Perks of Quercetin

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Abstract

Extensive research has been conducted on the utilization of quercetin, a type of bioflavonoid, as a therapeutic intervention for metabolic and inflammatory disorders. Flavonoids are a ubiquitous class of dietary compounds that can be sourced from a diverse range of food items, such as fruits (notably citrus), green leafy vegetables, seeds, nuts, flowers, trees, broccoli, olive oil, apples, onions, green tea, red grapes, red wine, dark cherries, and berries like blueberries and cranberries. Foods and beverages such as tea, red wine, apples, cherries, and berries are known to contain substantial quantities of flavonoids. Prior research has demonstrated the efficacy of this treatment in addressing a range of conditions, such as cancer, oxidative stress, inflammation, viral and bacterial infections, aging, and the SARS-CoV-2 virus. Although numerous in vitro and in vivo investigations have been conducted to explore the biological activity of quercetin across various cell lines and animal models, the metabolic mechanisms underlying its impact on human physiology remain elusive. Further clinical studies with a large sample size are required to establish the optimal dosage and administration regimen of quercetin for the management of red blood cell dysfunction.

Keywords: Quercetin**,** Dietary Flavonoids, Treatment**,** anti-SARS-CoV-2, Antiviral**,** Antioxidant, Anti-Inflammatory**.**

INTRODUCTION

The term "Quercetum" in Latin denotes an "oak forest," while "quercetin," scientifically referred to as 3,3,4,5,7-pentahydroxyflavone, is classified as a flavonol that is endogenously unattainable for humans.[1] The substance exhibits a slight yellow hue and displays partial solubility in boiling water while exhibiting complete solubility in alcohol and lipids. Quercetin has gained recognition as a bioflavonoid with therapeutic potential in the management of metabolic and inflammatory disorders. This flavonoid is highly abundant in the human diet and can be sourced from a diverse range of food items, such as fruits (notably citrus), leafy greens, nuts, seeds, flowers, trees, olive oil, onions, apples, red grapes, red wine, dark cherries, and berries such as blueberries and cranberries. Flavonoids were found to be abundant in fruits such as apples, cherries, and berries, as well as in beverages like tea and red wine. Abundant quantities of vegetables such as onions and broccoli were also available.[2]

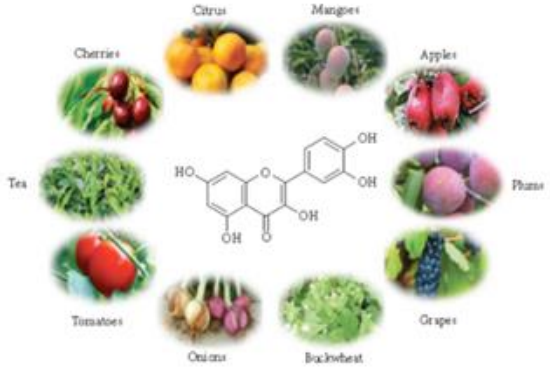

FIG 1: SOURCES OF QUERCETIN.[3]

PROPERTY

1. ANTIOXIDANT

Quercetin, a flavonoid aglycone derived from botanical sources, has been employed as a dietary adjunct and glycoside candidate for ameliorating a variety of health ailments.The beneficial effects of this substance include but are not limited to its anticancer, antitumor, antiulcer, antiallergy, antiviral, anti-inflammatory, anti-diabetic, gastroprotective, antihypertensive, immunomodulatory, and anti-infective properties.[1] Quercetin has the potential to counteract free radicals generated by various sources, apart from those produced by smoking and other environmental factors. Cigarette tar's free radicals possess the capability to cause harm to the membranes of erythrocytes. The study revealed that quercetin and its conjugate metabolites provided protection to erythrocytes against the detrimental effects of smoking-induced membrane damage.[4]

2. ANTI-INFLAMMATORY

According to a study, quercetin was found to have a dual effect of reducing inflammatory cytokine levels in the bloodstream and increasing the apoptosis of active neutrophils.[5] This molecule exhibits potential therapeutic applications in the management of rheumatoid arthritis due to its capability to reduce neutrophil activity. The protective effects of quercetin tea have been linked to its ability to stop the expression of NLRP3, lysate cysteine protease 1, IL-13, and N-GSDMD. This stops THP-1 macrophages from going through apoptosis.Quercetin exhibits the capability to impede the activation of the NLRP3 inflammasome. Additionally, it has been observed that the compound quercetin mitigates the increase in TLR2/MyD88 and p-AMPK resulting from the administration of lipopolysaccharide and adenosine triphosphate. The compound has been discovered to possess anti-inflammatory characteristics by obstructing the TLR2/MyD88/NF-6B and oxidative stress/AMPK signaling pathways.[6]

