Quercetin: Exploring Its Unique Flavonol Properties, Bioavailability, Safety Profile, and Therapeutic Potential in High-Impact Medical Conditions

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Abstract

Quercetin, an abundant flavonoid in various foods and plants, exhibits diverse therapeutic potential due to its antioxidant, anti-inflammatory, and anticancer properties. This review explores its biological and pharmacological activities, mechanisms of action, formulations, absorption, bioavailability, adverse effects, and potential therapeutic applications. Initially isolated in the 1800s as a dye and in 1936 as a polyphenol, quercetin has garnered attention for its antioxidant capabilities, particularly in preventing oxidative damage from low-density lipoprotein (LDL) cholesterol, reducing the risk of cardiovascular disease (CVD). Studies also suggest its efficacy in lowering blood glucose levels, improving insulin sensitivity, and inhibiting viral infections, including COVID-19.

Despite its promising benefits, quercetin's bioavailability is limited by factors such as poor water solubility and rapid metabolism. Researchers have...
Quercetin is a flavonoid— a plant pigment commonly found in many foods and plants such as fruits, vegetables, onions, capers, berries, seeds, and grains— with a bitter flavor profile. It is a bioactive compound and a member of the polyphenols group of flavonoids. The name and appellation of quercetin, which has been used since 1857, are derived from the Latin term “quercetum” (oak forest) after the oak genus Quercus due to its abundance in oak trees [1,2].

Quercetin was initially isolated in the early 1800s by the French chemist Michel Eugène Chevreul as a dye, while polyphenol quercetin was isolated in 1936 by the Hungarian biochemist Albert Szent-Györgyi [3,4]. Many studies have investigated quercetin’s potential therapeutic effects, including antioxidant, anti-inflammatory, and anticancer activities. In vitro studies show that quercetin may prevent oxidative damage from low-density lipoprotein (LDL) cholesterol [1]. Also, population studies indicate that people who consume flavonoids (like quercetin) in their diet may have a lower risk of cardiovascular disease (CVD) and cancer [5–7].

In vivo and human studies have shown that quercetin may lower blood glucose levels, improve insulin sensitivity, alleviate inflammation, and inhibit viral infections [5–7]. Moreover, quercetin has been found to possess three iron-chelating sites, making it a promising candidate for treating iron-induced toxicity [8]. Quercetin has also been identified as a potential treatment for COVID-19, with studies suggesting anti-SARS-CoV-2 activity [6]. Han et al. found no severe adverse effects from quercetin supplementation in a randomized clinical trial. This finding supports further considerations of quercetin’s safety for future therapeutic studies [9].

The first investigation on the oral bioavailability of quercetin in humans reported very poor bioavailability after a single dose [5]. When quercetin is consumed, only a small fraction of it is absorbed into the bloodstream and becomes available for use by the body. Factors contributing to its low bioavailability include poor water solubility, rapid metabolism, and swift elimination from the body.

Researchers have been exploring various methods to enhance quercetin’s bioavailability, such as using quercetin glycosides, complexing it with phospholipids (as in quercetin phytosome), or using nanoformulations and other delivery systems to improve its absorption and effectiveness [10,11]. Considerable research has identified quercetin’s potential therapeutic effects, including antioxidant, antiproliferative, and DNA damage inhibition. Some limited research has shown its safe supplementation. Further research is necessary to elucidate the efficacy and safety of quercetin for therapeutic use.

