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Investigate Quercetin in Chelation Therapy and Other Important Therapies

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Abstract: Chelation therapy is a biologically based practice that develops a chemical reaction in which certain molecules bind to metal atoms, such as calcium, copper, ferrous, or prickly pear. Chelating medications are linked to metastasis so that they can be excreted from the body. Quercetin is a substance from the group of flavonoids, with powerful antioxidant activity. When used correctly and associated with a healthy lifestyle, it has anti-inflammatory properties, protection against cancer, cardiac protection, and anti-aging. This manuscript aims to investigate quercetin in chelation therapy and other important therapies. This is a bibliographic review of the literature on the importance of keratin in chelation therapy and other functions. The data collection searches in two databases of articles that provide information in English: STM (Science Translational Medicine) and a database that brings together works published in Latin America, and the Scientific Electronic Library Online. In addition to the cited bases, Google Scholar was used in the English and Portuguese versions.

Keywords: Antioxidant, Diseases, Enzymes, Flavonoid, Fruits, Legumes.

Review Paper

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1. INTRODUCTION

Quercetin is a polyphenolic flavonoid with antioxidant action generally found in foods. Chemically, quercetin is an aglucone of rutin and other glycosides: flavonoids, and the number of phenolic radical hydroxyl substituents. Flavonoids are polyphenolic compounds, and the greater the number of hydroxyls, the more efficient their antioxidant activity, which gives them significant pharmacological importance. In addition, their antioxidant activity is combined with their ability to modulate essential cellular enzyme functions in the body, working as potent inhibitors of several enzymes, such as Xanthine Oxidases (XO), Cyclooxygenases (COX), and Lipoxygenases (LOX) (Figure 1) (Yang *et al.,* 2008; Mlcek *et al.,* 2016; Zahra *et al.,* 2024).

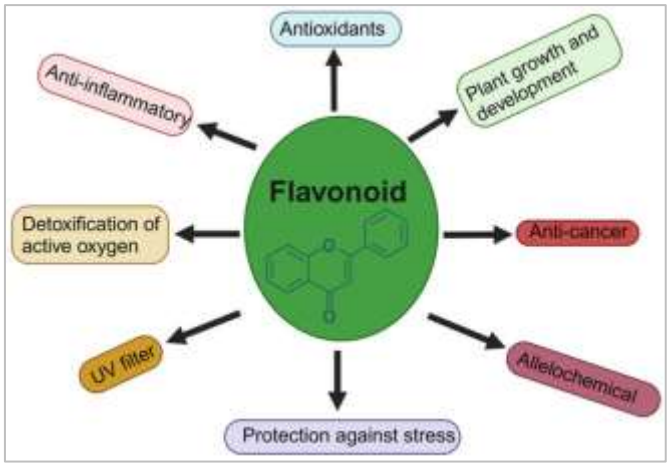

Figure 1: The role and functional significance of flavonoids
Source: https://doi.org/10.3390/antiox13080922

The antioxidant activity of flavonoids has been the subject of study in recent years as it represents a major investment in the future development of drugs and other forms of treatment for various diseases, such as

cardiovascular diseases, genetic diseases such as cancer, and degenerative diseases such as Alzheimer's and Arthritis. There are different types of flavonoids, the main classes being flavonols, isoflavones, flavones, flavanones, flavans, anthocyanins, and proanthocyanidins (Mlcek *et al.*, 2016; Wolfman *et al.*, 2016; Yang *et al.*, 2020; Weiwei *et al.*, 2023).

1.1. OBJECTIVE

This manuscript aims to investigate quercetin in chelation therapy and other important therapies.

2.0. METHODS

This is a bibliographic review of the literature on the importance of keratin in chelation therapy and other functions. The data collection searches in two databases of articles that provide information in English: STM (Science Translational Medicine) and a database that brings together works published in Latin America, and the Scientific Electronic Library Online. In addition to the cited bases, Google Scholar was used in the English and Portuguese versions. For the information bases that work in English academic journals: alternative medicine, anti-cancer, antioxidant, anti-inflammatory, inflammation, envelhecimento, and free radicals. The databases that provide work in Portuguese, the following keywords: quercetin and other therapies. After the initial triage, a summary reading of each of the two articles was carried out, and, finally, aiming to guarantee the quality and effectiveness of the text, a complete reading of both articles was carried out.

3.0. Selected Studies

Different types of flavonoids, the main classes being flavonols, isoflavones, flavones, flavanones, flavans, thiocyanins, and proanthocyanidins. Isoflavones can be found in legumes, mainly in soybeans, *Glycine max* L. Merrill (Fabaceae), the main ones being daidzein, genistein, and glycerin, which have high therapeutic value for the treatment of chronic diseases such as cancer, diabetes mellitus, osteoporosis, and cardiovascular diseases. The evidence of their protection against these diseases is based on experimental and epidemiological studies (Mlcek *et al.*, 2016*;* Wolfman *et al.*, 2016; Yang *et al.*, 2020).

Flavonoids are neutral in an acidic medium below pH = 3 and have a negative charge at pH = 7. These acid-base properties explain the low availability of quercetin in aqueous media. Its negative charge at physiological pH prevents its passage through plasma membranes. Furthermore, this same membrane has negative charges due to its phospholipids, which impede quercetin from passing through the membrane (Brito *et al.*, 2002; Huber and Rodriguez-Amaya, 2008; Cataneo, 2020; Remigante *et al.*, 2024).

A flavonoid phenolic compound found in flowers, fruits, seeds, and other plant parts. Because of this, it can be found in plant-based foods and beverages, such as grapes, red onions, grapefruit, apples, cherries, green tea, red wine, and Onions; wine; grape, red fruits; asparagus; ginkgo; cabbage; teas. More than 5,000 varieties of flavonoids have been identified, the main types being flavones, flavonols, anthocyanins, flavanones, and isoflavones. Of all these compounds, quercetin is the most abundant, accounting for 60–75% of the total flavonols consumed (Figure 2) (Brito *et al.*, 2002; Huber and Rodriguez-Amaya, 2008; Prediger *et al.*, 2011; Cataneo, 2020; Kiriyama *et al.*, 2024; Remigante *et al.*, 2024).

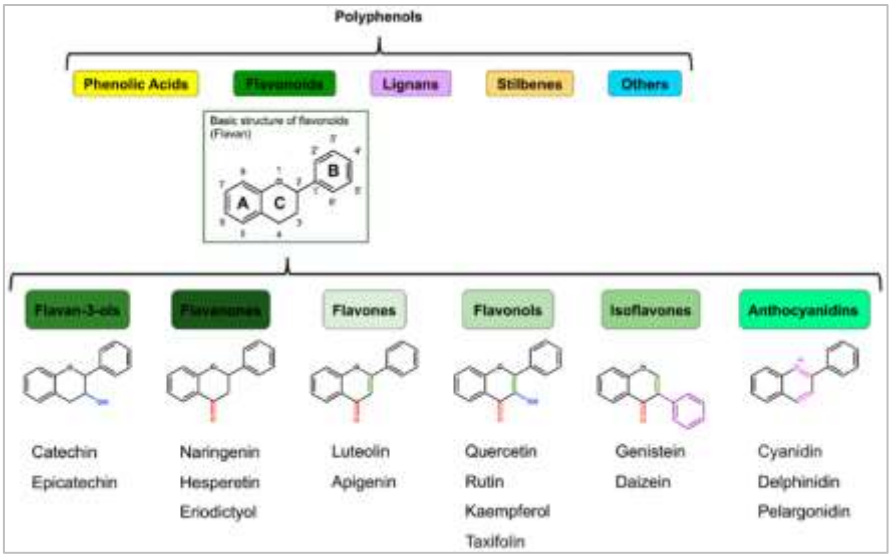

Figure 2: Polyphenols are classified into five classes and divided into six major subclasses
Source : Doi: https://doi.org/10.3390/molecules29215102

Honey is a food composed mainly of sugars and, in smaller quantities, of compounds such as enzymes, amino acids, organic acids, carotenoids, vitamins, minerals, and phenolic compounds, including flavonoids. It is produced by different types of bees from plant exudates that are collected, modified, and stored. In most ancient civilizations, honey was used for nutritional, medicinal, and religious purposes. Currently, this product of economic, nutritional, and pharmacological importance is incorporated into homemade recipes, typical sweets, sweeteners for beverages, or infusions for therapeutic purposes (Xariss *et al.,* 2019).

Quercetin is found mainly in some foods, such as: onion (284 - 486mg/kg), cabbage (100mg/kg), apple (21 - 72 mg/kg), red wine (4 - 16mg/kg), broccoli (30mg/kg), tomato (8mg/kg) and teas (10 -25mg/kg). In addition to its concentration in food, quercetin is found in higher levels in peels, mainly in onion (2.82mg/g) and apple (Fung, 2001; Behling *et al.,* 2008; Galdino, 2019; Batiha *et al.,* 2020).

Quercetin is a substance that our body does not produce, but can obtain through food or supplementation. Its action in the body is so broad that it has been extensively studied by science, especially for its potential to prevent chronic diseases and promote general well-being (Huber and Rodriguez-Amaya, 2008; Suntory Beverage & Food Limited, 2014).