The research suggests that quercetin has the potential to mitigate the progression of osteoarthritis by reducing oxidative stress responses and decreasing the degradation of cartilage extracellular matrix.[7] The administration of Quercetin has the potential to mitigate inflammation-induced mitochondrial dysfunction while simultaneously promoting mitochondrial fusion, as suggested by previous research.[8] "Regulators such as TXNIP, SIRT1, and Nrf2 have an impact on the activation or inhibition of the NLRP3 inflammasome. Quercetin has been observed to inhibit these regulators, thereby suppressing the NLRP3 inflammasome".[9] Quercetin has been observed to impede inflammatory responses. The substance in question exhibits anti-inflammatory properties by disrupting multiple signaling pathways, such as NF-6B, and not solely by impeding the synthesis of NLRP3 inflammasome constituents and pro-IL-13. The regulation of the NLRP3 inflammasome's activation or inhibition is primarily governed by regulators such as TXNIP, SIRT1, and Nrf2, which are influenced by various molecules. Quercetin has been observed to regulate the aforementioned factors through the inhibition of the NLRP3 inflammasome, thereby mitigating inflammation as well.[9] The production of NOX2 was suppressed by Quercetin, resulting in a reduction of inflammation and oxidative stress induced by ROS, as reported in reference.[10] "The M1 inflammatory responses that induce macrophages and microglial cells to enhance NO production, proinflammatory cytokine expression, and lipocalin-2 production are greatly reduced when quercetin is delivered. Quercetin treatment was observed to decrease the levels of chemokines C-C motif chemokine ligand (CCL)-2 and CCL-10, as reported in a previous study. Numerous research studies have demonstrated the anti-inflammatory properties of quercetin, both when administered internally and applied topically".[3]

"Recent studies have shown that quercetin inhibits TNF-production in lipopolysaccharide-stimulated macrophages by inhibiting the activity of monoclonal nonspecific suppressor factor 3".[10] "In one study, quercetin and the heat shock protein HSC70 affected the role of monoclonal nonspecific inhibitors. In the macrophage, like the cell line RAW264.7, quercetin showed dose-dependent inhibition of LPS/interferon-c-induced nitric oxide production without cytotoxicity. In addition, quercetin inhibits the production of the C-C chemokine RANTES in RAW264.7 cells as well as the rise in TNF-7. Quercetin may suppress MNSF3 activity by altering the activity of the chaperone HSC70. Quercetin has been shown in studies to be effective in the treatment of knee osteoarthritis. These studies show that quercetin reduces joint damage in rats with knee osteoarthritis by mediating the TSC2-RHBE-mTOR signal pathway and that quercetin also inhibits the expression of RHEB, p-mTOR, p-ULK1, and P62, as well as promoting fibroblast proliferation and migration.Studies have shown that quercetin inhibits

TNF-7, IL-13, and IL-6 expression in skin wounds, boosts the proliferation and migration of fibroblasts, inhibits involution in mice through the Wnt/3-catenin signal pathway and TERT, and successfully accelerates skin wound healing".[3]

"Quercetin has been shown to protect against inflammation by suppressing the activity of NF-B translocation, IB phosphorylation, AP-1, and reporter gene transcription. It also controls NF-6B, JNK1, and AP-1 signaling activity. TNF-e activity was reduced similarly when quercetin was used. Quercetin is an effective ferroptosis inhibitor that also reduces the degree of acute renal damage. Quercetin may have beneficial effects on type 2 diabetes by inhibiting pancreatic iron accumulation and ferroptosis in pancreatic 3 cells. Quercetin's metabolite, quercetin-3-O-glucuronide, has been shown to block the role of renal platinum in tubular cells in order to prevent tubular toxicity and perform a renal protective role".[3]

