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A review of the chemical, pharmacokinetic, and pharmacological aspects of quercetin

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Flavonoids, plant-derived phytochemicals, which are abundantly found in various fruits and vegetables, are potent antioxidants because of their ability to trap damaging free radicals. Among this phytochemical family, quercetin, which belongs to the flavonols subfamily, has garnered a lot of attention. Flavonoids, plant-derived phytochemicals which are abundantly found in various fruits and vegetables, are potent antioxidants because of their ability to trap damaging free radicals. Among this phytochemical family, quercetin, which belongs to the flavonols subfamily, has garnered a lot of attention. The trapping capacity of quercetin is thought to safeguard against a variety of aging-related diseases. The extent and mode of intestinal quercetin absorption have been identified recently. The glycosidic form of quercetin is hydrolyzed, affording the quercetin, which is subsequently transformed into one of its numerous metabolites. Recognizing the mechanism of quercetin as an antioxidant necessitates the synthesis and analysis of quercetin metabolites. This review examines the literature on flavonoids overall as well as quercetin in particular. To underline the relevance of flavonoids, their chemical backbones and antioxidant capabilities are described. However, because the degree of intestinal absorption of flavonoids is debatable, their antioxidant capacity may be an irrelevant matter. Many of the pharmacokinetic studies have indicated that superior absorbed antioxidants involving ascorbic acid are responsible for the antioxidant potential observed upon ingesting particular foods such as green apples. This review highlights the chemistry, pharmacokinetic, and pharmacological effects of flavonoids in general as well as quercetin and its metabolites in particular, by surveying the corresponding *in vitro* and *in vivo* studies.

KEYWORDS

Quercetin; chemistry; pharmacology; pharmacokinetic parameters; metabolites.

Introduction

Damaging free radicals are reactive chemical entities with odd electron numbers which stabilize themselves by abstracting electrons from other molecules. This abstraction generates a new free radical, causing a cascading sequence of free radical formation and stabilization [1]. Nucleic acids and essential cellular components including proteins, carbohydrates, and lipids can all be oxidized by free radicals. The results of this oxidation may include lipid peroxidation, protein denaturation, and mutagenesis [2]. Oxidative stress is the cellular degradation induced by free radicals, and it has been associated with numerous aging-related disorders, including cancer [3],

cardiovascular and inflammatory diseases [4], diabetes [5], and stroke [6].

Free radical moieties such as hydrogen peroxide, superoxide, and hydroxyl are continuously created under the influence of various internal and external factors [7]. The principal internal factor is the oxidative metabolic reactions, particularly when pre-oxidant metallic ions (e.g., iron and copper) participate in the electron transport chain [8]. On the other hand, air pollution, cigarette smoking, and radiation are among the important external factors [9].

In the oxygen-metabolizing organisms including humans, various physiological defense systems exist to prevent the creation of free radicals or neutralize their harm [10]. Pre-oxidant metallic ions, for instance, are prisoned in proteins to restrict their catalytic role in free radicals generation [11]. Also, molecular oxygen is associated to particular enzymes that control its reduction to damaging superoxide radicals which in the plants have also found ways to combat free radical harm. Dietary antioxidants can play a significant role in the combat with damaging free radicals [12]. Flavonoids, the plant-derived secondary metabolites, have a framework rich in the conjugated double bonds and hydroxyl groups enabling them to transfer electrons through resonance to neutralize these free radicals [13]. The scavenging characteristic of flavonoids can be employed in the protection and treatment of many oxidative stress-related disorders [14,15].

Based on their characteristic structural features, flavonoids are differentiated into various categories, including isoflavones, flavanones, flavones, anthocyanidins, flavanols, and flavonols. Isoflavones are explored in soy foods, whereas flavanones may be detected in citrus foods. Flavanols, flavones, anthocyanidins, and flavonols can be found in red grapes and red wine, green leafy spices, berries, and every meal option, respectively [16].

Quercetin (**QC**), a prominent flavonol category representative, has drawn a lot of interest. Approximately 60-75% of flavonoid consumption is driven by **QC** and its glycosides. By scavenging free radicals and chelating pre-oxidant metallic ions, **QC** has been demonstrated to inhibit the oxidation of low-density lipoproteins [17]. As a consequence, **QC** might help to prevent different disorders including diabetes, inflammatory diseases, Alzheimer's, cancer, and atherosclerosis [18].

This review gives a basic overview of flavonoid common chemical structure, its antioxidant properties and advantages, in order to emphasize the relevance of flavonoids. The debate over the absorption of flavonoids like **QC**, on the other hand, is the major emphasis. To successfully argue against the concept that the other antioxidants like ascorbic acid included in diets together with flavonoids, truly perform the antioxidant property, it is necessary to assess the extent of intestinal absorption and bioavailability of flavonoids and their metabolites.

Flavonoid common chemical structure

The typical flavonoid structure is made up of two aromatic rings connected by a three-carbon linker. Flavonoids are classified into two types based on the linker nature, as illustrated in Figure 1, including those ones with a linear linker and those with a heterocyclic ring, known as ring C. Variability in the latter ring and the substitution arrangements in the rings A and B offer a wider range of flavonoid structures [19].