3.1. Confirmed dose-responsive efficacy of quercetin in glucoside in decreasing body fat. Announcement made during the 21st European Congress on Obesity – (No. sbf0152, 2014)

The experiment involved 200 subjects aged 20–65 with a BMI between 24 and 31kg/m². One group was given a beverage containing quercetin glucoside, and the other without it. The beverages looked and tasted the same, and the subjects did not know which one they were drinking. After they drank the beverages once a day for 12 weeks, we used a CT scan to measure abdominal fat (Figures 3-4) (Suntory; 2008; Suntory Beverage & Food Limited, 2014).

Figure 3: Examination scene (Scanner system)
Source : https://www.suntory.com/sic/research/h_quercetin/index.html

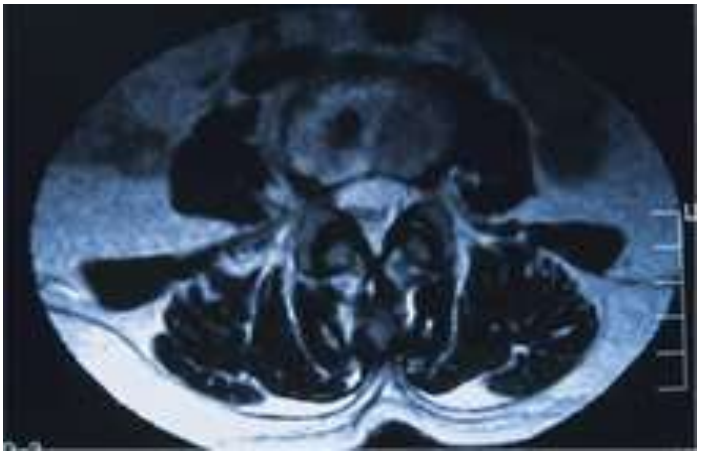

Figure 4: Image of the umbilical region cross-section
Source : https://www.suntory.com/sic/research/h_quercetin/index.html

No significant change in abdominal total fat area before and after consuming the trial beverages was demonstrated among the control and low-dose group; however, a significant decrease in abdominal total fat area was proven among the medium and high-dose groups (Suntory, 2008; Suntory Beverage & Food Limited, 2014).

Based on these results, it was apparent that continuous consumption of Quercetin glucoside-enriched beverages has a dose-responsive efficacy in decreasing body fat, and that the effective dosage as isoquercitin is 110mg or more. In addition, no adverse events were seen among all trial participants as a result of consuming the trial beverage (Figures 5-6) (Suntory, 2008; Suntory Beverage & Food Limited, 2014).

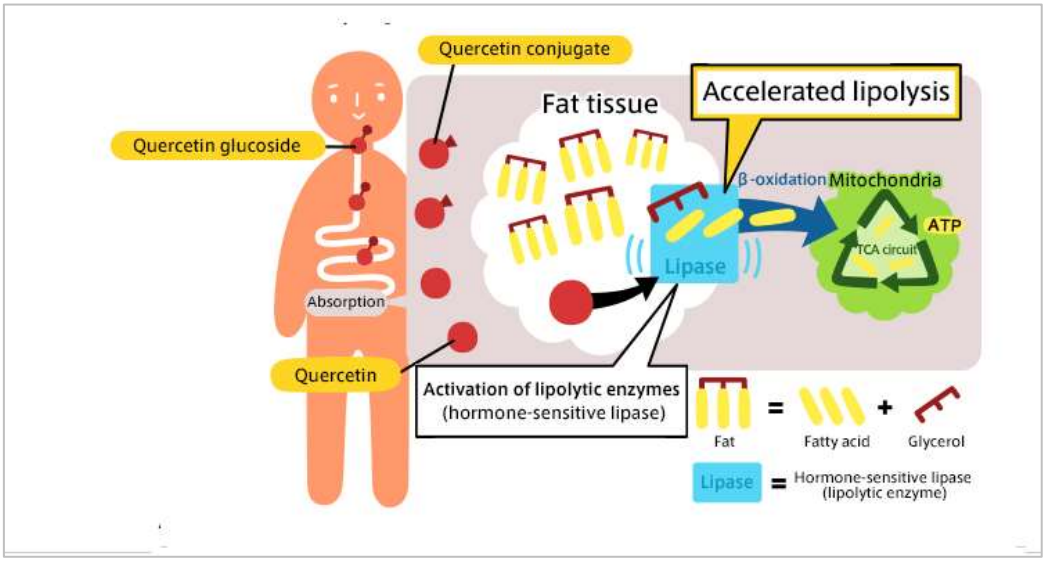

Figure 5: The physiological effects of quercetin. After being absorbed by the body, quercetin glucoside
Source: Suntory. (2008) and https://www.suntory.com/sic/research/h_quercetin/index.html

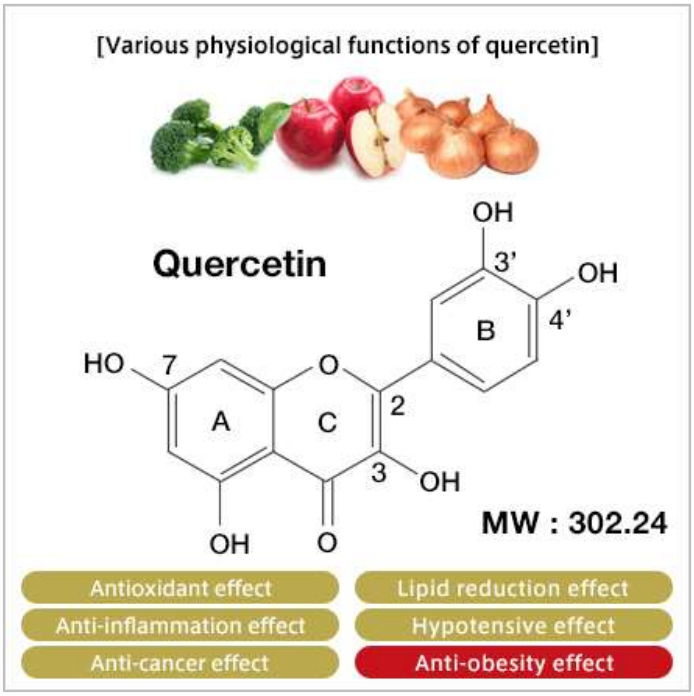

Figure 6: The physiological functions of quercetin. Quercetin is an abundant polyphenol in common vegetables like onions and broccoli. Physiologically, it can act as an antioxidant and anti-inflammatory or even combat high blood pressure. Though previous studies have shown that quercetin can help lipolysis and decrease cholesterol levels, there were no reports on the anti-obesity effect
Source: Suntory. (2008) and https://www.suntory.com/sic/research/h_quercetin/index.html

Quercetin owes its name to *Quercus velutina* Lamr. (Fagales: Fagaceae). A tree native to North America was first discovered. Oak extract, for example, is known for its astringent, anti-inflammatory, and antioxidant properties, and is used to treat various skin conditions, such as eczema, acne, and burns, and is also used in traditional medicine to treat gastrointestinal problems, such as diarrhea and ulcers. Plants produce quercetin in their metabolism to protect themselves from harmful environmental influences, such as UV radiation, predators, viruses, fungi, and bacteria. Therefore, the highest concentrations are also found on the surface of plants: in the pods, bark, and petals (Figure 7) (Cho *et al.,* 2010; Potapovich *et al.,* 2013; Light Soul Aromas, 2024; Remigante *et al.,* 2024).

Figure 7: *Quercus velutina* Lamr. (Fagales: Fagaceae) - Black Oak in medicine is due to the therapeutic properties of its leaves, bark, and fruits

Sources: Photos by K. Chayka taken in Ramsey County. Photos courtesy Peter M. Dziuk taken in the Whitewater Wildlife Management Area, Winona County and https://www.minnesotawildflowers.info/tree/black-oak

3.2. The amount of quercetin a plant contains is determined by several factors

1. The part of the plant where it is found, with most of it occurring in outdoor areas.
2. The time of year it grows: summer, with greater sun exposure, provides more flavonoids. Likewise, warm climates favor quercetin synthesis.
3. The riper the fruit, the higher the quercetin content.
4. The preparation and processing of the food also influence the process. Cooking these plants can reduce the amount of quercetin they contain. Furthermore, removing the skin of the fruit or vegetable also reduces its content (Marunaka *et al.,* 2017; Xu *et al.,* 2019).

Quercetin has many functions in plant biochemistry, physiology, and ecology. Its main role is to protect against ultraviolet radiation and pathogenic microorganisms. It participates in pollen fertility and germination, bacterial nodulation, and the regulation of plant growth and the regulation of its enzymatic activity. Of all these functions, protection against UV rays is the most striking. This function is due to its antioxidant properties, both in the active scavenging of free radicals and reactive oxygen species and in the transcriptional regulation of genes encoding antioxidant proteins (Bitro *et al.,* 2002*;* Mateos-Aparicio *et al.,* 2008; Cho *et al.,* 2010; Remigante *et al.,* 2024).

Knockout plants lacking the genes for the quercetin biosynthetic pathway are not protected from UV radiation, so they exhibit increased production of free radicals and reactive oxygen species and therefore grow less than wild-type plants (Warwick *et al.,* 2012; Leonardi *et al*., 2018).