3. ANTI-CANCER

"By inhibiting the red cell cycle and regulating signal molecules, quercetin in combination with a variety of small molecule drugs may reduce the dosage of anticancer therapies while improving their overall efficacy and safety".[3] "The combination of quercetin and cisplatin inhibits cervical cancer cells more efficiently".[12] "By inhibiting MMP-2, ezrin, METTL3, and P-Gp expression in cancer cells, quercetin may improve anticancer effects by weakening cell proliferation, migration, and invasion and enhancing apoptosis".[3] "Sunoqrot et al. (2019), mixed the hydrophilic anticancer compound curcumin with the natural polyphenol quercetin and functionalized it with poly(ethylene glycol) to improve drug distribution to cancer cell lines. This study demonstrates that the spherical form and excellent solubility in aqueous solutions improve the anticancer activity of nanomaterials based on quercetin".[13] "Furthermore, the effects of quercetin on glucose metabolism and cellular energy production contribute to its effects on cell viability decline, metastasis inhibition, and apoptosis induction in cancer cells".[14]

4. APOPTOSIS

Quercetin exhibits noteworthy anticarcinogenic properties by inducing apoptosis in various tissues such as the brain, liver, and colon, thereby impeding the proliferation of malignant cells.[15,16] "The efficacy of curcumin and quercetin in treating familial adenomatous polyposis (FAP) was investigated by Cruz-Correa et al. The patients were orally administered curcumin at a dosage of 480 mg and quercetin at a dosage of 20 mg, three times a day, for an average duration of 6 months. Upon conclusion of the research, it was observed that the administration of red curcumin and quercetin resulted in a decrease in both the quantity and dimensions of ileal and rectal adenomas while exhibiting minimal adverse reactions".[17]

5. ULCER & GASTRITIS

Research has indicated that quercetin possesses gastroprotective properties by impeding gastric acid secretion and lipid peroxidation. Moreover, it hinders the infection caused by Helicobacter pylori.[1] "Suzuki et al.'s study looked into the potential antioxidant and antiulcer properties of quercetin.The dosages of 50 and 100 mg/kg were administered to the rats. According to the data, it can be inferred that quercetin exhibits advantageous properties in terms of antiulcer activity. The anti-ulcer activity of quercetin is attributed to its ability to enhance gastric mucus production or potentially scavenge free radicals".[18,19]

6. ANTI-VIRAL & ANTI-BACTERIAL

"Various past studies showed that quercetin and its derivatives exhibit antiviral properties against a range of diseases, such as the Human Immunodeficiency Virus (HIV), poliovirus, respiratory virus, Sindbis virus, Mayar virus, and H5N1 virus".[20] Quercetin has been demonstrated in numerous studies to possess antiviral properties owing to its ability to impede early viral replication, interact with crucial viral replication proteases, and mitigate inflammation resulting from infection. In a study on Singapore grouper iridovirus particles, Liu et al. (2020) discovered that quercetin had a noteworthy detrimental effect. "Quercetin has been observed to impede SGIV's ability to bind to host cell targets by 76.14% and penetrate host cells by 56.03%."[21] Furthermore, it has been found to hinder virus replication within host cells. "Quercetin exhibits direct and host-mediated anti-Singapore grouper iridescence virus effects, indicating its potential for drug development aimed at effectively controlling Singapore grouper iridescence virus infection in aquaculture. The ethyl acetate fraction of Elaeocarpus sylvestris has been found to contain quercetin and isoquercitrin, which have demonstrated effective inhibition of human herpesvirus replication".[22] The combination treatment of ascorbic acid and quercetin has a synergistic antiviral impact due to their shared antiviral and immunomodulatory properties. Additionally, the potency of quercetin may be increased through its recycling by ascorbate.

"Furthermore, studies have shown interest and concluded that almost all strains of bacteria, particularly affecting gastrointestinal, respiratory,urinary, and dermal system. Their anti-infective and antireplicative ability possibly contributes to the antiviral characteristics".[3]

7. ANTI-AGING

"One recent study reviewed at the effects of quercetin on chicken pectoral muscle tenderness and the processes underlying these effects, and they found that quercetin may significantly reduce shear stress and improve the myofiber rupture index. Caspase-12 was activated, and levels of Bip, caspase-3 activity, p-IRE1/IRE1, and Bax/Bcl-2 were all improved by quercetin treatment".[23] "In addition, the effects of quercetin on autophagy and apoptosis include increased expression of ATG7 and Beclin-1 as well as activation of the cell cycle transition from LC3I to LC3II. The PI3K/AKT/mTOR signaling axis has been linked. These results suggest that administering quercetin to chickens after they have died may promote meat tenderness while simultaneously triggering apoptosis and autophagy pathways".[23]

