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EFFECTS AND MECHANISTIC UNDERSTANDING OF QUERCETIN AS AN ANTIOXIDANT, ANTIDIABETIC AND ANTI-INFLAMMATORY AGENT

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ABSTRACT

Quercetin is a flavonoid present in several fruits and vegetables. Quercetin is widely used in traditional and herbal medicine due to its numerous therapeutic characteristics, including anti-inflammatory, antioxidant, anti-diabetic, antihypertensive, vasodilator, anti-obesity, anti-hypercholesterolemic, and anti-atherosclerotic capabilities. Quercetin can help reduce inflammation and oxidative stress in the body, which can be beneficial for disorders like diabetes and other inflammatory ailments. Quercetin's antioxidant qualities help to manage blood sugar levels by lowering inflammation and oxidative stress in the body. However, further research is needed to properly understand quercetin's impact in these circumstances. Thus, the purpose of this review is to investigate the impacts and mechanistic knowledge of quercetin in these situations.

Keywords: Quercetin, Antioxidant, Antidiabetic, Anti-Inflammatory

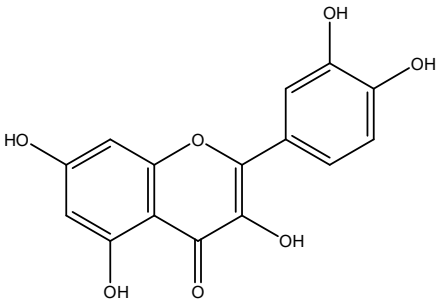
INTRODUCTION:

Antioxidants are vital for diabetes treatment because they help to reduce the body's inflammatory and oxidative stress. Furthermore, because free radical damage can increase diabetic symptoms, they can help protect cells from harm. People with diabetes may benefit from increasing their diet of antioxidant-rich foods such as fruits, vegetables, nuts, and whole grains. Furthermore, the potential therapeutic

benefits of a few specific antioxidants, such as vitamin C, vitamin E, and alpha-lipoic acid, have been studied **[1]**.

It is well recognized that inflammation produces reactive oxygen species and free radicals, which can set off a series of events that impede healing. Reactive oxygen species (ROS), which are produced in enormous quantities by the inflammatory process, have also been demonstrated to have a role in the pathophysiology of several chronic illnesses, including rheumatoid arthritis, cancer, cardiovascular disease, and neurological disorders. Antioxidants and anti-inflammatories are therefore crucial for the prevention and management of a wide range of human illnesses. Sadly, a variety of negative effects are linked to commonly used anti-inflammatory medications, such as NSAIDs (non-steroidal anti-inflammatory drugs), which limit their use. Therefore, plants or substances with antioxidant properties can help alleviate inflammatory diseases by absorbing reactive oxygen species and free radicals during the inflammatory process **[2]**.

Quercetin (3,3',4',5,7-pentahydroxyflavone), whose name is taken from the Latin word "Quercetum" (Oak Forest), is a substance that belongs to the class of substances known as flavonols. Its color is yellow, and insoluble in cold water. It is, however, quite soluble in lipids and alcohol. (Anand *et al*.,2016). Quercetin is a flavonoid found extensively in different fruits, vegetables, and herbs. Quercetin is known to possess several pharmacological activities including anti-diabetic, anti-inflammatory, analgesic, neuroprotective and antioxidant [**3]**.



Structure of Quercetin

Quercetin acts as an antioxidant, reducing oxidative stress and cell damage by helping the body break down free radicals. People with diabetes may benefit most from this, as oxidative stress is linked to the development and progression of diabetes. Additionally, quercetin has anti-inflammatory qualities that may aid in lowering bodily inflammation. The anti-inflammatory properties of quercetin may help manage diabetes because the disease is linked to

chronic inflammation, which affects many other health issues as well **[4]**.

MATERIALS AND METHODS:

The purpose of this study was to evaluate quercetin's benefits and potential mechanism of action as an anti-inflammatory, antidiabetic, and antioxidant. To achieve this, search terms including "quercetin," "antioxidant," "anti-diabetic," and "anti-inflammatory" were used to go through several databases, including PubMed, Google Scholar, Research Gate, Scopus, Medline, and Science Direct. The analysis only considered published, English-language articles that were pertinent to the goal of the study.