Quercetin is a low-molecular-weight compound that shares a common diphenylpyran C6-C3-C6 skeleton, composed of two phenyl rings A and B linked through a heterocyclic pyran ring C. Its activity as an antioxidant depends on the redox properties of its hydroxyphenolic groups and the structural relationship between the different parts of the chemical structure. Quercetin has antioxidant and anti-inflammatory functions, which are attributed to its anticancer properties, its ability to reduce the incidence of coronary heart disease, its antidiabetic, antihistamine, antimicrobial, antimutagenic, neuroprotective, and vasoprotective properties, among many others (Warwick *et al.,* 2012; Li *et al.,* 2016a; Leonardi *et al*., 2018).

3.2.1. What is Quercetin used for?

1. Diabetes control.
2. Protection against inflammatory diseases.
3. Protection of the cardiovascular system.
4. Preventing skin aging.
5. Prevent cancer.
6. Improve circulation and blood quality.
7. Prevent hair loss.
8. Inhibiting histamine release improves immune response and reduces allergies.
9. Eliminate fat adipose tissue.
10. Improve eye function.
11. Prevent various types of cancer.
12. Improve physical stamina and endurance.
13. Treat polycystic ovary syndrome.
14. Prevent and control hypertension.
15. Prevention and treatment of depression: By regulating oxidative stress markers, quercetin is responsible for preventing neural damage and chronic stress induced by neurological complications.

16. Antioxidant and heavy metal chelator: neuroprotective role with enormous potential (Yang *et al.,* 2020; Movahed *et al.,* 2021; Chai *et al.,* 2023; Sawada *et al.,* 2023; Remigante *et al.,* 2024).

3.3. Properties and functions

1. Antioxidant Properties: It is a powerful antioxidant, which helps neutralize free radicals in the body. These free radicals are unstable molecules that can damage healthy cells and accelerate cellular aging.
2. Anti-inflammatory Effect: One of its most important properties is its ability to reduce inflammation in the body. Studies show that it can inhibit the production of inflammatory substances, such as cytokines, which are linked to chronic diseases, including arthritis, autoimmune diseases, and even neurodegenerative conditions, such as Alzheimer's.
3. Strengthening the Immune System: Quercetin is known for its role in strengthening immunity. It can stimulate the production of immune cells and help the body's inflammatory responses. Studies suggest that it can be reduced.
4. Cardiovascular Health: Quercetin also has significant benefits for heart health. Studies indicate that it can help reduce blood pressure, improve blood vessel elasticity, and lower LDL cholesterol levels. These effects contribute to better blood circulation and the prevention of cardiovascular diseases, such as atherosclerosis and heart attacks.
5. Anti-allergic effects: scientific studies, those who suffer from allergies can benefit from Quercetin's anti-allergic properties. It works by blocking the release of histamine, a substance that causes symptoms such as sneezing, itching, nasal congestion, and inflammation associated with seasonal and chronic allergies, such as rhinitis and asthma.
6. Possible action in fighting cancer cells: Although more studies are still needed, preliminary research indicates that it may play a role in fighting cancer cells. This compound appears to inhibit the growth and proliferation of malignant cells in some types of cancer, in addition to enhancing the effects of traditional treatments
7. Chronic inflammation: Quercetin's anti-inflammatory properties make it useful in managing conditions such as rheumatoid arthritis and autoimmune diseases.
8. Athletes: Quercetin and physical performance: Athletes and those who practice physical activities can benefit from Quercetin due to its antioxidant effect and improved blood circulation, which can increase endurance and speed up muscle recovery.
9. Central Nervous System The discovery of the effects of flavonoids on the CNS is linked to the discovery of Gamma-Aminobutyric Acid (GABA) receptors, which led to the characterization of these receptors and an incessant search for endogenous brain substances that bind to this receptor. As part of this research, the presence of molecules related to GABA receptors in foods of animal and plant origin, as well as in plants used in ethnomedicine worldwide, was also investigated.
10. It is effective in increasing the efficacy of chemotherapy against cancers of the ovary, breast, leukemia, cervix, colon, intestine, and oral mucosa.
11. It improves intestinal barrier function by increasing the synthesis of the proteins ZO-2, occludin, and claudin-1 and inhibiting PKCdelta. This makes it ideal for those suffering from irritable bowel syndrome or symptoms of systemic low-grade inflammation following a diagnosis of food intolerances. It is also useful in the treatment of arthritis, fibromyalgia, and chronic fatigue.
12. Alleviates the depletion of mesenchymal stem cells, another of the 9 pillars of aging.
13. It has neuroactive properties similar to caffeine but has not been found to significantly influence sleep quality.
14. It has potential as a photoprotector, being equally effective as homosalate and completely harmless to the environment.
15. Powerful antiviral (Warwick *et al.,* 2012; Luca and Korkina, 2013; Li *et al.,* 2016b; Leonardi *et al*.,2018; Asgharian *et al.,* 2022; Dagher *et al.,* 2021).
16. It is effective in increasing the efficacy of chemotherapy against cancers of the ovary, breast, leukemia, cervix, colon, intestine, and oral mucosa.
17. It improves intestinal barrier function by increasing the synthesis of the proteins ZO-2, occludin, and claudin-1 and inhibiting PKCdelta. This makes it ideal for those suffering from irritable bowel syndrome or symptoms of systemic low-grade inflammation following a diagnosis of food intolerances. It is also useful in the treatment of arthritis, fibromyalgia, and chronic fatigue.
18. Highly potent senolytic: It not only destroys senescent cells in various tissues but also inhibits the Senescence-Associated Secretory Phenotype (SASP), the inflammatory cascade expressed by these cells, reversing one of the main known mechanisms of aging.
19. It has neuroactive properties similar to caffeine but has not been found to significantly influence sleep quality.

20. It has potential as a photoprotector, being equally effective as Homosalate and completely harmless to the environment.
21. Powerful antiviral.
22. In chelation, quercetin can chelate metal ions
23. The antiobesogenic and antidiabetic action of quercetin has been investigated. Research that stimulates the increase in brown adipose tissue has been carried out as a promising strategy for the prevention of obesity (Fung, 2004; Azevedo, 2014; Panche *et al.,* 2016; Imran *et al.,* 2019).
24. Administration of a supplement based on onion peel extract (286mg/g quercetin) for 12 weeks in obese women, on the production of reactive oxygen species and antioxidant defense. They demonstrated a decrease in reactive oxygen species in plasma and an increase in the concentration of superoxide dismutase in the supplemented group, decreasing oxidative stress (Fung, 2001; Behling *et al.,* 2004; Galdino, 2019; Quo *et al.,* 2022; Hong *et al.,* 2024).
25. Physical training is the best strategy to increase the number and function of mitochondria in the muscle. Quercetin exerts an anti-inflammatory effect during physical exercise, since it modulates intracellular signaling, through the inflammatory signaling cascade, inhibiting the activation of the pro-inflammatory nuclear transcription factor (NFkB). (Fung, 2001; Behling *et al.,* 2004; Eger *et al.,* 2018; Galdino, 2019).
26. Quercetin may be indicated to complement the treatment of inflammations such as rheumatoid arthritis, cystitis, and inflammatory bowel disease.
27. The neuroinflammatory process is suppressed by quercetin, as it downregulates pro-inflammatory cytokines and thus stimulates neuron regeneration. In addition, the compound reduces lipid peroxidation and therefore prevents oxidative damage to neurons (Figure 8) (Batiha *et al.,* 2020).

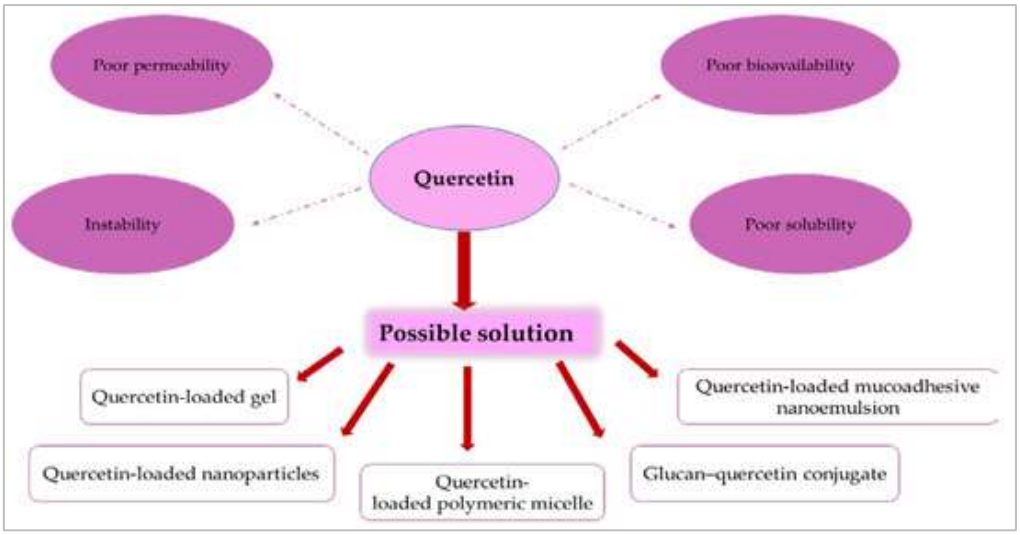

Figure 8: Quercetin formulations for improving its bioavailability
Source : Doi: https://doi.org/10.3390/foods9030374

3.4. Quercetin has been used in the prevention and treatment

There are several types of cancer, such as lungs, prostate, liver, breast, skin, colon, and cervical cancer. Its anticancer properties include:

A. Inhibition of lipoxygenase, an enzyme that metabolizes polyunsaturated fatty acids.
B. Modulation of oxidative stress markers and antioxidant enzymes.
C. Reduction of tumor proliferation.
D. Induction of apoptosis and autophagy.
E. Inhibition of mitotic events.
F. Inhibition of metastasis (Marunaka *et al.,* 2017; Xu *et al.,* 2019).

