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Fisetin — An Unsung Hero in the Fight Against Vascular Calcification

Analysis by Dr. Joseph Mercola | May 26, 2026

STORY AT-A-GLANCE

- Fisetin, naturally found in strawberries, apples, and onions, prevents artery stiffness by halting harmful calcium buildup in blood vessels
- Regular consumption of fisetin-rich foods significantly reduces inflammation and oxidative stress, effectively lowering your risk of heart disease and stroke
- Fisetin enhances your body's natural defenses by activating enzymes that switch off dangerous signals responsible for arterial calcification
- Eliminating ultraprocessed foods from your diet protects your arteries from chronic inflammation and metabolic damage
- Daily physical activity and targeted carbohydrate intake help maintain healthy insulin levels, which is essential for preserving flexible arteries and good cardiovascular health

One of the most overlooked threats to your cardiovascular health is vascular calcification, meaning your arteries harden and stiffen as calcium builds up within their walls.

When your arteries lose flexibility, your heart works harder to pump blood, significantly raising your risk for hypertension, heart attack, and stroke. In fact, you could have it right now. Research indicates that nearly half of all adults over the age of 60 have some level of calcification throughout their body, also known as diffuse calcification.[1]

To manage the issue, researchers are turning towards fisetin, a natural flavonol found abundantly in foods like strawberries, apples, and onions. Interestingly, fisetin also exhibits antioxidant and anti-inflammatory properties that promote better overall health.

Fisetin Prevents Calcium Buildup in Arteries

In a study published in Aging,[2] researchers investigated how fisetin helps prevent vascular calcification, a process that makes your blood vessels stiff and less able to function properly. To conduct their study, they used human vascular smooth muscle cells, segments of mouse arteries, and a special mouse model that mimics calcification caused by too much vitamin D.

The team treated cells and tissues with high levels of calcium and phosphate, which simulates conditions that promote artery hardening, and then added fisetin. They closely monitored changes in calcification markers, such as genes and proteins involved in calcium deposition.

- **The impact of fisetin on cardiovascular health —** When fisetin was added, it dramatically reduced the buildup of calcium in the artery cells and in artery segments from mice. Specifically, it lowered activity levels of genes known to promote calcification, including BMP2, ALPL, and CBFA1.

  For context, BMP2 is a gene that signals your body to start depositing calcium, ALPL promotes mineralization, and CBFA1 is crucial in transforming smooth muscle cells into bone-like cells — none of which you want happening in your arteries. In other words, fisetin directly interrupts the dangerous transformation of your artery cells from smooth, flexible structures into hardened, calcium-filled tissues.

- **Going deeper into fisetin's effectiveness —** The researchers observed that fisetin significantly reduced calcification markers across all experimental setups, proving it is consistently beneficial, and this wasn't a minor improvement at all. It was

substantial enough to suggest that regular intake of fisetin-rich foods or supplementation could effectively shield your arteries from harmful calcium buildup.

Interestingly, these benefits hinged strongly on one crucial enzyme called dual-specificity phosphatase 1 (DUSP1). When researchers turned it off, fisetin lost its protective effects completely. Even worse, shutting down this enzyme increased calcification, showing that DUSP1 is what fisetin activates to halt the hardening of arteries.

- **Fisetin works right away —** Time-related specifics were equally striking. In mouse models overloaded with vitamin D (a known way to rapidly induce artery calcification) the introduction of fisetin led to visible improvements in as little as two weeks. Calcium deposits were lower, showing fisetin works swiftly to prevent artery stiffening from progressing once introduced.

- **Groups who will benefit the most from fisetin —** The research strongly indicates that anyone already at risk from conditions like kidney disease, diabetes, or vitamin D overload (which excessively raises calcium levels) will likely see significant heart-health benefits from fisetin. These groups typically face higher risks of rapid vascular calcification.

  Conversely, the effectiveness of fisetin compared to untreated scenarios was stark. Cells and tissues exposed to high phosphate and calcium without fisetin quickly became calcified, mirroring the conditions that lead to stiff, blocked arteries in people. But with fisetin treatment, those same tissues remained flexible and significantly less mineralized.

- **A look into the biological processes —** The central player in vascular calcification is a protein called p38 mitogen-activated protein kinase (p38 MAPK). Think of this protein as a harmful switch that, when activated by stress signals like excess calcium and phosphate, instructs your artery cells to harden and calcify.