RESULTS AND DISCUSSION:

Antioxidant Effects of Quercetin:

Multiple research projects have been conducted to study the antioxidant properties of quercetin in vitro and in vivo. Quercetin has been demonstrated to scavenge free radicals, prevent lipid peroxidation, and improve the activity of antioxidant enzymes. Quercetin has also been shown to protect cells from oxidative stress-induced damage **[5]**.

Quercetin has been found to have considerable antioxidant properties in animal studies. In one study, quercetin treatment lowered the levels of oxidative stress indicators while increasing the activity of antioxidant enzymes in rats with induced oxidative stress **[6]**. Similarly, quercetin treatment enhanced glutathione levels and decreased lipid peroxidation in research utilising mice with induced oxidative stress **[7]**.

Mechanisms of Action of Quercetin as Antioxidant:

The precise methods through which quercetin exerts its antioxidant properties are unknown. Several possible processes, however, have been hypothesised, including:

1. Free radical scavenging: Quercetin has been shown to scavenge free radicals such as superoxide anion, hydroxyl radical, and singlet oxygen, all of which can cause oxidative damage. Because of the presence of many hydroxyl groups that may contribute electrons to destroy free radicals, quercetin is a potent antioxidant **[8]**.

2. Lipid peroxidation inhibition: Quercetin has been proven to decrease lipid peroxidation, which is the oxidative breakdown of lipids that can cause cellular harm. Quercetin can directly scavenge lipid peroxyl radicals, preventing lipid peroxidation from spreading **[9]**.

3. Induction of antioxidant enzymes: It has been discovered that quercetin increases the activity of antioxidant enzymes such as superoxide dismutase (SOD), glutathione peroxidase (GPx), and catalase (CAT). These antioxidant enzymes may neutralize ROS and RNS, therefore protecting cells from oxidative stress-induced damage **[10]**.

4. Heat shock protein induction: Quercetin has been demonstrated to promote the production of heat shock proteins (HSPs), which are chaperone proteins that aid in the prevention of protein misfolding and aggregation. Induction of HSP may boost cellular antioxidant defenses and protect against oxidative damage **[11]**.

Antidiabetic Effects of Quercetin:

Several research in both animal models and people have looked at the possible anti-diabetic properties of quercetin. A meta-analysis of randomized controlled trials found that quercetin supplementation lowered fasting blood glucose levels in type 2 diabetic patients **[12]**. Similarly, another clinical trial meta-analysis discovered that quercetin supplementation improved glycemic control and insulin sensitivity in overweight or obese persons with prediabetes or metabolic syndrome **[13]**.

Quercetin has been proven in animal models to have anti-diabetic effects by boosting insulin release from pancreatic beta-cells and enhancing glucose absorption in insulin-sensitive tissues. In one research of diabetic rats, for example, quercetin administration enhanced glucose tolerance and raised insulin sensitivity **[14]**. Similarly, another study discovered that giving rats quercetin boosted glucose absorption in muscle cells and improved insulin signaling **[15]**.

Quercetin may also protect pancreatic beta-cells, which are important for insulin production. Quercetin was discovered to protect against oxidative stress and inflammation in rat pancreatic beta-cells, which are known to lead to beta-cell malfunction and death **[16]**.

Mechanisms of Action of Quercetin as antidiabetic:

The precise methods through which quercetin exerts its anti-diabetic benefits are unknown. Several plausible processes, however, have been hypothesised, including:

1. AMP-activated protein kinase (AMPK), a major regulator of glucose metabolism, has been demonstrated to be activated by quercetin. AMPK activation improves glucose tolerance and increases glucose absorption in muscle cells **[17]**. Quercetin has also been demonstrated to block alpha-glucosidase, an enzyme that converts complex carbs into simple sugars, causing postprandial hyperglycemia **[18]**.

2. Insulin secretion regulation: Quercetin has been shown to stimulate pancreatic beta-cell insulin secretion by activating the transient receptor potential cation channel subfamily V member 1 (TRPV1). TRPV1 activation causes calcium influx in beta cells, resulting in insulin secretion **[19]**.