Liver fibrosis is a major cause of death nowadays. It has been shown that quercetin significantly reduces liver fibrosis. "Human liver stellate cells treated with fructose showed lower expression of fibrosis genes after treatment with quercetin, suggesting that this antioxidant may protect against fibrosis by inhibiting the conversion of growth factor – β and Smad3 signal pathways".[24] Hepatic astrocytic cells exhibit an increased erythropoietic response in the context of chronic liver injury, which is attributed to the upregulation of transforming growth factor 3, collagen 17, and actin-7-smooth muscle. In addition, it has been observed that quercetin has the ability to impede the process of mesenchymal progenitor cell differentiation into adipocytes. Quercetin has been observed to decrease fat deposition and the expression of the lipid-forming genes CEBPA and ADIPOQ in PDGFR7+/CD201+ cells by impeding CREB phosphorylation during the adipocyte differentiation stage. Quercetin is observed to significantly decrease the expression of probromine red (TIMP1, ACTA2, COL1A1, and COL3A1) by inhibiting Smad2 phosphorylation. Quercetin has been observed to impede the differentiation of muscle-derived PDGFR7+/CD201+ cells into adipocytes and fibroblasts within the spectrum of quantities that can be obtained from dietary sources and supplements.[25]The findings of this study indicate that quercetin could potentially serve as a therapeutic or preventative measure against muscle atrophy. The anti-aging properties of quercetin have been demonstrated through the targeted elimination of aged endothelial cells.[26]

8. ANTI- SARS-CoV -2

"The possibility of utilizing quercetin, a significant therapeutic component in traditional Chinese medicine, for the treatment and prevention of COVID-19 has been suggested".[27] Infectious diseases have historically presented a substantial impediment to the advancement of human society. The SARS-CoV-2 pandemic poses a substantial threat to numerous underdeveloped nations that are deficient in adequate medical resources. The creation of biosensors that are rapid, uncomplicated, and not reliant on specific devices is of utmost importance in addressing this dilemma. "Several academic studies have demonstrated the potential of utilizing CRISPR/Cas technology in conjunction with biosensors and bioassays for the purpose of nucleic acid detection. The criticality of drug development for therapeutic treatment is emphasized".[28] Theoretically, it has been suggested that quercetin has the potential to restrict the replication of SARS-CoV-2 and mitigate the inflammatory and toxic consequences of COVID-19 vaccines.[29,30] "Moreover, it has been reported that quercetin mitigates the intensity of symptoms and unfavorable prognostic factors associated with COVID-19, thereby accelerating the conversion of molecular tests from positive to negative".[31] "In a recent clinical investigation, a cohort of 42 outpatients exhibiting COVID-19 symptoms were segregated into two groups. One group was subjected to standard care (SC) treatment, while the other group was administered quercetin as an adjuvant treatment".[3] "The patient's blood indicators revealed that the inclusion of quercetin red supplementation resulted in a reduction of lactate dehydrogenase (LDH) by 35.5%, ferritin (FER) by 40%, C-reactive protein (CRP) by 54.8%, and D-dimer by 11.9%".[3] According to recent research, the severity of COVID-19 symptoms can be reduced and the duration of molecular testing can be shortened by supplementing with quercetin.[31] The administration of a combination of quercetin and vitamins has been proposed as a potential therapeutic approach for individuals afflicted with COVID-19.[32] "According to existing research, quercetin has the potential to serve as a useful intervention in mitigating the frequency and severity of respiratory tract

infections. However, additional studies are required to confirm these findings".[3]

9. ASTHMA, ALLERGIES, HAY FEVER

Quercetin operates as a natural antihistamine through the inhibition of histamine release from allergic substances and other cells involved in allergic reactions. The potential of quercetin to mitigate allergic reactions could have significant therapeutic and prophylactic implications for asthma and bronchitis. The membranes of mast cells play a crucial role in serving as an immunological interface to the brain while also responding to environmental and psychological stressors.[2]