**Discussion**

Quercetin has diverse biological and pharmacological activities, including anti-tumor, anti-inflammatory, immunomodulatory, and antioxidant properties (Table 1). In vitro studies have identified its potential as a therapeutic agent for cardiovascular disease (CVD), cancer, diabetes, and viral infections [1,2,5–7]. Quercetin has been found to have potential neuroprotective effects and may alleviate symptoms of depression and anxiety. Preclinical studies have reported its possible role in managing neurodegenerative disorders such as Alzheimer’s and Parkinson’s disease [12]. In human studies, quercetin has been associated with enhanced exercise performance and reduced inflammation, blood pressure, and blood sugar levels [11].
### Table 1: Quercetin’s Effects on Diverse Body Systems

<table>
<thead>
<tr>
<th>Body System</th>
<th>Effects and Activities of Quercetin</th>
</tr>
</thead>
</table>
| Cardiovascular   | - Potential therapeutic agent for CVD  
- Associated with reduced blood pressure                                                      |
| Neurological     | - Potential neuroprotective effects  
- May alleviate symptoms of depression and anxiety  
- Possible role in managing neurodegenerative disorders such as Alzheimer’s and Parkinson’s disease |
| Metabolic        | - Potential therapeutic agent for diabetes  
- Associated with reduced blood sugar levels                                                      |
| Immune           | - Immunomodulatory effects                                                                       |
| Oncological      | - Antitumor properties  
- Potential therapeutic agent for viral infections                                                |
| Musculoskeletal  | - Associated with enhanced exercise performance  
- Reduced inflammation                                                                          |
| General Health   | - Antioxidant properties  
- Anti-inflammatory effects                                                                       |

However, excessive supplementation of quercetin may lead to side effects such as headache, tingling, and heart palpitations, particularly when administered intravenously [13]. Nevertheless, such side effects are rare, and generally, quercetin is considered safe when supplemented through food and drinks [14].

Table 2 summarizes quercetin’s various biological and pharmacological activities, safety considerations, and side effects.

### Table 2: Quercetin’s Biological and Pharmacological Activities

<table>
<thead>
<tr>
<th>Biological and Pharmacological Activities</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antioxidant</td>
<td>Quercetin has antioxidant properties</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>It exhibits anti-inflammatory effects</td>
</tr>
<tr>
<td>Immunomodulatory</td>
<td>Quercetin can modulate the immune system</td>
</tr>
<tr>
<td>Antitumor</td>
<td>It has properties that may help in fighting tumors</td>
</tr>
<tr>
<td>Therapeutic potential for diseases</td>
<td>In vitro studies suggest quercetin could be therapeutic for cancer,</td>
</tr>
<tr>
<td></td>
<td>CVD, diabetes, and viral infections</td>
</tr>
<tr>
<td>Neuroprotective effects</td>
<td>Quercetin may have neuroprotective effects, potentially alleviating</td>
</tr>
<tr>
<td></td>
<td>depression and anxiety symptoms</td>
</tr>
<tr>
<td>Neurodegenerative disorder management</td>
<td>Preclinical studies indicate it might help manage Alzheimer’s and</td>
</tr>
<tr>
<td></td>
<td>Parkinson’s disease</td>
</tr>
<tr>
<td>Exercise performance</td>
<td>Associated with enhanced exercise performance</td>
</tr>
<tr>
<td>Inflammation, blood pressure, and blood</td>
<td>Quercetin has been linked to reduced inflammation, blood pressure, and</td>
</tr>
<tr>
<td>sugar</td>
<td>blood sugar levels in human studies</td>
</tr>
<tr>
<td>Side effects</td>
<td>Excessive supplementation may lead to headaches, tingling, and heart</td>
</tr>
<tr>
<td></td>
<td>palpitations, especially when administered intravenously</td>
</tr>
<tr>
<td>Safety</td>
<td>Generally considered safe when consumed through food and drinks, with</td>
</tr>
<tr>
<td></td>
<td>rare side effects</td>
</tr>
</tbody>
</table>

Quercetin has diverse biological and pharmacological activities, making it a promising therapeutic supplement for various diseases. However, further research is necessary to evaluate its efficacy and safety, especially when consumed in high doses.