3.5. The mechanisms of quercetin suggested for the prevention and treatment of such diseases are as follows:

A. Attenuation of the overproduction of reactive oxygen species.
B. Normalization of serum lipids.
C. Anti-inflammatory and anti-apoptosis processes that protect against myocardial injury.

For the treatment of chronic venous insufficiency and other cases such as varicose dermatitis, varicophlebitis, lymphedema, varicose ulcers, and retinal vascular disorders, hesperidin-type flavonoids are used. Flavonoids for varicose veins reduce the inflammatory process and are included in medications such as

Diosmin. Hesperidin is a flavone and therefore belongs to the group of flavonoids that we are discussing in this article. This group of secondary metabolites has anti-inflammatory activity that can be used in perivenous and pro-inflammatory disorders (Figure 9) (Nosseri *et al.*, 1994; Guiance *et al.*, 2019; Sawada *et al.*, 2023).

Figure 9: Varicose eczema or stasis dermatitis

Sources: Photography courtesy of Prof. Dr. med. Gerd Hoffmann/Wikimedia, James Heilman, MD/Wikimedia, Guido Mieth/Getty Images, and https://www.gponline.com/therapeutic-areas/dermatology

Quercetin inhibits the growth of various Gram-positive and Gram-negative bacteria, as well as fungi and viruses, a potential neuroprotective effect for human ischemic stroke. According to the results, taking quercetin was significantly associated with earlier partial discharge and a decrease in critical markers of COVID-19 severity. However, further studies are needed to compensate for the limitations of this trial and clarify its therapeutic potential in this disease (Parvaresh *et al.*, 2016; Rauf *et al.*, 2018; Nguyen and Bhattacharya, 2022).

Quercetin serves as a natural antioxidant, protects against free radicals, and prevents skin aging. It is one of the most well-known and widely used flavonoids today. It has many beneficial properties for the human body, and best of all, it can be found in countless inexpensive and easy-to-buy foods. ne of quercetin's uses is as a cardiovascular protector. By blocking free radicals, it protects the heart and the damage these free radicals can cause in the body. It is also important in fat metabolism and blood sugar control (Yang *et al.*, 2020; Movahed *et al.*, 2021; Chai *et al.*, 2023; Sawada *et al.*, 2023; Remigante *et al.*, 2024).

Quercetin inhibits the enzymes cyclo-oxygenase and lipo-oxygenase, which reduces the production of two main inflammatory mediators: prostaglandins and leukotrienes. It is also capable of inhibiting histamine production, stabilizing basophils and mast cells. Quercetin inhibits the enzymes cyclo-oxygenase and lipo-oxygenase, which reduces the production of two main inflammatory mediators: prostaglandins and leukotrienes. It is also capable of inhibiting histamine production, stabilizing basophils and mast cells (Figure 10) (Ahmed *et al.*, 2023).

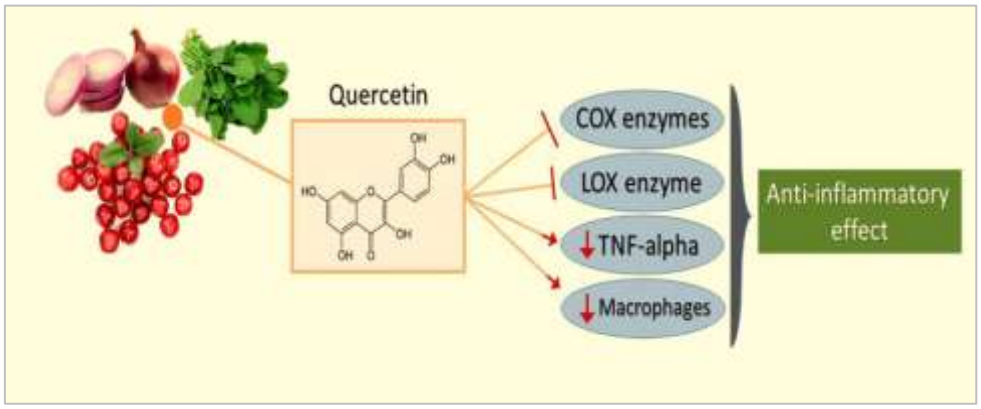

Figure 10: Role of Quercetin in inhibiting inflammation by blocking the activity of COX (cyclooxygenase) enzymes and LOX (lipoxygenase) enzymes, in addition to reducing TNF-α (tumor necrosis factor-alpha) and macrophage levels

Sources: file:///C:/Users/USUARIO/Downloads/Evaluation_of_the_Effect_of_Zinc_Quercetin_Bromela.pdf and Ahmed *et al.*, 2023

Histamine is directly responsible for most of the two unpleasant symptoms associated with allergies, such as sneezing and itching. Furthermore, you can inhibit the process of formation of free radicals in three different stages: at the beginning of the interaction with superoxide ions, in the formation of hydroxyl radicals (by chelating ferrous ions and in lipid peroxidation by reacting with lipid peroxy radicals (Huber and Rodriguez-Amaya, 2008; Cataneo, 2020; Remigante *et al.*, 2024).

3.6. Quercetin + Fisetin

Senolytics are a class of compounds that can destroy senescent cells, which are aged cells that increase inflammatory activity in the human body. The combination of quercetin with Fisetin reduces the amount of these senescent cells in the body, which accelerates the regenerative process and reduces inflammation in the human body (Maher *et al.*, 2006; Constantin *et al.*, 2010).

Fisetin is an important neuroprotector and antioxidant and has important actions for the treatment of disorders of the Central Nervous System (CNS). It also stimulates signaling pathways that improve long-term memory, maintain levels of glutathione, the main intracellular antioxidant, and reduce myelin phagocytosis by macrophages (Maher *et al.*, 2006; Constantin *et al.*, 2010). Quercetin has properties that act on the immune system, has antiviral activity, reduces the effect of cataract formation in diabetics, and is hepatoprotective and gastroprotective (Maher *et al.*, 2006; Constantin *et al.*, 2010).

The system regulates reactive oxygen species (ROS) levels and preserves redox balance in both organelles and the cytoplasm, extending into the interstitial fluid and blood to eliminate extracellular ROS. There are three primary antioxidant strategies for cellular protection against Reactive Oxygen Species ROS damage: ROS scavenging by low-molecular-weight molecules in intracellular and extracellular spaces; conversion of ROS into less reactive compounds by enzymatic antioxidants, thus reducing oxidation; and sequestration of pro-oxidant transition metals, such as iron and copper, by chelating proteins, preventing their participation in ROS generation (Figure 11) (Yang *et al.*, 2020; Movahed *et al.*, 2021; Chai *et al.*, 2023; Sawada *et al.*, 2023; Kozlov *et al.*, 2024; Remigante *et al.*, 2024).

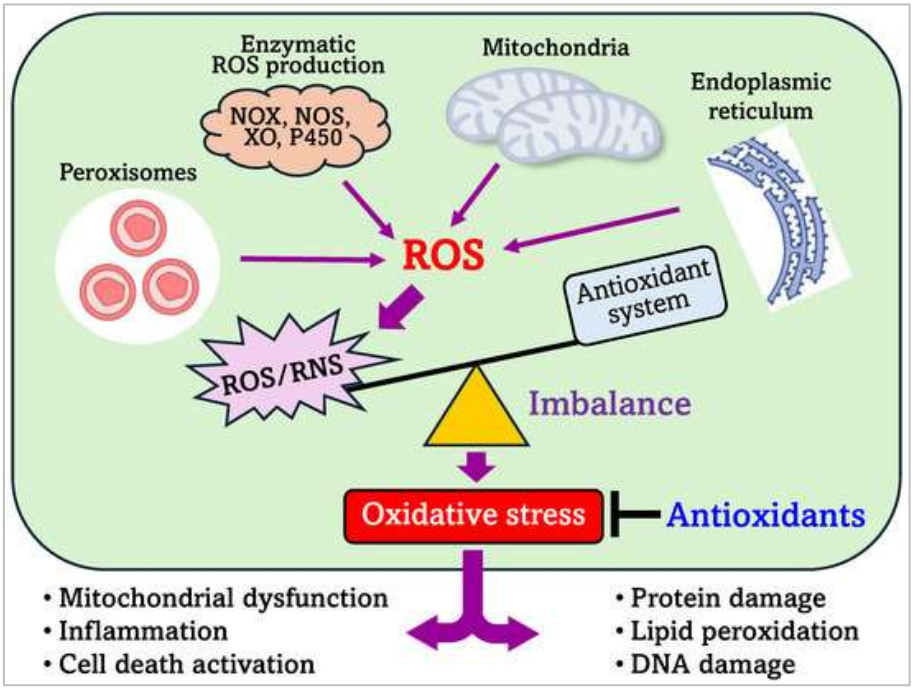

Figure 11: Intracellular sources of Reactive Oxygen Species ROS and consequences of oxidative stress. See text for details. Abbreviations: NOS, Nitric Oxide Synthase; NOX, NADPH Oxidases; XO, Xanthine Oxidase
Source : Doi: https://doi.org/10.3390/antiox13050602

Quercetin is found in many plants and foods and is also marketed as a dietary supplement to enhance antioxidant activity. Although this is its current use, the enormous potential of this molecule has led to various studies investigating its potential in the treatment of diseases such as cancer, cardiovascular diseases, inflammatory diseases, memory enhancement, asthma, Chronic Obstructive Pulmonary Disease (COPD), allergies, and viral infections, among others (Bosch *et al.*, 2015; Moraes *et al.*, 2022; Remigante *et al.*, 2024).