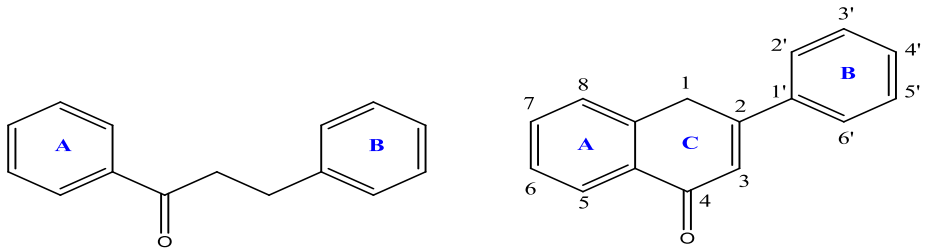

FIGURE 1 Typical two chemical structures of flavonoids

Many categories of flavonoids differ in terms of the substituent linked to ring C. Flavanols and anthocyanidins seem to be the only two categories lacking a 4-oxo group and including a 3-hydroxyl group, in addition to flavonols. Anthocyanidins have two double bonds at 1-2 and 3-4 of ring C, while isoflavones, flavones, and flavonols have double bond lies between positions 2 and 3. Except for isoflavones which are bridged at carbon 3, the C ring in the other categories is connected to ring B through carbon 2. These varied substitutional styles of flavonoids not only determine the category, but also influence the absorption and antioxidant activity [20].

The flavonol **QC**, with a chemical name of 3',4',5,7-tetrahydroxyflavan-3-ol and a structure illustrated in Figure 2, can contribute a proton upon reacting with the free radical. This contribution converts **QC** into its radical form, in which the resultant unpaired electron is delocalized by resonance, rendering the **QC** radical inactive. The catecholic B ring, the, α,β-unsaturated cyclic ketone substituted with hydroxyl group of ring C, and the resorcinolic A ring enable **QC** to retain its stability and function as an antioxidant when interacting with free radicals [26]. These structural characteristics can contribute electrons among the rings of **QC**, increasing its possible resonance configurations [21].

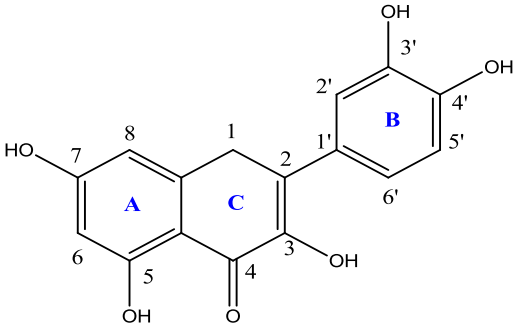

FIGURE 2 The chemical backbone of QC

Almost all flavonoids are naturally found in the O-glycoside form, where glycosylation can functionalize at any hydroxyl group, yielding glycosidic flavonoids. One of the most prevalent **QC** glycosides is **QC**-3-O-glucoside which has a monosaccharide moiety at position 3 [22].

Plants' biosynthesis of phytochemicals involving flavonoids is a legitimate reaction to the plant atmosphere. Plant-derived flavonoids are frequently involved in the protection against ultraviolet rays and lipid peroxidation. When dill cell culture was exposed to UV-B radiation, the predominant flavonoid synthesized was **QC**-3-O-β-glucuronide, according to Mohle *et al.* (1985). These researchers proposed which ultraviolet light may regulate the biosynthesis of flavonoids, and their accumulation serves as a defense mechanism [23].

Many *in vitro* studies looked into the antioxidant potential of natural **QC** in its aglycone form. However, the blood analysis after **QC** consumption revealed that **QC** metabolites, particularly **QC**-3-O-β-D-glucuronide are frequently detected. Because of the limited commercially available **QC** metabolites, the aglycone form of **QC** is commonly applied in research, despite the fact that these metabolites can be chemically synthesized [24].

In 2002, Bouktaib *et al.* created **QC**-3-O-β-glucuronide from its aglycone precursor (**QC**), as illustrated in Figure 3. The synthesis was initiated by the selective protection of the ring B hydroxyl groups using dichlorodiphenylmethane. The resultant ketal containing compound (**1**) was subsequently glucosylated at the hydroxy group of ring C by using K_2CO_3 in DMF to afford compound (**2**). The hydroxyl groups of the latter were protected using benzyl bromide and K_2CO_3 in DMF resulting in the formation of compound (**3**). The acetoxy protecting groups of the sugar moiety were hydrolyzed by sodium methoxide, and the excess of basicity was neutralized by anionic resin. The resultant compound, named **QC**-3-glucoside, was oxidized by sodium hypochlorite in the presence of sodium bromide. This oxidation is promoted by 2,2,6,6-tetramethyl piperidine-1-oxy (TEMPO) yielding compound (**4**) which is a glucuronic acid-based derivative. Upon a reduction reaction promoted by Pd/C, the crude was purified via column chromatography, affording the pure **QC**-3-O-β-glucuronide [25].