**Quercetin: Structure, Forms, and Mechanism**

**Chemical and Molecular Structure**

Quercetin is a flavonoid from the flavonol group of polyphenols, which has a basic structure following the flavonol family. Quercetin’s molecular formula is C_{15}H_{10}O_{7}, and it has five hydroxyl groups placed at the
3-, 3’-, 4’-, 5- and 7-positions, making it a pentahydroxyflavone (Figure 1) [7]. Also, its chemical structure contains functional groups, such as a catechol ring in ring B and hydroxyl groups in ring A, which contribute to its potent scavenging activity against reactive oxygen species (ROS) [15].

Figure 1: Quercetin’s Structural Chemical Formula and Molecule Model
Image credit: bacsica / Adobe Stock, File ID: 214131672

Quercetin is classified under the subclass of flavonols, along with myricetin and kaempferol [7].

Various Forms Found in Plants
Quercetin is synthesized via the phenylpropanoid metabolic pathway, where it forms from the initial cinnamic acid synthesized from phenylalanine. This process eventually leads to the formation of 4-coumaroyl-CoA and entrance into the flavonoid biosynthesis pathway [16]. Plants produce quercetin in different forms, including free quercetin, glycosidic-bond quercetin, and acylated quercetin. Quercetin glycoside is the most common form found in plants, where the sugar molecule is attached to the hydroxyl group of the flavonoid structure [7]. Free quercetin exists in cells in limited amounts and is commonly derived from the hydrolysis of quercetin glycoside. Acylated quercetin represents a combination of both forms where the sugar molecule is attached to a hydroxyl group substituted with an acyl group [17]. In plants, different forms of quercetin serve as an essential constituent of the antioxidant machinery and facilitate several plant physiological processes (e.g., photosynthesis, seed germination, and pollen growth). Quercetin contributes to plant stress tolerance against various biotic and abiotic stresses [17].

Quercetin can occur in different forms in plants, including free, glycosidic-bond, and acylated quercetin. These forms facilitate several plant physiological processes and promote plant stress tolerance.

Mechanism of Action
Quercetin has several pharmacological activities and mechanisms of action, including antioxidant, anti-inflammatory, antitumor, antibacterial, and antiviral properties, primarily attributed to its potent antioxidant capabilities (Table 3) [2,18].

Quercetin’s antioxidant capabilities are derived from its ability to scavenge ROS and inhibit the expression of pro-inflammatory cytokines, thereby reducing inflammation [2,18].

Quercetin’s anticancer mechanisms are mainly attributed to its ability to inhibit cancer cell proliferation, induce apoptosis and autophagy, and alter gene expression in cancer cells [6]. Quercetin is a specific quinone reductase 2 (QR2) inhibitor (an enzyme that catalyzes the metabolism of toxic substances) and is involved in detoxifying carcinogens in cells [19,20].

Quercetin’s antibacterial mechanisms involve disrupting bacterial cell walls, altering cell permeability, and inhibiting bacterial cell growth. Its antiviral effects involve inhibiting virus replication during the viral life cycle and suppressing the inflammatory cascade induced by the infection [2,18].

Table 3: Quercetin Effects and Mechanisms of Action

<table>
<thead>
<tr>
<th>Effects</th>
<th>Mechanisms Resulting in the Effect</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antitumor</td>
<td>- Inhibition of cancer cell proliferation</td>
</tr>
<tr>
<td></td>
<td>- Induction of apoptosis and autophagy in cancer cells</td>
</tr>
<tr>
<td></td>
<td>- Alteration of gene expression in cancer cells</td>
</tr>
<tr>
<td></td>
<td>- Inhibition of QR2 enzyme activity, involved in the metabolism of</td>
</tr>
<tr>
<td></td>
<td>toxic substances and detoxification of carcinogens</td>
</tr>
<tr>
<td>Antioxidant</td>
<td>- Scavenging ROS</td>
</tr>
<tr>
<td></td>
<td>- Inhibition of pro-inflammatory cytokine expression, reducing inflammation</td>
</tr>
<tr>
<td>Anti-inflammatory</td>
<td>- Inhibition of pro-inflammatory cytokine expression, reducing inflammation</td>
</tr>
</tbody>
</table>
Quercetin has several pharmacological activities and mechanisms of action, including antioxidant, anti-inflammatory, anticancer, antibacterial, and antiviral effects, derived from its potent antioxidant capabilities and interactions with specific enzymes and cellular pathways.