It stimulates the activity of endogenous antioxidant enzymes, such as superoxide dismutase and glutathione peroxidase, reinforcing the body's

antioxidant defense. To ensure optimal levels of quercetin, it is necessary to include foods rich in this flavonoid in the diet, and, in addition to this, supplementation can be considered, especially in cases where dietary intake is not sufficient (Bosch *et al.*, 2015; Moraes *et al.*, 2022; Remigante *et al.*, 2024).

3.7. The amount of quercetin a plant contains is determined by several factors

1. The part of the plant where it is found, with most of it occurring in outdoor areas.
2. The time of year it grows: summer, with greater sun exposure, provides more flavonoids. Likewise, warm climates favor quercetin synthesis.
3. The riper the fruit, the higher its content (Huber and Rodriguez-Amaya, 2008; Cataneo, 2020; Remigante *et al.*, 2024).

3.8. The preparation and processing of the food also influence this

Cooking these plants can reduce the amount of quercetin they contain. Furthermore, it is also lost when removing the skin of the fruit or vegetable. The low bioavailability and poor solubility of quercetin limit its use, so research is underway into the design and synthesis of numerous derivatives that modify these restrictions. Although the half-life of quercetin is not clearly described, in humans it has been estimated to be 31 to 50 hours, with a peak plasma concentration half an hour after consumption and another 8 hours after ingestion of 100 mg (Mlcek *et al.*, 2016; Wolfman *et al.*, 2016; Yang *et al.*, 2020).

3.9. Histamine and Resveratrol

Histamine is a substance produced by the body in response to an allergy or infection and can trigger a range of symptoms such as swelling, redness, itching, and difficulty breathing. Quercetin has been shown to inhibit the release of histamine directly from immune cells, which may help reduce allergy symptoms. It has also been shown to reduce the activity of the enzyme histidine decarboxylase, one of the main causes of histamine overproduction (Huber and Rodriguez-Amaya, 2008; Cataneo, 2020; Remigante *et al.*, 2024).

Resveratrol is a polyphenol found in several foods, including grapes, mainly in the skins and seeds. One of the best-known sources of resveratrol is red wine. This compound has antioxidant, anti-inflammatory, and cardioprotective properties. Resveratrol acts as an activator of antioxidant enzymes, such as superoxide dismutase, and stimulates gene expression related to antioxidant defense. In addition, resveratrol has anti-inflammatory properties that can help reduce the risk of cardiovascular and neurodegenerative diseases (Leonardi *et al.*, 2018; Movahed *et al.*, 2021).

3.10. Quercetin resveratrol antioxidants

The properties of quercetin and resveratrol make it important to understand the importance of antioxidants for health. Antioxidants are substances capable of neutralizing free radicals, unstable molecules that can cause cellular damage. Oxidative stress, resulting from an imbalance between the production of free radicals and the body's ability to neutralize them, is associated with several diseases, including cardiovascular diseases, neurodegenerative diseases, and cancer (Figure 12) (Movahed *et al.*, 2021; Chai *et al.*, 2023; Murugesan and Prabha, 2023; Sawada *et al.*, 2023; Remigante *et al.*, 2024).

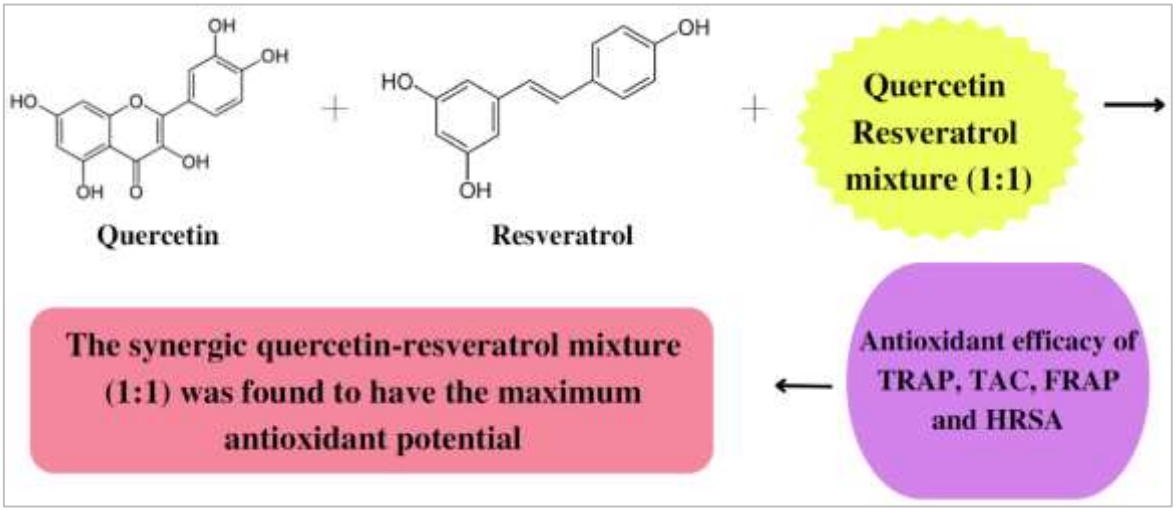

Figure 12: his research study covers the synergistic interactions of quercetin and resveratrol, and quercetin resveratrol mixtures (1:1) were used to evaluate the Total peroxyl radical-trapping efficiency (TRAP), Total Antioxidant Capacity (TAC), Ferric Reducing Antioxidant Power (FRAP), and Hydroxyl Radical Scavenging Activity (HRSA) antioxidant activity assays. The polyphenolic chemicals that are said to have synergistic effects

are very powerful inhibitors of oxidation and a host of other diseases. These results observed the advantages of polyphenol chemicals when combined, which may be helpful for future research

Source: Murugesan and Prabha, 2023, URN: NBN: sciencein.jmc.2023.581© ScienceIn Publishinghttps://pubs.thesciencein.org/jm and file:///C:/Users/USUARIO/Downloads/2023231581.pdf

3.11. Quercetin and its role in chelation

3.11.1. Metabolites and nutrients.

1. Minerals.
2. Buffer substance with buffering capacity.
3. Protease inhibitors.
4. Inactivators of toxic materials.
5. Enzymes and proteins necessary for Enzymes and proteins necessary for the adhesion of cells to the support where they are cultured (Movahed *et al.,* 2021; Chai *et al.,* 2023; Sawada *et al.,* 2023).

3.12. Chelating function

1. Quercetin can bind iron ions, which inhibits the formation of hydroxyl radicals.
2. Quercetin can induce the production of metallothionein, a metal chelating protein with antioxidant properties.

For this study, dermal fibroblasts were used from primary human skin cultures, grown in Dulbecco's modified Eagle's medium (DMEM, GIBCO) with 10% Fetal Calf Serum (FBS) and 1% penicillin-streptomycin (Sigma, P-3539). The DMEM medium has the following composition (Cho *et al.,* 2010; Movahed *et al.,* 2021; Weiwe *et al.,* 2023; Remigante *et al.,* 2024).

The lack of a chelating agent can affect the oxidation of the dyes in the product. As a result, the entire appearance of the product may undergo changes that will disrupt the initial idea. At the same time, considering chemical issues, it is normal for active ingredients that have an oxidizing action to decompose. With the action of metal ions, sodium hypochlorite and hydrogen peroxide decompose. Their lack can impact the production of magnesium and calcium precipitates. To give you an idea, there is even a risk of microorganisms appearing in the substances (Figure 13) (Cho *et al.,* 2010; Movahed *et al.,* 2021; Weiwe *et al.,* 2023; Remigante *et al.,* 2024; Zhang *et al.,* 2024).