Prevalence of flavonoids in foods

Many investigators have qualified and quantified flavonoids in a variety of foods. When D'Abrosca *et al.* (2007) compared the total flavonoids of apple peel and flesh; the authors discovered that the peel had the greatest proportion of flavonoids. Green and black tea phenotypes were studied by Rietveld and his colleague Wiseman (2003), who found that these types of tea contained around 200 mg/cup for a traditional beverage [26]. Hollman *et al.* detected flavonoids in a variety of beverages, vegetables, and fruits in 1996. To determine the precursor of the present flavonols, Hollman and colleagues hydrolyzed the glycoside forms isolated from plants and used high-performance liquid chromatography (HPLC) to detach and evaluate the isolated flavonols. These phytochemicals were found in the highest concentrations in fruits like apples, cherries, and berries, vegetables like onions and broccoli, and beverages like tea and red wine. The US Department of Agriculture (USDA) compiled in 2014 a more comprehensive list of **QC** aglycone content in foods, as recorded in Table 1, using HPLC as a robust instrument for the qualification and quantification of natural products [29].

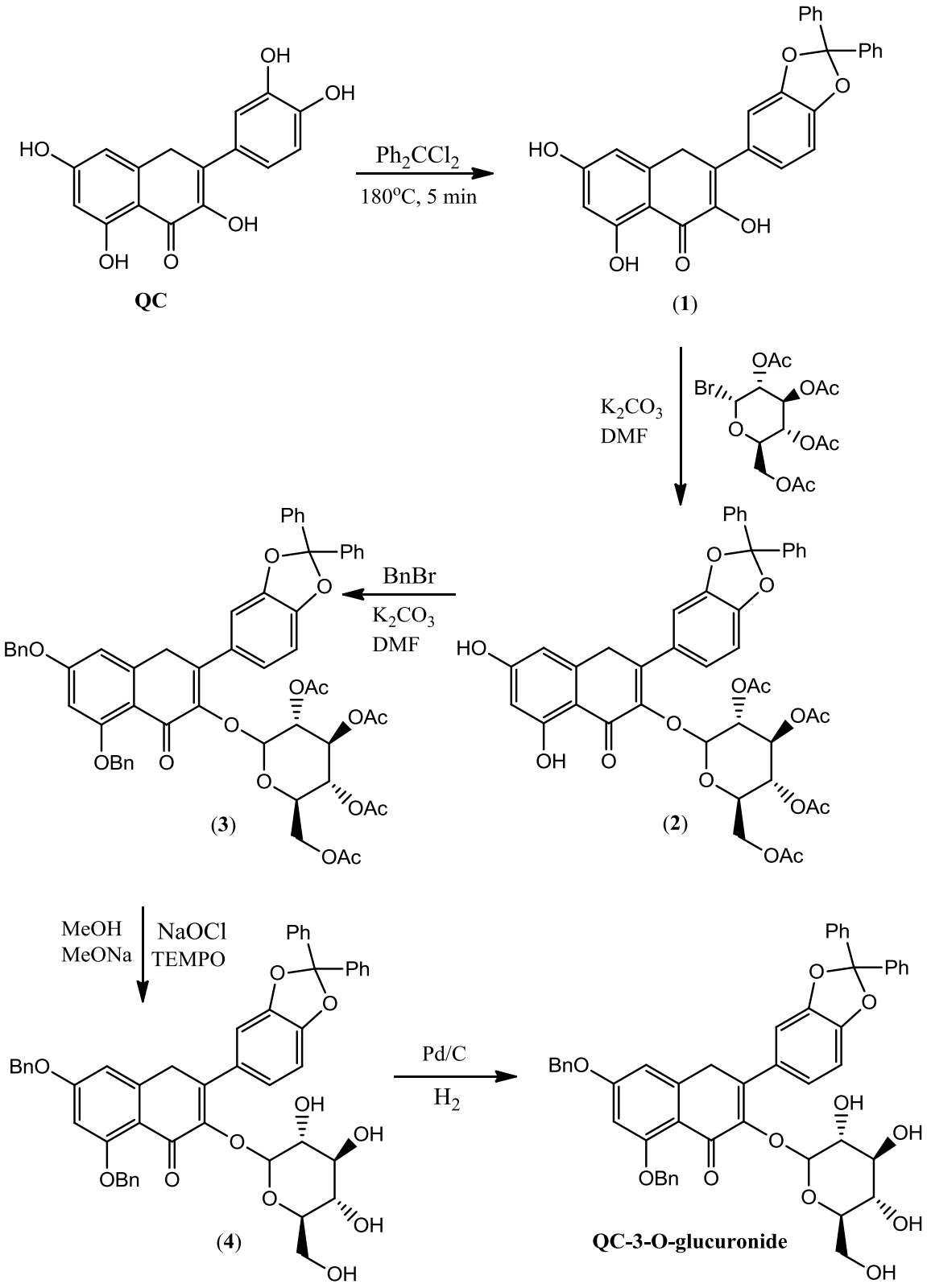

FIGURE 3 Chemical synthesis of QC-3-O-β-glucuronide from its QC, as described by Bouktaib *et al*