**Quercetin: Formulations, Absorption, Bioavailability, Adverse Effects, and Recommendations**

**Formulations**
Quercetin is available in various forms on the market, including pure aglycone form and glycoside compounds. Different formulations have been used to study its pharmacokinetics in humans. The oral bioavailability of ingested quercetin varies depending on the formulation and the carrier used. Quercetin glucuronides are bioavailable in humans, and their circulating levels are similar regardless of whether they are ingested as aglycone or glycoside, with bioavailability five times higher when ingested as glycosides [21–23].

Various quercetin supplements, with differing doses and formulations, are available to consumers, including capsules, tablets, powders, and liquids. Some supplements are formulated with other compounds, such as vitamin C and bromelain, that can enhance absorption and effectiveness [1,24].

**Factors Affecting Absorption and Bioavailability**
Quercetin absorption varies depending on the source and the food matrix. It may occur in several forms, including free aglycone, glycoside, and conjugates, with glycoside forms better absorbed [5,25]. However, some studies indicate that aglycones of flavonols, such as quercetin, are more readily absorbed due to their higher lipophilicity [26].

Several factors, such as the dietary source, processing, dosage, and administration route, affect quercetin’s absorption rate and extent [25]. The bioavailability of quercetin is enhanced when it is ingested in combination with other compounds, such as bromelain, vitamin C, and phospholipids, which facilitate its absorption and entry into the bloodstream [27].

After absorption, quercetin is extensively metabolized in the liver and undergoes conjugation with glucuronic acid or sulfate for excretion through bile or urine [28]. Some studies have suggested that quercetin metabolites may play a more significant role in exerting its health benefits than the parent molecule [29].

Quercetin absorption depends on the form and the dietary matrix, while its bioavailability is affected by other chemical compounds in the diet. Following absorption, it undergoes significant liver metabolism before excreting in the bile or urine.

**Enhancing Bioavailability with Phytosomes**
A phytosome is a complex of a natural active ingredient and a phospholipid. This complex enhances the absorption and bioavailability of the active ingredient when taken orally. Phytosomes are used to improve the delivery of various plant-derived compounds, such as flavonoids like quercetin, making them more effective in therapeutic applications [30].

**Adverse Effects of Quercetin Supplementation**
Quercetin supplementation has possible adverse effects in humans. High doses can cause gastrointestinal effects such as mild stomach discomfort, diarrhea, nausea, and vomiting, which may lower tolerability at supra-physiological doses (>1000 mg/day) [31,32]. At higher doses, quercetin supplementation does not seem to alter immunity significantly and can even increase pro-inflammatory cytokine TNF concentrations in some studies [33].

**Daily Intake and Recommendations**
Currently, there is no established minimum daily requirement (MDR) for quercetin. The dietary consumption of foods containing quercetin varies widely among different geographical regions, countries, and populations. Quercetin is available as a dietary supplement, with manufacturers’ recommending daily doses of 200 to 1200 mg [33].

**Potential Therapeutic Applications of Quercetin**

**Cardiovascular Diseases**
Quercetin has multiple cardioprotective effects against several CVDs by various molecular mechanisms. The antioxidant and anti-inflammatory properties of quercetin are responsible for most of its cardioprotective effects [13,34]. The specific effects are highlighted as follows:

- Reduces systolic blood pressure significantly but has no effect on other cardiovascular risk factors and inflammatory markers in humans [35]
- Protects against atherosclerosis by interfering with multiple pathways [13]
- Improves endothelial function and reduces oxidative stress, inflammation, and apoptosis [34]

**Metabolic Syndrome**
Quercetin can maintain metabolism and treat metabolic syndrome, including obesity, insulin
Th2-related cytokines, which play a crucial role in therapeutic option for respiratory conditions, including eosinophilic inflammation [42]. The specific effects are highlighted as follows:

- Improves metabolic syndrome by regulating insulin secretion, enhancing glucose uptake by tissues, and improving glucose metabolism through modulating key enzymes and antioxidant and anti-inflammatory properties [36,37]
- Protects against oxidative stress and chronic inflammation and enhances adiponectin levels, regulating lipid and glucose metabolism [38]
- Ameliorates dyslipidemia by reducing oxidative stress, lowering blood pressure, and improving systolic blood pressure and insulin levels [14]
- Improves various metabolic abnormalities related to metabolic syndrome, such as dyslipidemia, adiposity, and glucose intolerance [39]
- Improves insulin sensitivity and secretion and reduces blood glucose levels in diabetic animal models [39]

Neurodegenerative Disorders
Quercetin has therapeutic applications in neurodegenerative disorders, including Alzheimer’s disease, Parkinson’s disease, and Huntington’s disease, due to its antioxidant, anti-inflammatory, and neuroprotective effects [12]. The specific effects are highlighted as follows:

- Exerts neuroprotective effects by suppressing oxidative stress, reducing inflammation, and inhibiting the formation of β-amyloid, which is responsible for the neurodegeneration observed in Alzheimer’s disease [12]
- Inhibits the aggregation of α-synuclein, an important protein implicated in Parkinson’s disease [40]
- Modulates various molecular targets in neurodegenerative disorders, such as sirtuins, mitogen-activated protein kinase (MAPK) signaling pathways, and nuclear factor kappa B (NF-κB), and affects brain-derived neurotrophic factor (BDNF) and neuroinflammation [41]

Respiratory Conditions
Quercetin has been found to exhibit antiallergic and anti-inflammatory activities, making it a potential therapeutic option for respiratory conditions, including allergies. Quercetin has been studied for its effects on Th2-related cytokines, which play a crucial role in allergic diseases and have been shown to suppress eosinophilic inflammation [42]. The specific effects are highlighted as follows:

- Reduces the symptoms of allergic rhinitis, seasonal allergies, and asthma, as suggested by in vivo and in vitro studies [42]
- Inhibits histamine release and modulates immune responses by suppressing the activity of specific enzymes and transcription factors [42]
- Reduces polinosis symptoms, according to a randomized trial [43]
- Reduces the severity and frequency of respiratory infections, which can exacerbate respiratory conditions in allergic individuals [42]
- Reduces inflammation, modulates immune responses, suppresses eosinophilic inflammation, and inhibits histamine release in respiratory conditions and disorders [42,43]

Skeletal Conditions
Quercetin has therapeutic applications in skeletal conditions, including arthritis and osteoporosis, due to its anti-inflammatory, antioxidant, and antiresorptive effects [44,45]. The specific effects are highlighted as follows:

- Inhibits the formation of osteoclast-like cells and bone resorption and promotes bone formation, making it useful for preventing osteoporosis [44]
- Prevents the progression of osteoarthritis by inhibiting the expression of pro-inflammatory cytokines and matrix metalloproteinases and acts as a chondroprotective agent [45]
- Exerts anti-inflammatory effects in arthritis by suppressing the release of inflammatory cytokines and decreasing the production of ROS [46]
- Reduces pain and inflammation in arthritis [45]
- Inhibits osteoclastic differentiation, promotes osteoblastic differentiation, reduces inflammation, and inhibits oxidative stress in skeletal conditions [44–46]

Bacterial Infections
Quercetin has significant antibacterial activity against various pathogenic bacteria by multiple molecular mechanisms, such as inhibition of bacterial growth, biofilm formation, and virulence factors [47]. The specific effects are highlighted as follows:

- Demonstrates broad-spectrum antibacterial effects against both gram-positive and gram-negative bacteria, as shown in several in vitro and animal studies [2]
- Exhibits a synergistic effect with various antibiotics, such as ampicillin, enhancing inhibitory activity against pathogenic bacteria like Staphylococcus aureus [48]
- Interferes with the formation of bacterial biofilms, which are resistant to most conventional antibiotics, thereby increasing the effectiveness of antibiotic therapy [47]
- Inhibits the expression of virulence factors in pathogenic bacteria, which plays a significant role in the pathogenesis of bacterial infections [2]

Cancer
Quercetin has been shown to have potential anticancer effects by various molecular mechanisms. Quercetin
has been documented to inhibit the proliferation of various types of cancers such as prostate, cervical, lung, breast, colon, and ovarian [7]. The specific effects are highlighted as follows:

- Affects multiple pathways involved in cancer development and progression, such as inducing apoptosis, inhibiting angiogenesis, reducing oxidative stress, and inhibiting the NF-κB and PI3K/Akt pathways [7]
- Inhibits cancer cell migration and invasion [6]
- Enhances the effect of chemotherapeutic agents, such as gemcitabine, and prevents drug resistance [49]

**Diabetes**

Quercetin has antidiabetic effects through various molecular mechanisms such as improving insulin sensitivity and glucose metabolism, promoting pancreatic β-cell function, decreasing oxidative stress, and regulating key signaling pathways involved in diabetes [37]. The specific effects are highlighted as follows:

- Improves insulin sensitivity, glucose metabolism, and insulin secretion in diabetic animal models by promoting pancreatic β-cell function in vivo studies [37]
- Acts on multiple targets of diabetes by activating AMP-activated protein kinase (AMPK) and peroxisome proliferator-activated receptor-γ (PPAR-γ) and reducing blood glucose levels [37]
- Reduces complications related to diabetes, such as neuropathy and inflammation [37]
- Synergizes with other antidiabetic agents, such as resveratrol and metformin, to exert significant antidiabetic effects [37]
- Reduces insulin resistance without decreasing body weight, an ideal characteristic of an antidiabetic agent [50]
- Improves oxidative stress and insulin sensitivity in human studies [37]

**Fungal Infections**

Quercetin has been recognized as a potent antifungal compound with potential therapeutic applications in managing fungal infections. The mechanism of antifungal action of quercetin involves the induction of apoptosis in yeasts through mitochondrial pathways, inhibition of virulence factors, and interference with fungal metabolic pathways [2]. The specific effects are highlighted as follows:

- Sensitizes fluconazole-resistant Candida albicans strains, making it a potential therapeutic option for treatment-resistant candidiasis [2]
- Inhibits Candida albicans biofilm formation, which contributes to the virulence and persistence of these fungal infections, according to in vitro studies [2]
- Shows potential as a food additive in inhibiting fungal growth and serving as a natural preservative [2]

**Inflammation**

Quercetin has potent anti-inflammatory effects through multiple molecular mechanisms, modulating various inflammatory pathways. Quercetin is beneficial in several inflammation-related conditions, such as prostatitis, autoimmune diseases, and CVDs [5]. The specific effects are highlighted as follows:

- Inhibits inflammatory cytokines and enzymes, modulates the TLR4/NF-κB signaling pathway, and scavenges ROS, reducing oxidative stress and inflammation [5]
- Reduces symptoms of prostatitis, according to preliminary evidence [51]
- Attenuates rheumatoid arthritis, inflammatory bowel disease, multiple sclerosis, and systemic lupus erythematosus [52]

**Iron-Induced Toxicity**

Quercetin can attenuate iron-induced toxicity by chelating iron, inhibiting iron overload, regulating iron homeostasis, and preventing oxidative damage [8]. The specific effects are highlighted as follows:

- Reduces iron-induced toxicity in the heart and brain, possibly through protein aggregation inhibition and iron-chelating activity [54]
- Acts as a potent iron chelator, attenuating lipid peroxidation and oxidative stress by chelating iron in vitro and in vivo [54]
- Inhibits iron overload by increasing fecal excretion of iron and decreasing serum ferritin levels [55]
- Inhibits the Fenton reaction by reducing the generation of ROS [54]
- Inhibits intestinal non-heme iron absorption and regulates the expressions of iron-related genes [54]