3. Antioxidant and anti-inflammatory qualities: Quercetin possesses powerful antioxidant and anti-inflammatory capabilities that may protect against beta-cell malfunction and apoptosis. Diabetes

patients have higher levels of oxidative stress and inflammation, which can lead to beta-cell malfunction and insulin resistance **[20]**.

4. Gut microbiota regulation: Quercetin has been demonstrated to regulate the makeup of gut microbiota, which can have a substantial influence on metabolic health. In one study, quercetin supplementation reduced the quantity of pro-inflammatory bacteria while increasing the abundance of anti-inflammatory bacteria in mice fed a high-fat diet. This change in the makeup of the gut microbiota was linked to better glucose tolerance and insulin sensitivity **[21]**.

Anti-inflammatory Effects of Quercetin:

Numerous research has been conducted to study the anti-inflammatory properties of quercetin in vitro and in vivo. Quercetin has been proven to decrease the generation and release of inflammatory cytokines such tumour necrosis factor-alpha (TNF-α), interleukin-1 beta (IL-1β) and interleukin-6 (IL-6) (IL-6) **[22]**. Quercetin has also been demonstrated to inhibit immune cell activation and migration, including macrophages, neutrophils, and T cells **[23]**.

Quercetin has been shown to have considerable anti-inflammatory effects in animal studies. In a study, quercetin administration reduced the intensity of inflammation and the production of inflammatory cytokines in rats with colitis **[24]**. Similarly, quercetin treatment decreased airway hyperresponsiveness, eosinophil infiltration, and cytokine production in mice with allergic airway inflammation **[25]**.

Mechanisms of Action of Quercetin as Anti-inflammatory:

The precise processes through which quercetin exerts its anti-inflammatory properties are unknown. Several plausible processes, however, have been hypothesised, including:

1. Inhibition of inflammatory cytokine production: Quercetin has been discovered to limit the activation of nuclear factor-kappa B (NF-κB), which inhibits the synthesis and release of inflammatory cytokines such as TNF-α, IL-1β, and IL-6. NF-κB is a transcription factor that controls inflammation-related genes **[26]**.

2. Immune cell activation inhibition: Quercetin has been demonstrated to inhibit the activation and migration of a variety of immune cells, including macrophages, neutrophils, and T lymphocytes. Quercetin treatment decreased the production of inflammatory cytokines and chemokines in human macrophages **[27]**. Similarly, in a study of mice with acute lung injury, quercetin administration reduced neutrophil recruitment to lung tissue **[28]**.

3. Antioxidant properties: Quercetin contains significant antioxidant capabilities that can help protect against oxidative stress-induced inflammation. Quercetin is said to

scavenge free radicals and reduce lipid peroxidation, both of which can cause cell membrane damage and inflammation **[29]**.

4. Immunomodulatory characteristics: Quercetin has been reported to have immunomodulatory qualities, which can aid in immune response regulation. In a study using sepsis mice, quercetin treatment boosted anti-inflammatory cytokine expression while decreasing pro-inflammatory cytokine expression **[30]**.

CONCLUSION:

Quercetin has demonstrated potential antioxidant, anti-diabetic and anti-inflammatory properties in both in vitro and in vivo experiments. It has been shown to scavenge free radicals, decrease lipid peroxidation, and improve antioxidant enzyme activity. It has also been shown to boost insulin secretion, improve glucose metabolism, and decrease immune cell activation, prevent the generation and release of inflammatory cytokines to exert its anti-diabetic and anti-inflammatory activity respectively. The actual processes by which quercetin exerts its antioxidant properties need to be investigated further, although its propensity to generate HSPs may potentially play a role. The precise methods through which quercetin exerts its anti-diabetic and anti-inflammatory benefits are unknown, although its capacity to regulate gut microbiota composition and its capacity to influence the immune response may potentially play a crucial role**.** Quercetin is a naturally occurring molecule present in a range of foods and plants, and due to its low toxicity, it is a good option for the creation of new antioxidants. More clinical research is needed, however, to identify the appropriate dosage, duration, and safety of quercetin supplementation in people.

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