate the ability of quercetin to prevent or treat episodes of asthma.

Antibacterial effect

Quercetin alone or in combination form shown antibacterial property with other supplements or antibiotics. Quercetin shown antibacterial properties in vitro against actinomyces nasselundi, actinobasils actinomycetamittins, fusobacterial nuclei, porphyromoneous gingivilles and actinomyces viscosus in alone form.[30] Helicobacter pillori was considered to be sensitive to quercetin's antimicrobial effects in both vitro and vivo. In combination with dose, quercetin morin and rutin and antibiotics, including amoxicillin, ampicillin, cephradine, ceftriaxone, imipenem, and methicillin, showed a synergistic effect against methicillin-resistant Staphylococcus aureus (MRSA) in vitro. when natural compounds quercetin and

epigallocatechin gallate were administered together shown a synergistic effect against MRSA in in-vitro studies.[31]

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