TABLE 1 Natural sources of QC aglycone with their content

Source	QC amount (mg/100g)	Source	QC amount (mg/100g)
Fresh broccoli	3.21	Apple with its peel	4.42
Fresh onion	13.27	Fresh spinach	4.86
Dry black tea leaves	204.66	Dry green tea leaves	255.55

Quercetin concentration levels in foods can be affected by food processing and preservation. Foods which have been cooked or boiled contain less **QC** than fresh ones. Due to the heat deterioration and the draining movement of boiling water, cooking causes an immense loss of the contained **QC** [28]. This is not a rule, but differs according to the type of food. For instance, onions contain **QC** hybrids which can withstand versus temperatures as high as 1000 °C. The amount of **QC** in food products is also affected by preservation conditions. For example, onions can lose up to 33 % of their **QC** composition in the first 12 days of storage, but only slightly after that period of time [28].

Contrarily, once strawberries are preserved at -200 °C for 9 months, the extent of **QC** increases by about 32 %. It is also essential to consider how the foods are cultivated. Flavonol content, for instance, is greater in plants that have prolonged exposure to the high levels of ultraviolet-B radiation due to their role as plausible UV light protective factors [44]. Through the use of green-houses, which prevent ultraviolet-B radiation, crops cultivated in the United Kingdom had lower flavonol content than those ones cultivated in Southern Africa [30].

As displayed in Table 2, flavonols found in a variety of foods are quantitatively different depending on geography and culture [46]. In Italy, red wine is the primary source, while tea is the major source in Dutch and Japanese cultures. Onions and apples are the main nutritional sources of flavonols in the United States, Greece, Finland, and Slovenia. In Finland, an individual's daily total flavonoid consumption is limited to 24 mg, while in Holland; the quantity is extended to 73 mg. The high consumption of isoflavones is coherent with Japanese culture, as soy foods are abundant in their dietary habits, whereas tea, a source of flavanols, seems to be prevalent in Holland [31].

TABLE 2 The variation in the amounts of flavonols and flavonoids based on the country

Country	Mean of the daily flavonols intake (mg)	Mean of the daily flavonoids intake (mg)
Denmark	15-30	23-46
Poland	4	24
Holland	23	73
Japan	16	63
United states	20-22	20-34

Antioxidant characteristic of QC

Because of its ability to quench free radicals and tie transition metal ions, **QC** is considered an effective antioxidant. The conversion of polyunsaturated fatty acids to free radicals via hydrogen abstraction is known as lipid peroxidation, as illustrated in (Figure 4) [32]. The lipid peroxy radicals that form as a result of this process extract hydrogen from other unsaturated fatty acid molecules causing more free radicals to form. The presence of trace amounts of transition metallic ions assists in initiating the reaction. Lipid peroxidation can exert negative

consequences on the body's functions, resulting in various disorders including diabetes, cardiovascular and neurodegenerative diseases, and cancer. However, dietary antioxidants such as quercetin, when combined with internal defense mechanisms can combat the oxidative stress by reacting with the formed harmful radicals [33].

