Quercetin Reduces Atherosclerosis

BY RICHARD TEMPLETON

It's difficult to overstate just how dangerous and common **atherosclerosis** is.

Atherosclerosis is the progressive buildup of plaque in the arteries and is a leading cause of cardiovascular disease, including coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease.[1]

Preclinical research over the last few years has shown that **quercetin** can play a role in mitigating the development and progression of atherosclerosis, helping to protect the heart and potentially reduce risk for these dangerous conditions.

How Atherosclerosis Drives Cardiovascular Disease

Atherosclerosis-driven coronary artery disease develops over time as lipids, inflammatory cells, smooth muscle cells, and dead cell debris accumulate beneath the vessel's inner endothelial lining.

Its major complications, including myocardial infarction and stroke, substantially contribute to morbidity, loss of independence, and reduced quality of life.[2]

Nearly half of U.S. adults have at least one major risk factor for coronary heart disease, such as high blood pressure, high lipids, or smoking. Meanwhile, **12%** have diabetes, a serious risk factor; and 115 million adults have prediabetes, yet another potential contributor.[4]

As plaque accumulates, several pathological changes can occur:[2]

- **Endothelial dysfunction**, in which the endothelium loses its protective role, leading to reduced vasodilation, increased inflammation, and endothelial cell senescence.[5] Endothelial dysfunction is also the first step in the process that initiates atherosclerosis.[6]
- **Narrowing of blood vessels** (often **> 50%**), which reduces blood flow and causes angina, particularly during physical exertion or stress,[2] and
- **Blood clot formation** can be triggered by rupture-prone fat and inflammation-rich plaques, blocking blood flow to the heart, causing a heart attack, or traveling to the brain resulting in stroke.[2]

Emerging preclinical research suggests that quercetin may influence several biological processes involved in atherosclerosis progression.

What Is Quercetin?

Quercetin is a naturally occurring compound found in a variety of plant foods, including onions, leafy green vegetables such as kale, cruciferous vegetables like broccoli and cabbage, as well as tea, berries, and certain herbs.[7]

Quercetin has been studied for its role in mitigating age-related deterioration and disease, largely because of its **antioxidant** and **anti-inflammatory** effects.[7] Preclinical studies also suggest quercetin may have **senolytic activity**, meaning it may help target **senescent cells**, though this has primarily been demonstrated in experimental models.[8,9]

Recent research suggests that quercetin may influence key biological processes involved in atherosclerosis. Evidence from animal and human cell studies indicates that quercetin reduces plaque formation and improves vascular health.

Activating Cellular Defenses

Preclinical studies suggest that quercetin's antioxidant[10] and anti-inflammatory effects[11,12] target key processes involved in atherosclerotic plaque formation.

Quercetin also activates specific cell pathways critical to cellular defense and rejuvenation in blood vessels.

One way quercetin may support cellular defenses is by increasing activity of a protein called **Nrf2**. When activated, Nrf2 *switches on protective genes* that defend cells against threats like oxidative damage.[13,14]

Nrf2 activity can be suppressed when it binds to another protein, **KEAP1**. A study found that quercetin binds to KEAP1 and causes it to separate from Nrf2, allowing Nrf2 to activate cellular defenses. As a result, Nrf2 activation helps reduce inflammatory cell death in macrophages.[13]

Quercetin also increases the production and activity of another cellular defender, **SIRT1**.[15-17] SIRT1 and other sirtuins are proteins vital to cellular defense and rejuvenation.

Activating SIRT1 has been associated with prolonged cellular lifespan in experimental models.[15,18] Quercetin boosts SIRT1 expression and activity, which may contribute to its observed effects in atherosclerosis.[17]

In preclinical studies, quercetin has also been shown to increase the activity of **AMPK**, an enzyme that plays a key role in metabolic regulation (including blood sugar, lipids, and insulin resistance).[15,19,20] *Reduced* AMPK activity is tied to insulin resistance and metabolic syndrome, major risk factors for cardiovascular disease including atherosclerosis.[21]

Through all these actions, quercetin can further block the oxidative damage and inflammation that contribute to atherosclerosis.

For example, it impedes the **oxidation of LDL cholesterol**, which contributes to fat deposits in arterial plaques.[14,15]

These effects of quercetin have been associated with protection against atherosclerosis in animal models.

Blocking Dangerous Abnormalities

Several types of cells are damaged or altered in **atherosclerosis**, worsening the condition.

Quercetin has been shown in preclinical studies to protect against damage to:

- **Macrophages**. A type of immune system cell, damaged macrophages can invade arterial plaques and transform into **foam cells**, which rapidly accelerate plaque buildup. Quercetin has been shown to *reduce* transformation of macrophages into forms that promote atherosclerosis.[13,15,22]
- **Endothelial cells**. These cells line the inside of arteries and are critical to healthy blood flow. When these cells become damaged, they drive atherosclerosis. Quercetin has been shown to *block* endothelial cell damage and death.[12,14,15]
- **Vascular smooth muscle cells**. Smooth muscle cells in arterial walls allow the vessel to constrict or dilate to regulate blood flow. In atherosclerosis, these cells spread and migrate to abnormal locations within the vessel. This is associated with inflammation, calcification, and thickening of the plaque.[23] Quercetin has been shown to *inhibit* the harmful proliferation and migration of these cells.[24,25]

Improving Gut Health

A healthy mix of gut microbes benefits the heart and overall health.[26]

In preclinical models, quercetin intake has been associated with improvements in gut microbial

composition.[27-29] In turn, healthy gut microbes metabolize quercetin into bioactive compounds that circulate throughout the body.

Higher levels of these metabolites have been linked to reduced atherosclerosis in experimental animals.[26] In one animal study quercetin intake not only altered the gut microbiota but also reduced harmful lipid metabolites.[30]

A review of 30 preclinical studies suggests that quercetin supplementation, across a range of doses, may exert cardioprotective effects in experimental high-fat diet models.[31] Clinical trials are needed to determine whether these findings translate to human atherosclerosis.

Summary

Cardiovascular disease is the leading killer in the world. Atherosclerotic **plaque** in blood vessels is its most common driver.

Quercetin has been studied for its potential effects on atherosclerosis formation and progression. By boosting cellular defenses and blocking damaging processes that contribute to atherosclerosis in cell and animal models, it shows promise for lowering the burden of atherosclerosis in humans. •

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