**Oxidative Stress**

Quercetin has significant antioxidant effects due to its ability to reduce oxidative stress and scavenge free radicals by multiple molecular mechanisms [2,24]. The specific effects are highlighted as follows:

- Activates the Nrf2-ARE pathway, regulates GSH-related redox balance, prevents mitochondrial dysfunction, increases low-density lipoprotein (LDL) resistance to oxidation, and inhibits oxidative modification of LDL by scavenging ROS [2,24,53,56]
- Attenuates oxidative stress-related conditions such as sarcoidosis, neurodegenerative diseases, and exercise-induced oxidative stress [53,56,57]
- Exhibits a protective effect against oxidative stress-induced apoptosis in various cell lines, such as PC-12 cells, as shown in in vivo studies [58]
- Significantly reduces oxidative stress biomarkers such as malondialdehyde and increases antioxidant status in humans [53]
**Viral Infections**
Quercetin has antiviral effects by inhibiting different stages of virus infections through various molecular mechanisms such as inhibition of viral entry, replication, protease activity, and modulation of the immune response [6]. The specific effects are highlighted as follows:

- Exhibits broad-spectrum antiviral activity against several viruses, including Human metapneumovirus (hMPV), O’nyong-nyong virus (ONNV), Ebola virus, Zika virus, and Coronaviruses [6,59–61]
- Impairs viral infection in host cells by reducing the viral RNA load, inhibiting viral-induced cytokine release, and boosting the innate immune response, as shown in in vitro studies [6,59–61]
- Enhances the therapeutic efficacy of antiviral agents such as Remdesivir [62]
- Shows promising antiviral activity in treating viral infections, particularly COVID-19, by inhibiting NLRP3 inflammasome activation [6,11]. However, the optimal dosage and efficacy in human viral infections have yet to be established. Clinical trials evaluating the use of quercetin for the prevention and treatment of viral infections are still needed.

Quercetin has been investigated for its potential therapeutic applications in diverse medical conditions, disorders, and diseases, spanning high-impact, medium-impact, and low-impact categories (Table 4).

**Table 4: Impact Levels of Various Medical Conditions**

<table>
<thead>
<tr>
<th>Impact Category</th>
<th>Conditions</th>
</tr>
</thead>
<tbody>
<tr>
<td>High</td>
<td>Cardiovascular diseases, neurodegenerative disorders (Alzheimer’s disease, Parkinson’s disease, Huntington’s disease), cancer (various types), diabetes, viral infections (including COVID-19), respiratory conditions (including allergies and asthma), skeletal conditions (arthritis, osteoporosis), metabolic syndrome, iron-induced toxicity</td>
</tr>
<tr>
<td>Medium</td>
<td>Inflammation (various inflammatory conditions), fungal infections, bacterial infections</td>
</tr>
<tr>
<td>Low</td>
<td>Iron-induced toxicity (compared to other conditions), fungal infections (in comparison to bacterial and viral infections), bacterial infections (in comparison to viral infections)</td>
</tr>
</tbody>
</table>

Note: The impact level represents the severity of a condition on the individual and its burden on society and is not indicative of quercetin’s influence on such conditions.

There is growing interest in quercetin’s novel applications and potential therapeutic uses. Quercetin-based hybrids have been investigated for their bioimaging and biosensing activity [63]. Also, there is interest in the phytosome-based delivery of quercetin, which may increase its bioavailability and efficacy [30].

**Summary of Quercetin’s Therapeutic Advantages and Disadvantages**
Quercetin has shown numerous potential health benefits due to its diverse pharmacological activities, including antioxidant, anti-inflammatory, immunomodulatory, anticancer, cardioprotective, and neuroprotective effects [1,2,5–7,12]. It has been linked to improved exercise performance, reduced inflammation, blood pressure, and blood sugar levels, and a lower risk of age-related diseases [11].