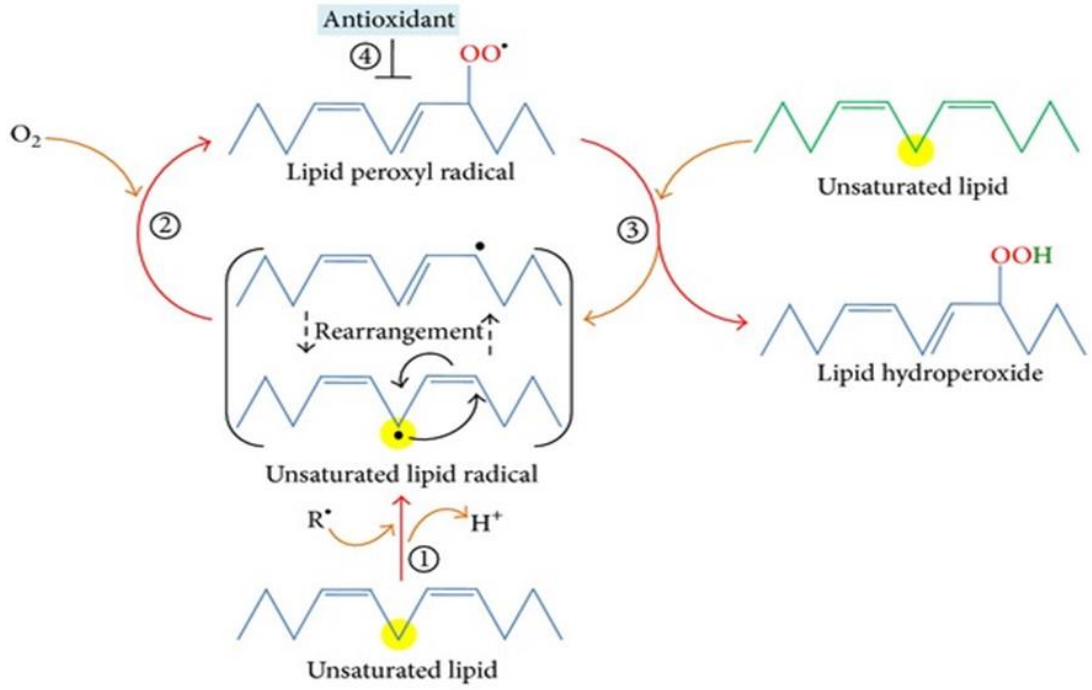

FIGURE 4 The process of lipid peroxidation and the role of antioxidant

Low-density lipoprotein (LDL) oxidation can contribute to the emergence of atherosclerotic plaques, which is the primary cause of many cardiovascular diseases. Multiple studies have indicated the QC's ability to prevent this oxidation. Graf and colleagues reported that the 4 mg daily consumption of QC resulted in a 21% reduction in mortality due to cardiovascular diseases [34].

Chopra *et al.* (2000) investigated the effects of QC and red wine powdered extract (Rp) on plasma levels of LDL and vitamins C and E, as well. Each attendee acted as a control for himself, and then the male-attendees were divided into two groups. The first received 30 mg of QC daily for two weeks, whereas the second group took 1 g of Rp daily for the same duration. It was estimated that, besides other flavonoids, there was 3.5 mg of QC/g of Rp. Also, each attendee should maintain a dietary plan that includes certain foods, such as vegetables, fruit and their juices, milk, and alcohol. From the gathered findings, the investigators concluded that QC and Rp can lower the plasma LDL without affecting the plasma levels of the studied vitamins.

Neurological disorders, including Alzheimer's and Parkinson's diseases, are believed to be caused by the frailty of brain lipid membranes to lipid peroxidation. Balazs and co-worker discovered that this oxidation type is linked to extracellular amyloid β-peptide accumulation which occurs before neural damage in Alzheimer's patients. Antioxidants, on the other hand, can help to prevent the establishment of amyloid plaques. In this circumstance, QC not only prevents lipid peroxidation from spreading, but it also raises glutathione (GSH) levels. The latter is a prominent protective factor for neuron protection versus lipid peroxidation. When a superoxide radical is formed, an

antioxidant enzyme named superoxide dismutase can transform this radical species into a hydrogen peroxide radical. GSH can switch the resultant radical to water and molecular oxygen, and can break the free radical formation chain.

By trapping free radicals, QC can reduce the inflammatory process. Free radicals can stimulate transcription factors, resulting in the production of pro-inflammatory cytokines, which are frequently found at higher levels in patients suffering from chronic inflammatory diseases. Alexander *et al.* measured the levels of the cytokines, including interleukin-1β and tumor necrosis factor-α, in sperm samples from healthy males and those with chronic prostatitis. According to the findings, the authors concluded that the males with this inflammatory disorder had higher levels of both investigated pro-inflammatory cytokines in their seminal fluid than healthy men [35].

Shoskes and colleagues gave patients suffering from chronic prostatitis 0.5 g of QC in the morning and evening for 30 days to investigate the effect of QC on this inflammatory disorder. As a result, the clinical signs of 67 % of the volunteers improved by 25 %. Accordingly, the investigators concluded that when the patients were administrated QC in combination with Prosta-Q, an absorption enhancer of QC composites of papain and bromelain, the disorder signs improved by 82 % for at least one quarter of the involved patients.

By provoking a continuous elevation in cytosolic Ca^{2+} accumulation, oxidative stress can cause cell damage. Increased Ca^{2+} thresholds cause a rise in metabolic rate and the commencement of cytoskeletal deterioration, which can result in strokes and acute neuronal losses. Quercetin, on the other hand, can safeguard cells from oxidative stress, preventing Ca^{2+}-dependent apoptosis. In a 15-year study of 550 middle-aged men, those who consumed more than 30 mg/day of QC had a significantly lower risk of cerebral hemorrhage.

QC can also safeguard against oxidative stress caused by more conspicuous exposures, such as tobacco smoke. Cigarette tar contains reactive oxygen species, which have been shown to harm the membranes of erythrocytes. According to Sangai and co-workers (2018), the QC and its conjugated metabolic products can protect erythrocytes from smoking-induced membranous destruction. Flavone, which had the same core structure as QC but no hydroxyl groups, was employed as a control in this investigation and had no negative impact on the investigated cells. This indicates that the QC-OH groups play a role in its antioxidant properties [36].