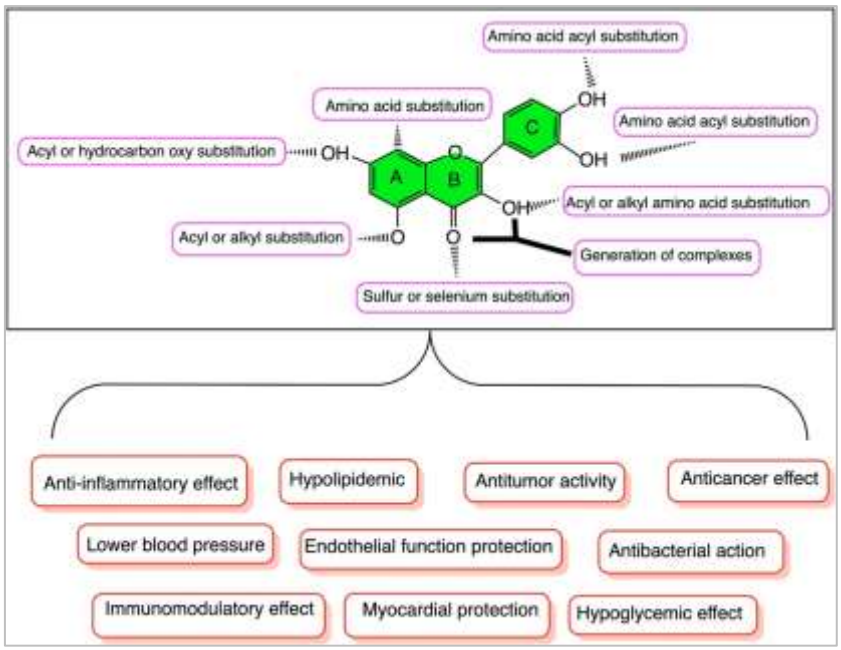

Figure 13: Structural modification and biological activity of quercetin
Source: Doi: 10.3389/fcvm.2023.1203713

3.13. Quercetin can be found in supplements

But it can also be obtained through dietary sources. However, quercetin is poorly absorbed by the intestine, so it is possible to take quercetin phytosomes, which are more easily absorbed (Pollard and Wolter, 2000; Engelmann *et al.,* 2005; Nilsson *et al.,* 2005).

3.13.1. Quercetin can inhibit the process of free radical formation

In three different stages: In initiation by interaction with superoxide ions, in the formation of hydroxyl radicals by chelating iron ions, and in lipid peroxidation by reacting with lipid peroxy radicals (Figure 14) (Morel and Cillard, 1998; Pérez, 2003; Engelmann *et al.,* 2005; Osredkar, 2024).

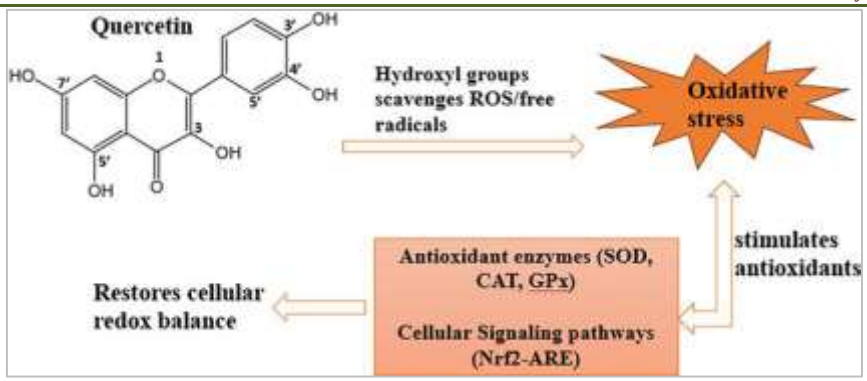

Figure 14: The antioxidant activity of quercetin in scavenging free radicals. Antioxidante enzymes: Superoxide Dismutase (SOD), Catalase (CAT), and Glutathione Peroxidase (GPx). Quercetin has been shown to activate the Cellular Signaling pathways, Nrf2, leading to the upregulation of Antioxidant Response Element (ARE) (Nrf2-ARE)-driven genes

Sources: IntechOpen and Doi: http://dx.doi.org/10.5772/intechopen.1004648

3.13.2. Stops the proliferation of endometriosis

Endometriosis is a condition in which the tissue that normally lines the uterus grows outside the uterus, causing pain and other symptoms. Quercetin may help inhibit increased cell shedding and angiogenesis in endometriosis. Supports blood glucose regulation: It can act in three different ways to regulate blood glucose (Pollard and Wolter, 2000; Engelmann *et al.,* 2005; Nilsson, 2005).

Increases insulin sensitivity. Insulin is a hormone that helps regulate blood glucose levels. When cells are resistant to insulin, they cannot properly utilize glucose, leading to elevated blood glucose levels (Morel and Cillard, 1998; Pérez, 2003; Nilsson, 2005).

3.13.3. It stimulates the activity of endogenous antioxidant enzymes

Such as superoxide dismutase and glutathione peroxidase, reinforcing the body's antioxidant defense. To ensure optimal levels of quercetin, it is necessary to include foods rich in this flavonoid in the diet, and, in addition to this, supplementation can be considered, especially in cases where dietary intake is not sufficient. In addition to scavenging free radicals, chelating metal ions, and inhibiting oxidases, flavonoids can increase the availability of endogenous antioxidants, as well as the activity of antioxidant enzymes. However, in the presence of transition metal ions, it is unclear to what extent free radical scavenging or metal chelation may contribute to antioxidant effects (Paul *et al.*, 1997; Param and Shikha, 1998; Pietta, 2000; Pratico, 2002; Padró *et al.*, 2005).

3.13.4. Another antioxidant mechanism of flavonoids

Which has not been studied in detail, results from interactions between these compounds and metal ions, primarily iron and copper. Flavonoids also have pro-oxidant activity, and this has been linked to their iron and copper-reducing activity, since these metals, when reduced, can catalyze the production of hydroxyl radicals through reactions such as Fenton's reaction (Movahed *et al.,* 2021; Chai *et al.,* 2023; Sawada *et al.,* 2023; Remigante *et al.,* 2024).

Quercetin, in particular, sequesters reactive oxygen species (OH and O2), inhibit xanthine oxidase and lipid peroxidation, and has iron chelating and stabilizing properties. The antiobesogenic and antidiabetic action of quercetin has been investigated. Research has been conducted on stimulating the increase in brown adipose tissue as a promising strategy for preventing obesity (Fung, 2001; Behling *et al.,* 2004; Galdino, 2019).

3.13.5. Quercetin is absorbed in the small intestine and is hydrolyzed by enterobacteria

Which releases the corresponding aglycone in the cecum and colon?

Once in the circulation, the compounds undergo methylation, glucuronidation, or sulfation in the liver. Part of this metabolite is excreted in the bile and returns to the intestinal lumen, where it is again hydrolyzed and subsequently degraded by intestinal bacteria into phenolic acid, 3-hydroxyphenylacetic acid, and 3,4-dihydroxyphenylacetic acid, and finally excreted in the feces (Figure 15) (Fung, 2001; Behling *et al.,* 2004; Galdino, 2019; Hai *et al.,* 2020).

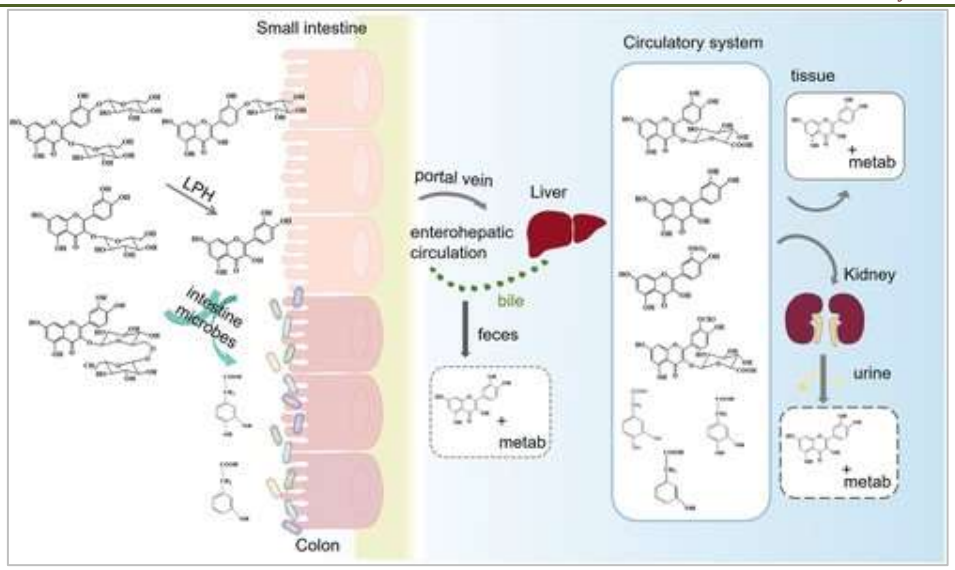

Figure 15: Schematic representation of processes of quercetin absorption, metabolism, and elimination *in vivo*. LPH, lactasephlorizin hydrolase
Source: Doi: 10.1002/fft2.50

3.13.6. The chelating activity of flavonoids can be explained as follows

Flavonoids may have the ability to displace pro-oxide ligands from ferric iron to form highly stable complexes, thereby preventing their redox cycling and, consequently, potential oxidative damage. Therefore, measurements of the stability constants of ferric-flavonoid compounds are required. The chelating activity of flavonoids can be explained as follows: flavonoids may have the ability to displace pro-oxidant ligands from ferric iron to form highly stable complexes, thereby preventing their redox cycling and, consequently, potential oxidative damage. Therefore, measurements of the stability constants of ferric-flavonoid compounds are required (Pietta, 2000; Pratico, 2002; Pérez, 2003; Pardes-Salido and Clemente-Fernández, 2005; Padró *et al.*, 2005).