10. NEURODEGENERATIVE DISORDER

"The occurrence of neuronal damage within the central nervous system has been linked to the development of neurodegenerative conditions such as Alzheimer's and Parkinson's disease, as well as inflammatory processes of the system that are associated with stroke".[3] "Quercetin not only hinders red oxidative harm to neurons but also mitigates the likelihood of red damage to human lymphocytes and skin neurovascular structures". Research has demonstrated that it possesses the ability to safeguard neurons from oxidative stress, a process that is implicated in the destruction of tissues and the onset of neurological disorders such as Alzheimer's.[1] The protective effects of flavonoids on neuronal injury are widely acknowledged.[33] Flavonoids exhibit neuroprotective properties in the central nervous system, which may confer neuroprotection against neurotoxic insults. Furthermore, it has the ability to reduce neuroinflammation and enhance cognitive abilities such as memory retention and learning. Flavonoids exhibit preventive properties that can avert severe degenerative ailments and various cerebrovascular diseases linked with dementia and stroke, primarily affecting the geriatric population. Foods and supplements that are rich in flavonoids have been found to enhance cognitive functions and offer protection to vulnerable neurons. "This is achieved through the enhancement of pre-existing neuronal function or the stimulation of neuronal regeneration".[34]

PHARMACOKINETIC

The pharmacokinetic characteristics of quercetin were investigated by Ferry et al. in cancer patients who were administered intravenous doses of the compound within the range of 60 to 2000 mg/m2. According to the research findings, the administration of 945 mg/m2 quercetin was deemed a safe dosage for human consumption. Quercetin elicited adverse effects such as emesis, hypertension, nephrotoxicity, and hyperkalemia at toxic concentrations. Upon intravenous administration, quercetin exhibits a distribution half-life ranging from 0.7 to 7.8 minutes and an elimination half-life ranging from 3.8 to 86 minutes. The measured clearance falls within the range of 0.23-0.84 L/min/m2, while the volume of distribution is determined to be 3.7 L/m2.[35] The pharmacokinetic properties of quercetin aglycone at doses of 8, 20, and 500 mg were investigated by Erlund et al. in a cohort of healthy volunteers.[36] The pharmacokinetic properties of quercetin at 200 mg dose levels were investigated by Graefe et al. The attainment of the maximum concentration (C_{max}) of quercetin occurred at the time of (T_{max},) which was 0.7–0.3 hours.[37]

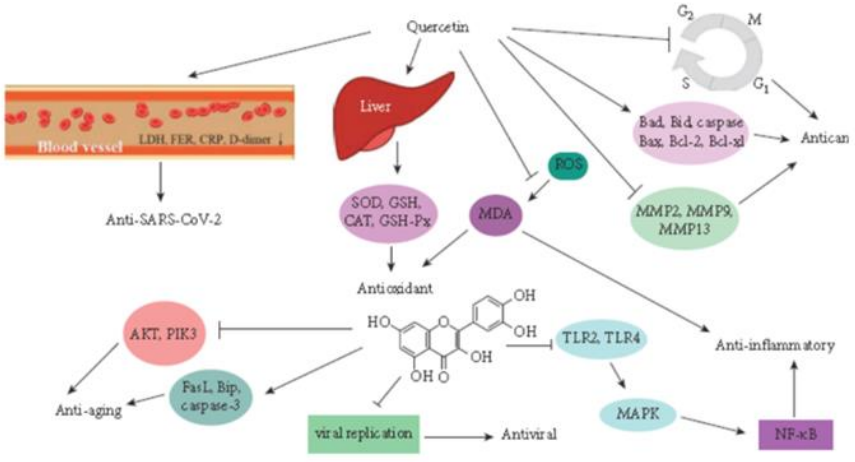

FIG 2: PHARMACOLOGICAL ACTIVITY AND THE POSSIBLE MECHANISMS OF QUERCETIN.[3]

BENEFITS

1. Studies have proved the protective mechanism against various diseases such as osteoporosis, lung cancer like chronic obstructive pulmonary disease cardiovascular disease .
2. It reduces systolic blood pressure
3. Reduce plasma oxidized Low Density Lipoprotein concentrations in overweight
4. Effective against oral lichen planus

CONCLUSION

Research has demonstrated that the flavonoid quercetin possesses antioxidant characteristics. Quercetin has been advocated as a potential remedy for a range of maladies and conditions, such as cardiovascular disease, lung cancer, and osteoporosis. According to a study, there is a correlation between a substantial consumption of flavonoids and a reduced likelihood of cardiovascular ailments, including vascular disease. Flavonoids exist in diverse forms, with flavonol being a prominent variant that is widely distributed across a range of fruits and vegetables. The human diet comprises a variety of flavonols, with quercetin being the most commonly occurring among them. The metabolic pathways through which quercetin exerts its effects in humans remain unknown, despite extensive in vitro and in vivo investigations of its biological activity in various cell lines and animal models. Further clinical studies with larger sample sizes are required to establish the optimal dosage and administration regimen for quercetin in addressing red blood cell dysfunction.

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