Oral absorbability of QC

The free radical scavenging potential of flavonoids is believed to be due to their chemical backbones, however because few evidence pieces are established regarding their absorption, it is unclear whether certain biomedical effects result from their absorption inside the body. Flavonoids are assumed to be inadequately absorbed since the saccharide moieties in the naturally occurring flavonoids increase their hydrophilicity, and no enzyme has been identified to breakdown the glycosidic linkage. The aglycones afforded from hydrolyzing this linkage can be easily absorbed, but flavonoids themselves are infrequently found in plants as aglycones. Normal flora bacteria in the colon are capable to hydrolyze the glycosidic linkage, forming the aglycone, but this hydrolytic reaction also deteriorates the aglycones [37].

The glycosyl flavonoids are assumed to access the colon and be hydrolyzed to the aglycone by enterobacteria. Because of its lipophilicity, the aglycone is readily taken up in the colon and then hepatically metabolized

via glucuronidation, O-methylation, and/or sulfation. Since the QC aglycone can act as a pro-oxidant, converting it to metabolites could assist in reducing the negative impacts, and the metabolites have also been shown to preserve their antioxidant properties. Although glycosyl QC can transfer through the epithelial cell surface, its performance is reduced compared to QC aglycone. As a result, QC absorption is accelerated by the hydrolysis of the glycosidic bond [37].

Numerous research findings concerned with the bioavailability of flavonoids and QC have yielded conflicting results. Because of the activity of the glucose transporter-1, investigators suggested that the glycosyl form absorbs better than its aglycone. Another study found that QC-4'-O-glucoside was more lipophilic than its two congeners, QC-3-O-glucoside and QC-3,4'-di-O-glucoside, and that it was assimilated more efficiently [58]. According to many research outcomes, QC absorption is influenced by the type and location of saccharides attached. Many researchers discovered that before intestinal absorption, glycosyl QC was totally catabolized to its aglycone form, promoting the more globally acknowledged theory [38].

Human blood does not contain the aglycone or glucoside form of QC, but it contains quercetin conjugates involving isorhamnetin-3-glucuronide, QC-3-glucuronide, and QC-3'-sulfate. In 2021, the last two metabolites were detected in human blood 90 minutes after consuming onions. After digesting fried onions, the research group encountered 5 distinct QC conjugates, not the aglycone or glucoside form of QC. In the next year, when the researchers nourished QC to rats, two of its metabolic conjugates, named QC-4'-O-β-D-glucuronide and QC-3-O-β-D-glucuronide, were encountered in the blood of the test animals. Further testing revealed that the latter metabolic conjugate can retard the Cu^{+2}-induced oxidation of LDL in human plasma, indicating that this QC metabolite can act as a potential antioxidant candidates [39].

It has been suggested, in 2022, that flavonoids involving QC would not need to be absorbed in order to have a biomedical influence. Scientists concluded that elevated levels of flavonoids in the intestinal lumen of rats nourished teas and wines (significant sources of QC), reducing DNA-oxidative damage in caecal mucosal cells. The outcomes of this research concluded that certain natural flavonoids could have a beneficial medical effect despite their poor intestinal absorption [36].

Although QC consumption ordinarily aligns with the intake of the other natural products, few research attempts have been found about how these products can influence QC absorption. According to the investigation published in 2022, the concurrent consumption of QC and lipids (e.g., beef tallow, fish oil, and lecithin) or emulsifiers (e.g., sucrose-fatty acid ester and sodium caseinate) can enhance the deposition of its metabolites in the human blood [32].

The extent of flavonoids absorption is still a point of contention. Consequently, a few research has linked the free-radicals trapping properties of flavonoid-rich food products to other compounds. According to a research paper, fructose may be to blame for the higher antioxidant impacts after eating apples; participants who ingested fructose at comparable levels to those observed in apples also showed elevated plasma antioxidant functionality. A rise in plasma urate, a metabolic antioxidant, was observed after the fructose treatment. As a consequence, the researchers hypothesized that the antioxidant effect was due to increased urate levels rather than flavonoids in apples.

The limited absorption of flavonoids in comparison to certain other dietary antioxidants like ascorbic acid has sparked refutes. The blood concentration of

flavonoids in humans is commonly detected in the range of 0.06-7.6 μM after intake of food enclosing flavonoids; that's also the spectrum for QC. While the concentration of ascorbic acid ranges between 30 and 150 μM, according to a research paper published in 2022 [40].

According to a published article, the blood free-radical trapping potential increased just after participants' ingested cranberry juice rather than fructose or blueberry as a control. The principal flavonoids found in cranberries are flavonols and anthocyanidins. Nevertheless, ascorbic acid was responsible for the greatest increase in blood free-radical trapping potential. They blamed the lack of effect on low ascorbic acid levels in the blueberries. These findings, which endorse the refutation of flavonoid free-radical trapping potential *in vivo*, emphasize the significance of proper design of experiments and differentiating between the effects of antioxidants other than flavonoids once presented in the same food products [21].

Conclusion

Flavonoids, involving **QC,** have the chemical backbone to be potent free-radical trapping applicants, and this has been demonstrated *in vitro* many times. **QC**, as a principal component of flavonoid intake could combat a variety of degenerative diseases. However, the amount of **QC** absorbed and its pharmacokinetics raise questions over whether it can impose a free-radical trapping potential *in vivo*. More research is needed to understand the effects of **QC** in the body, as well as its extent and absorption rate. In addition, the research interest should focus on the principal metabolic products of **QC** occurring in the human blood and their role in these internal effects.