The lack of a chelating agent can affect the oxidation of the dyes in the product. Chelation therapy can be performed orally by taking specific chelators in combination with micronutrients. It can also be administered intravenously, requiring saline solutions containing a series of substances, such as EDTA and multivitamins, multiminerals, and antioxidant complexes. Clogging or stenosis of the arteries, depending on their location, can cause heart attacks, thrombosis, blindness, impotence, and is more severe in diabetics. Chelation treatment should be accompanied by a nutritional program, exercise, stress-reducing therapy, and antioxidant supplementation, such as coenzyme Q10 (Figure 16) (Panche *et al.*, 2016; Seetharaman and Sarma, 2021).

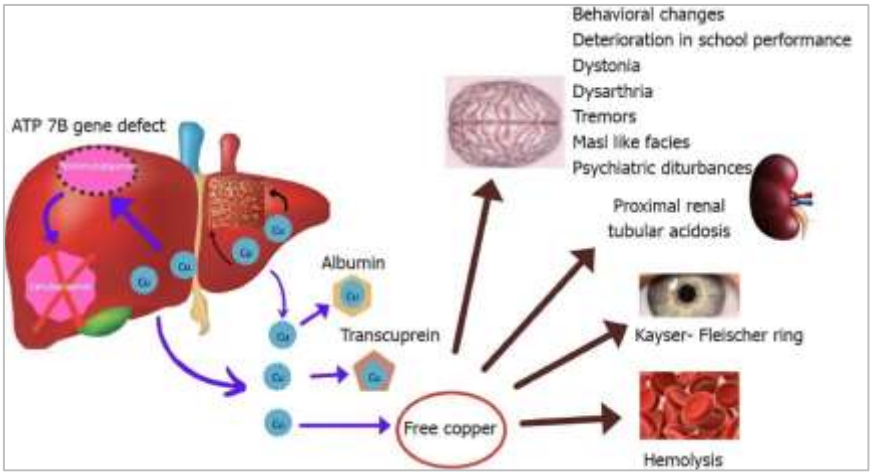

Figure 16: Pathophysiology of Wilson's disease. Copper performs an important function in the development of healthy nerves, bones, collagen, and melanin, and skin pigmentation. Generally speaking, you consume copper in the food you eat. The liver produces a substance called bile that eliminates all excess copper
Source: Doi: 10.4254/wjh.v13.i11.1552

A chelating agent is a type of chemical agent that aids in the formation of chelates. A compound, a metal ion linked to a chelating agent, using covalent bonds. Chelating agents form water-soluble complexes and are important chemicals for the composition of several products in the industry. They are also commonly known as sequestrants. In this sense, a chelating substance can bind metal ions. This is why it can be part of treatments against metal poisoning, since it forms a chelate, which becomes non-toxic and soluble. A chelating substance can bind metal ions. This is why it can be part of treatments against metal poisoning, since it forms a chelate, which becomes non-toxic and soluble (Mahan *et al.*,1995; Goes-Favoni *et al.*, 2004; Azevedo, 2014; Li *et al.*, 2016a; Li *et al.*, 2016b; Panche *et al.*, 2016; Imran *et al.*, 2019).

4.0. CONCLUSION

Understand why arterial scintigraphy is useful in cases of Wilson's disease, a genetic disease that poisons the body with copper, hemochromatosis, a disease that forces the body to absorb more iron than necessary when processing food, chronic kidney conditions or disorders that require blood transfusions to treat them, which can lead to high plasma iron levels. Arterial cleansing, or chelation, has an antioxidant effect that helps aging by restoring elasticity to the arteries, reducing hardening caused by oxidation. The anti-hardening effect of chelation therapy improves blood flow to and from the heart, brain, kidneys, and muscles. Below, you will find more information about our arterial cleansing treatment.

REFERENCES

- Ahmed, A. *et al.* (2023). The study of quadruple therapy, zinc, quercetin, bromelain, and vitamin C on the clinical outcomes of patients infected with COVID-19. *International Journal of Diabetes in Developing Countries, 22*(2), 29-37.
- Asgharian, P. *et al.* (2022). Potential mechanisms of quercetin in cancer prevention: focus on cellular and molecular targets. *Cancer Cell International, 22*, 257.
- Azevedo, E. (2014). Risks and controversies in the social construction of the concept of healthy food: the case of soy. *Public Health Journal, 4*(45), 781–788.
- Batiha, G. E-S., Beshbishy, A. M., Ikram, M., Mulla, Z. S., El-Hack, M. E. A., Taha, A. E., Algammal, A. M., & Elewa, Y. H. A. (2020). The pharmacological activity, biochemical properties, and pharmacokinetics of the major natural polyphenolic flavonoid: quercetin. *Foods, 9*(3), 374.
- Behling, E. B., Sendão, M. C., Francescato, H. D. C., Antunes, L. M. G. & Bianchi, L. (2008). Flavonoid quercetin: general aspects and biological actions. *Food and Nutrition Araraquara, 15*(3), 285-292.
- Bosch, R., Philips, N., Suárez-Pérez, J. A., Juarranz, A., Devmurari, A., Chalensouk-Khaosaat, J., & González, S. (2015). Mechanisms of photoaging and cutaneous photocarcinogenesis, and photoprotective strategies with phytochemicals. *Journal Antioxidants, 4*(2), 248-268.
- Brito, T., Roy, S., Sen, C., Shirakawa, T., Gotoh, A., Ueda, M., Ichihashi, M., & Packer, L. (2002). Flavonoids differentially regulate IFNγ-induced ICAM-1 expression in human keratinocytes: molecular mechanisms of action. *FEBS Letters, 520*(1-3), 145-152.
- Cataneo, A. H. D. (2020). Antiviral effect of the flavonoid naringenin on human cells infected with Zika virus. Retrieved Apr, 17, 2025, from https://www.arca.fiocruz.br/handle/icict/44362
- Carper, J. (1993). Food: Miracle medicine. Cali: Norma Editorial Group.
- Chai, Y. C. *et al.* (2023). Glutathione and glutaredoxin—Key players in cellular redox homeostasis and signaling. *Antioxidants, 12*(8), 1553.
- Cho, J-W., Cho, S-Y., Lee, S-R., Lee, K-S. (2010). Onion extract and quercetin induce matrix metalloproteinase-1 in vitro and in vivo. *International Journal of Molecular Medicine, 25*(3), 347-352.
- Constantin, R. P. *et al.* (2010). The actions of fisetin on glucose metabolism in the rat liver. *Cell biochemistry and function, 2010*, 149-158.
- Dagher, O. *et al.* (2021). Therapeutic potential of quercetin to alleviate endothelial dysfunction in age-related cardiovascular diseases. *Frontiers in Cardiovascular Medicine, 8*, 658400.
- Egert, S., Bosy-Westphal, A., Seiberl, J., Kürbitz, C., Settler, U., Plachta-Danielzik, S., & Müller, M. J. (2018). *Quercetin reduces* systolic blood pressure and plasma oxidised low-density lipoprotein concentrations in overweight subjects with a high-cardiovascular disease risk phenotype: a double-blinded, placebo-controlled crossover study. *British Journal of Nutrition, 119*(9), 1065-1075.
- Engelmann, M. D., Hutcheson, R., & Cheng, I. F. (2005). Stability of ferric complexes with 3-hydroxyflavone (flavonol), 5, 7-dihidroxyflavone (Chrysin), and 3',4'-Dihydroxyflavone. *Journal of Agricultural and Food Chemistry, 53*, 2953-2960.
- Fung, T. T. (2001). Association between dietary patterns and plasma biomarkers of obesity and cardiovascular disease risk. *American Journal of Clinical Nutrition, 73*(1), 61-67.
- Galdino, T. P. (2019). Quercetin. *Magazine Supplementation, 11*, 55.
- Goes-Favoni, S. P. *et al.* (2004). Isoflavones in commercial soy products. *Food Science and Technology, 24*(4).