Quercetin may benefit various health conditions such as CVDs, metabolic syndrome, neurodegenerative disorders, respiratory conditions, skeletal conditions, bacterial and fungal infections, cancer, diabetes, iron-induced toxicity, oxidative stress, and viral infections. Despite its potential health benefits, quercetin may have side effects such as gastrointestinal disturbances, headache, and tingling sensation [13,31,32]. The optimal therapeutic dose of quercetin is yet to be established, and its bioavailability varies depending on factors such as formulation and individual differences [11].

**Limitations of Research**
Most of the current research on the therapeutic application of quercetin has been conducted in vitro and in animal models, with limited clinical studies in humans. The limited research in humans and the lack of standardization in the formulations used and dosage hinder the ability to draw conclusive evidence regarding the therapeutic effects of quercetin [2,11,64].

Another limitation is the variability in quercetin’s bioavailability. Quercetin is poorly absorbed by the body and has low bioavailability, affecting its therapeutic efficacy. The optimal therapeutic dose and mode of administration of quercetin remain to be established [10,11,64].

Further investigation is required on the safety of long-term use of quercetin supplements. Studies have suggested that high doses of quercetin supplements may have potential side effects on liver and kidney function and interactions with other medications [11,32]. Moreover, the potential of quercetin to interact with other medications and alter their pharmacokinetics warrants further investigation. Some studies have suggested that quercetin may interact with drugs used for treating cardiovascular, neurodegenerative, and cancer-related diseases [64,65].
Forward-Looking
Quercetin’s therapeutic and diagnostic applications require further exploration. Future research should focus on identifying the optimal dosage, formulation, and delivery methods. Studies are needed to identify potential side effects and clarify quercetin’s mechanism of action [1,2,6,66,67]. Investigating the potential of quercetin to interact with other medications and affect their pharmacokinetics is also a valuable topic for future research [11,32,64].

Conclusion
Quercetin, a flavonoid found abundantly in plants, exhibits various biological and pharmacological activities, making it a promising therapeutic agent for different diseases. Its effects include antitumor, anti-inflammatory, immunomodulatory, and antioxidant properties. In vitro studies have demonstrated its potential in treating cardiovascular disease (CVD), cancer, diabetes, and viral infections. Notably, quercetin shows promise in neuroprotection, potentially alleviating symptoms of depression, anxiety, and neurodegenerative disorders like Alzheimer’s and Parkinson’s disease. Human studies suggest benefits in enhancing exercise performance and reducing inflammation, blood pressure, and blood sugar levels. However, caution is warranted regarding excessive supplementation, which may lead to side effects such as headache, tingling, and heart palpitations, particularly when administered intravenously. Nevertheless, such side effects are rare, and quercetin is generally considered safe when consumed through food and drinks.

Structurally, quercetin belongs to the flavonol group of polyphenols, characterized by its molecular formula C15H10O7 and pentahydroxyflavone structure. It exists in various plant forms, including free, glycosidic-bond, and acylated quercetin, each contributing to different plant physiological processes and stress tolerance mechanisms. Quercetin exerts its effects through multiple mechanisms, including antioxidant, anti-inflammatory, anticancer, antibacterial, and antiviral actions. It modulates specific enzymes and cellular pathways, contributing to its diverse therapeutic potential. Various formulations of quercetin supplements are available, with differing bioavailability depending on the source, processing, dosage, and route of administration. Combining other compounds like bromelain and vitamin C can enhance absorption and effectiveness. Despite its potential benefits, research on quercetin’s therapeutic applications is limited to in vitro and animal studies, with few clinical trials in humans. Standardization in formulations and dosage and investigations into long-term safety and potential drug interactions are essential for optimizing its therapeutic use. Future research should clarify its mechanism of action and interactions with other medications and establish optimal dosages and formulations for therapeutic applications.

Conflict of Interest Statement
The authors declare that this paper was written without any commercial or financial relationship that could be construed as a potential conflict of interest.

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