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Ethical issues[1]

The scientific committee of the Pharmaceutical Chemistry Department was approved this work.

Competing interests

We have no conflicts of interest to disclose.

Authors' contributions

All authors contributed toward data analysis, drafting and revising the paper and agreed to responsible for all the aspects of this work.

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References

[1] F. Ciampi, L.M. Sordillo, J.C. Gandy, M. Caroprese, A. Sevi, M. Albenzio, A. Santillo, *J. Dairy Sci.,* **2020**, *103*, 8938–8947. [Crossref], [Google Scholar], [Publisher]
[2] Y.F. Mustafa, *J. Glob. Pharma Technol.,* **2019**, *11*, 1–10. [Pdf], [Google Scholar], [Publisher]
[3] Y.F. Mustafa, M.A. Najem, Z.S. Tawffiq, *J. Appl. Pharm. Sci.,* **2018**, *8*, 49–56. [Crossref], [Google Scholar], [Publisher]
[4] Y.F. Mustafa, M.K. Bashir, M.K. Oglah, *Syst. Rev. Pharm.,* **2020**, *11*, 598–612. [Pdf], [Google Scholar], [Publisher]

[1] The second scientific session for the academic year 2020-2021 on Sunday 11 September 2020.

[5] H. Aldewachi, Y.F. Mustafa, R. Najm, F. Ammar, *Syst. Rev. Pharm.,* **2020**, *11*, 289–296. [Pdf], [Google Scholar], [Publisher]
[6] A. Gościniak, M. Paczkowska-Walendowska, A. Skotnicka, M.A. Ruchała, J. Cielecka-Piontek, *Pharmaceutics,* **2021**, *13*, e2185. [Crossref], [Google Scholar], [Publisher]
[7] Y.F. Mustafa, N.T. Abdulaziz, *Syst. Rev. Pharm.,* **2020**, *11*, 438–452. [Pdf], [Google Scholar], [Publisher]
[8] Y.F. Mustafa, N.T. Abdulaziza, M.H. Jasim, *Egypt. J. Chem.,* **2021**, *64*, 1807–1816. [Crossref], [Google Scholar], [Publisher]
[9] C.G. Fraga, K.D. Croft, D.O. Kennedy, F.A. Tomás-Barberán, *Food Funct.,* **2019**, *10*, 514–528. [Crossref], [Google Scholar], [Publisher]
[10] Y.F. Mustafa, *NeuroQuantology,* **2021**, *19*, 99–112. [Crossref], [Google Scholar], [Publisher]
[11] S. Hajirezaee, A. Abed-elmdoust, N. Alekhina, S. Chupradit, Y.F. Mustafa, *Comp. Biochem. Physiol. - Part D Genomics Proteomics,* **2021**, *40*, 100917. [Crossref], [Google Scholar], [Publisher]
[12] J. Jumintono, S. Alkubaisy, D. Yánez Silva, K. Singh, A. Turki Jalil, S. Mutia Syarifah, Y.F. Mustafa, I. Mikolaychik, L. Morozova, M. Derkho, *Arch. Razi Inst.,* **2021**, *76*, 981–989. [Crossref], [Google Scholar], [Publisher]
[13] M.K. Oglah, Y.F. Mustafa, M.K. Bashir, M.H. Jasim, *Syst. Rev. Pharm.,* **2020**, *11*, 472–481. [Pdf], [Google Scholar], [Publisher]
[14] J.J. Peterson, J.T. Dwyer, P.F. Jacques, M.L. McCullough, *Nutr. Rev.,* **2015**, *73*, 553–576. [Crossref], [Google Scholar], [Publisher]
[15] Y.F. Mustafa, *Appl. Nanosci.,* **2021**. [Crossref], [Google Scholar], [Publisher]
[16] Y.F. Mustafa, S.M. Kasim, B.M. Al-Dabbagh, W. Al-Shakarchi, *Appl. Nanosci.,* **2021**. [Crossref], [Google Scholar], [Publisher]
[17] Y.F. Mustafa, E.T. Mohammed, R.R. Khalil, *Egypt. J. Chem.,* **2021**, *64*, 4461–4468. [Crossref], [Google Scholar], [Publisher]
[18] Y.F. Mustafa, R.R. Khalil, E.T. Mohammed, *Egypt. J. Chem.,* **2021**, *64*, 3711–3716. [Crossref], [Google Scholar], [Publisher]
[19] Y.F. Mustafa, M.K. Bashir, M.K. Oglah, R.R. Khalil, E.T. Mohammed, *NeuroQuantology,* **2021**, *19*, 129–138. [Crossref], [Google Scholar], [Publisher]
[20] J. Terao, *Biochem. Pharmacol.,* **2017**, *139*, 15–23. [Crossref], [Google Scholar], [Publisher]
[21] Y.F. Mustafa, N.T. Abdulaziz, *NeuroQuantology,* **2021**, *19*, 175–186. [Crossref], [Google Scholar], [Publisher]
[22] Y.F. Mustafa, N.A. Mohammed, *Biochem. Cell. Arch.,* **2021**, *21*, 1991–1999. [Google Scholar], [Publisher]
[23] P. Asgharian, A.P. Tazehkand, S.R. Soofiyani, K. Hosseini, M. Martorell, V. Tarhriz, H. Ahangari, N. Cruz-Martins, J. Sharifi-Rad, Z.M. Almarhoon, A. Ydyrys, A. Nurzhanyat, *Oxid. Med. Cell. Longev.,* **2021**, *2021*. [Crossref], [Google Scholar], [Publisher]
[24] M.K. Oglah, Y.F. Mustafa, *J. Glob. Pharma Technol.,* **2020**, *12*, 854–862. [Google Scholar], [Publisher]
[25] E.T. Mohammed, Y.F. Mustafa, *Syst. Rev. Pharm.,* **2020**, *11*, 64–70. [Google Scholar], [Publisher]
[26] I. Raya, T. Chen, S.H. Pranoto, A. Surendar, A.S. Utyuzh, S. Al-janabi, A.F. Alkaim, N.T. Danh, Y.F. Mustafa, *Mater. Res.,* **2021**, *24*, e20210245. [Crossref], [Google Scholar], [Publisher]
[27] R.R. Khalil, Y.F. Mustafa, *Syst. Rev. Pharm.,* **2020**, *11*, 57–63. [Pdf], [Google Scholar], [Publisher]
[28] Y.F. Mustafa, E.T. Mohammed, R.R. Khalil, *Syst. Rev. Pharm.,* **2020**, *11*, 570–576. [Pdf], [Google Scholar], [Publisher]
[29] Y.F. Mustafa, M.K. Oglah, M.K. Bashir, *Syst. Rev. Pharm.,* **2020**, *11*, 482–489. [Pdf], [Google Scholar], [Publisher]
[30] B. D'Abrosca, S. Pacifico, G. Cefarelli, C. Mastellone, A. Fiorentino, *Food Chem.,* **2007**, *104*, 1333–1337. [Crossref], [Google Scholar], [Publisher]
[31] Y.F. Mustafa, R.R. Khalil, E.T. Mohammed, *Syst. Rev. Pharm.,* **2020**, *11*, 382–387. [Pdf], [Google Scholar], [Publisher]