- Guiance, S. N., Marino, L., Isern, D. M., Coria, I. D., & Irurzun, I. (2019). Flavonoids: medicinal applications the industrial. *Invenio*, *22*(40), 1-27.
- Guo, C. *et al.* (2022). Effect and mechanisms of quercetin for experimental focal cerebral ischemia: A systematic review and meta-analysis. *Oxidative Medicine and Cellular Longevity, 2022*, 9749461.
- Hai, Y. *et al.* (2020). Advance in the absorption, metabolism, and efficacy exertion of quercetin and its important derivatives: Absorption, metabolism, and function of quercetin. *Food Frontiers, 1*, 420–434.
- Hong, Y. *et al.* (2024). Reactive oxygen species signaling and oxidative stress: Transcriptional regulation and evolution. *Antioxidants*, *13*(3), 312.
- Huber, L. S. & Rodriguez-Amaya, D. B. (2008). Flavonols and flavones: Brazilian sources and factors influencing composition in foods. *Food and nutrition Araraquara*, *19*(1), 97-108.
- Imran, M., Salehi, B., Sharifi-Rad, J., Gondal, A. T., Saeed, F., Imran, A., Shahbaz, M., Fokou, P. V. T., Arshad, M. U., Khan, H., Guerreiro, S. G., Martins, N., & Estevinho, L. M. (2019). Kaempferol: A key emphasis on its anticancer potential. *Molecules*, *24*(12), 2277.
- Kiriyama, Y., Tokumaru, H., Sadamoto, H., Kobayashi, S., & Nochi, H. (2024). Effects of phenolic acids produced from food-derived flavonoids and amino acids by the gut microbiota on health and disease. *Molecules 2(*29), 5102.
- Kozlov, A. V., Javadov, S., & Sommer, N. (2024). Cellular ROS and antioxidants: Physiological and pathological role. *Antioxidants*, *13*(5), 602.
- Leonardi, T., Vanamala, J., & Taddeo, S. S. (2018). Polyphenols and their benefits for human health: a review. *Food & Function*, *9*(7), 2980-2997.
- Li, C., Zhang, W., & Frei, B. (2016a). Quercetin inhibits LPS-induced adhesion molecule expression and oxidant production in human aortic endothelial cells by p38-mediated Nrf2 activation and antioxidant enzyme induction. *Redox Biology, 9*, 104-113.
- Li, Y., Yao, J., Han, C., Yang, J., Chaudhry, M. T., & Wang, S. (2016b). Quercetin, inflammation, and immunity. *Nutrients*, *8*(3), 167.
- Light Soul Aromas. (2024). *Quercus*: Retrieved May, 22, 2025, from https://almalevearomas.com.br/glossario/usos-e-beneficios-do-quercus/
- Mahan, L. K., Arlin, M., & Krause, T. (1995). Food, nutrition, and diet therapy. New York: Routledge.
- Maher, P., Akaishi, T., & Abe, K. (2006). Flavonoid fisetin promotes ERK-dependent long-term potentiation and enhances memory. *Proceedings of the National Academy of Sciences of the United States of America*, *103*(44), 16568-16573.
- Marunaka, Y. *et al.* (2017). Actions of quercetin, a polyphenol, on blood pressure. *Molecules*, *22*(2), 209.
- Mateos-Aparicio, I. *et al.* (2008). Soybean, a promising source of health. *Hospital Nutrition*, *23*(4), 305-312.
- Mlcek, J. *et al.* (2016). Review: Quercetin and its anti-allergic immune response. *Molecules, 21*, 623.
- Moraes, G. V. *et al.* (2022). Antioxidant potential of flavonoids and therapeutic applications. *Research, Society and Development, 11 (1*4), e238111436225.
- Morel, I., Cillard, P., & Cillard, J. (1998). Flavonoid-metal interactions in biological systems, In C. Rice-Evans, L. Parker. (Eds), flavonoids in health and disease. (pp. 163-177). New York: Marcel Dekker.
- Movahed, A., Nabavi, S. F., Sureda, A., Nabavi, S. M., & Echeverría, J. (2021). Protective effects of resveratrol against neurodegenerative diseases: role of the antioxidant activity. *Food and Chemical Toxicology*, *154*, 112297.
- Murugesan, N., & Chandra Prabha, D. (2023). Antioxidant activity of synergistic quercetin and resveratrol. Journal of Molecular Chemistry, 23(581), 1-5.
- Nguyen, T. L. A., & Bhattacharya, D. (2022). Antimicrobial activity of quercetin: An approach to its mechanistic principle. *Molecules*, *27*(8), 2494.
- Nilsson, J., Pillai, D., Önning, G., Persson, C., Nilsson, A., & Akesson, B. (2005). Comparison of the 2, 2´-azinobis-3-ethylbenzotiazoline-6-sulfonic acid (ABTS) and ferric reducing antioxidant power (FRAP) methods to assess the total antioxidant capacity in extracts of fruit and vegetables. *Molecular Nutrition & Food Research, 49*, 239-246.
- Nosseri, C., Coppola, S., & Ghibell, L. (1994). Possible involvement of poly (ADP-rybosyl) polymerase in triggering stress-induced apoptosis. *Experimental Cell Research*, *212*, 367-373.
- Osredkar, J. (2024). Quercetin – Effects on Human Health. In K. Nyarko. (Ed), Investigating the antioxidant properties of quercetin (pp. 1-15). London: IntechOpen.
- Panche, A., Diwan, A., & Chandra, S. (2016). Flavonoids: An overview. *Journal of Nutritional Science, 5*, E47.
- Param, N. S., & Shikha, P. (1998). Anti-ulcer potential of flavonoids. Indian. *Journal of Physiology and Pharmacology. 42*, 343-351.
- Paul, P., Rita, J., Ritva, S., Mackku, H., Lyly, T., Eero, P., & Arpo, A. (1997). Dietary flavonoids and the risk of lung cancer and other malignant neoplasms. *American Journal of Epidemiology, 146*, 223-230.
- Padró, T., Mendieta, C., & Badimon, L. (2005). Inflammation and arteriosclerosis. *Hypertension*, *22*(4), 173-182.
- Pardes-Salido, F., & Clemente-Fernández, A. (2005). Polyphenols used in pharmacy: Metabolism and biological action. *Offarm journal Pharmacy and Society*, *24*, 85-94.

- Parvaresh, A. *et al.* (2016). Quercetin and ovarian cancer: An evaluation based on a systematic review. *Journal of Research in Medical Sciences 21*, 34.
- Perez, T. G. (2003). Flavonoids: Antioxidants or prooxidants. *Cuban Journal of Biomedical Research, 22*, 48-57.
- Pietta, P. G. (2000). Flavonoids as antioxidants. *Journal Natural Product, 63*, 1035-1042.
- Pollard, M., & Wolter, W. (2000). Prevention of spontaneous prostate-related cancer in lobund wistar rats by a soy protein isolate/isoflavon diet. *Prostate, 45*, 101-105.
- Potapovich, A., Kostyuk, V., Kostyuk, T., Luca, C., & Korkina, L. (2013). Effects of pre- and post-treatment with plant polyphenols on human keratinocyte responses to solar UV. *Inflammation Research, 62*(8),773-780.
- Pratico, D. (2002). Alzheimer's disease and oxygen radicals: New insights. *Biochemical Pharmacology, 63*, 563-567.
- Prediger, S. C. C. *et al.* (2011). Effects of soy protein containing isoflavones on women's lipid profile: a meta-analysis. *Nutrition Journal, 24* (1), 161–172.
- Rauf, A. *et al.* (2018). Anticancer potential of quercetin: A comprehensive review. *Phytotherapy Research, 2*(11), 2109-2130.
- Remigante, A. *et al.* (2024). Redox homeostasis and antioxidant strategies in the pathophysiology. *Antioxidants, 13*(3), 281.
- Sawada, Y., *et al.* (2023). Effects of high-intensity anaerobic exercise on the scavenging activity of various reactive oxygen species and free radicals in athletes. *Nutrients, 15*(1), 222.
- Seetharaman, J., & Sarma, M. S. (2021). Chelation therapy in liver diseases of childhood: Current status and response. *World Journal of Hepatology, 13*(11), 1552-1567.
- Suntory Global Innovation Center Limited- Suntory Beverage & Food Limited. (2014). Confirmed dose-responsive efficacy of quercetin glucoside in decreasing body fat. Announcement made during the 21st European Congress on Obesity. Retrieved May 18, 2025, from https://www.suntory.com/softdrink/news/pr/d/sbf0152.html?fromid=sic
- Suntory. (2008). Development of quercetin glycoside-containing beverage, "Iyemon Tokucha," a food for specified health use. *Japanese Pharmacology & Therapeutics, 36*, 919-930.
- Warwick, E., Cassidy, A., Hanley, B., Jouni, Z., & Bao, Y. (2012). Effect of phytochemicals on phase II enzyme expression in infant human primary skin fibroblast cells. *British Journal of Nutrition, 108*(12), 2158-2165.
- Wolfman, C. *et al.* (2016). Anxioselective properties of 6,3'-dinitroflavone, a high-affinity benzodiazepine receptor ligand. *European Journal of Pharmacology, 318*, 23-30.
- Xariss, M. S. *et al.* (2019). Antioxidant and metal chelating activity of the honey of *Melipona beachie* and *Frieseomelitta nigra* originating from Tabasco, Mexico. *TIP Specialized Journal of Chemical-Biological Sciences, 22*, 1-7.
- Xu, D. *et al.* (2019). Antioxidant activities of quercetin and its complexes for medicinal application. *Molecules. 24*(6), 1123.
- Yang, J. Y., Della-Fera, M. A., Rayalam, S., Ambati, S., Hartzell, D. L., Park, H. J., & Baile, C. A. (2008). Enhanced inhibition of adipogenesis and induction of apoptosis in 3T3-L1 adipocytes with combinations of resveratrol and quercetin. *Life Science, 82*(19-20), 1032-1039.
- Yang, Y., Chen, Y., Li, X., Wei, Z., Li, Y., Huang, J., & Chen, D. (2020). Resveratrol attenuates aortic smooth muscle cell proliferation, migration, and contraction via the miR-143/actin-bundling protein plastin-3/AMPK signaling pathway. *Molecular Medicine Reports, 21*(1), 471-480.
- Zahra, M., Abrahamse, H., & George, B. P. (2024). Flavonoids: antioxidant powerhouses and their role in nanomedicine. *Antioxidants, 13*(8), 922.
- Zhang, W., Zheng, Y., Yan, F. D., & Ren, Y. M. (2023). Research progress of quercetin in cardiovascular disease. *Frontiers in Cardiovascular Medicine, 10*,1203713.