[32] A.M. Nejres, Y.F. Mustafa, H.S. Aldewachi, *Int. J. Pavement Eng.,* **2022**, *23*, 39–45. [Crossref], [Google Scholar], [Publisher]
[33] A.M. Nejres, H.K. Ali, S.P. Behnam, Y.F. Mustafa, *Syst. Rev. Pharm.,* **2020**, *11*, 726–732. [Pdf], [Google Scholar], [Publisher]
[34] M.K. Bashir, Y.F. Mustafa, M.K. Oglah, *Period. Tche Quim.,* **2020**, *17*, 871–883. [Pdf], [Google Scholar], [Publisher]
[35] Y.F. Mustafa, *J. Med. Chem. Sci.,* **2021**, *4*, 612–625. [Crossref], [Google Scholar], [Publisher]
[36] Y.A. Atia, D.O. Bokov, K.R. Zinnatullovich, M.M. Kadhim, W. Suksatan, W.K. Abdelbasset, H.A. Hammoodi, Y.F. Mustafa, Y. Cao, *Mater. Chem. Phys.,* **2022**, *278*, 125664. [Crossref], [Google Scholar], [Publisher]
[37] M.J. Ansari, S.A. Jasim, T.Z. Taban, D.O. Bokov, M.N. Shalaby, M.E. Al-Gazally, H.H. Kzar, M.T. Qasim, Y.F. Mustafa, M. Khatami, *J. Clust. Sci.,* **2022**, *4*, 44–47. [Crossref], [Google Scholar], [Publisher]
[38] H.S. Budi, M.F. Jameel, G. Widjaja, M.S. Alasady, T. Mahmudiono, Y.F. Mustafa, I. Fardeeva, M. Kuznetsova, *Braz. J. Biol.,* **2022**, *84*, e257070. [Crossref], [Google Scholar], [Publisher]
[39] Y.F. Mustafa, M.K. Oglah, M.K. Bashir, E.T. Mohammed, R.R. Khalil, *Clin. Schizophr. Relat. Psychoses,* **2021**, *15*, 1–6. [Pdf], [Google Scholar], [Publisher]
[40] A.B. Roomi, G. Widjaja, D. Savitri, A.T. Jalil, Y.F. Mustafa, L. Thangavelu, G. Kazhibayeva, W. Suksatan, S. Chupradit, S. Aravindhan, *J. Nanostructures,* **2021**, *11*, 514-523. [Crossref], [Google Scholar], [Publisher]

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