Fisetin's primary action involves activating DUSP1. When it raises the levels of DUSP1, p38 MAPK gets turned off, blocking the harmful signal pathway.

- **Fisetin also helps maintain balance in cell signaling —** Normally, cells in your arteries carefully regulate their internal calcium levels, but certain conditions disrupt this balance. High phosphate, chronic inflammation, and metabolic disorders upset calcium regulation, pushing smooth muscle cells toward calcification. By enhancing DUSP1 activity, fisetin restores balance, preserving the natural state of your arteries and safeguarding your cardiovascular system from unnecessary strain.

- **The dual role of fisetin for your overall health —** Not only does fisetin halt calcium buildup, it also addresses inflammation and oxidative stress, which are powerful contributors to artery disease.

Other Health Benefits of Increasing Fisetin Intake

In a meta-analysis published in Acta Scientific Nutritional Health,[3] researchers investigated the different health-promoting effects of fisetin. Moreover, they highlighted its specific advantages for your cardiovascular system.

- **Maintain lipid balance —** This means your cholesterol and triglyceride levels become healthier. Animal studies showed substantial reductions in LDL cholesterol, commonly called "bad cholesterol," and triglycerides after fisetin administration. This improvement is essential because lower LDL and triglycerides directly reduce your risk of plaque buildup in arteries, thereby dramatically lowering your chance of heart attack or stroke.

- **Improve insulin sensitivity —** This is a critical factor for managing and preventing Type 2 diabetes and its related cardiovascular complications. Laboratory tests showed improvements within weeks of fisetin supplementation, particularly on animal models of insulin resistance.

- **Manage blood pressure —** Several studies cited in the review demonstrated significant drops in blood pressure after fisetin was administered regularly. High blood pressure puts relentless strain on your heart and arteries, increasing risks of severe cardiac events.

- **Control metabolic dysfunction —** The most substantial cardiovascular benefits of fisetin appeared among test animal models. In these groups, fisetin not only normalized cholesterol levels and blood pressure, but also reduced inflammation. These benefits could also translate for human applications, too.

- **Modulate the MAPK pathway —** As noted in the previous study, this pathway triggers inflammatory responses in your blood vessels, contributing to plaque buildup and vascular damage if unchecked. Studies reviewed showed that fisetin blocks these inflammatory signals at their source, creating powerful protection against heart disease.

- **Antioxidant capabilities —** Antioxidants help neutralize harmful free radicals, and fisetin stands out because it specifically protects cardiovascular tissues. Previously published literature outlined in the featured study illustrated that fisetin directly scavenges damaging free radicals in heart cells, reducing oxidative stress and minimizing tissue damage.

  When oxidative stress is controlled, your heart stays healthier and functions more effectively, significantly reducing your risks of long-term cardiovascular conditions.

- **Anticancer properties —** Interestingly, the researchers noted that fisetin helps fight cancer, specifically by activating tumor suppressor pathways through the p53 protein:[4]

  > *"P53 is often referred to as the 'guardian of the genome' because it regulates critical cellular processes, such as DNA repair, cell cycle arrest, and apoptosis (programmed cell death), in response to cellular stress or DNA damage.*

In many cancers, p53 is either mutated or downregulated, leading to uncontrolled cell growth and evasion of apoptosis. Fisetin has been shown to restore or enhance the function of p53, promoting cell cycle arrest and apoptosis in cancer cells."

- **Endothelial function support —** Healthy endothelial cells are crucial for proper circulation, blood pressure control, and overall heart health, and fisetin was shown to help keep endothelial cells functioning optimally, maintaining healthy blood vessel dilation and smooth blood flow.

How to Protect Your Arteries and Improve Cardiovascular Health

If you're dealing with early signs of arterial stiffness or simply want to ensure your cardiovascular system remains strong, tackling the root causes is your best strategy. Here are my recommendations to help you effectively improve your heart health naturally:

1. **Boost your fisetin intake through diet —** Start incorporating more fisetin-rich foods into your meals daily. Strawberries, apples, onions, cucumbers, and even persimmons contain significant amounts of this beneficial flavonol. As the prior studies have shown, increasing your fisetin intake will help reduce the risk of artery calcification, as well as lower inflammation, and improve overall heart health.

2. **Cut out ultraprocessed foods from your life —** Avoiding ultraprocessed foods, especially those high in linoleic acid (LA) is one of the most effective steps to protect your cardiovascular system.

   These synthetic products directly fuel inflammation and oxidative stress, which are major drivers of artery stiffness. Instead, replace these harmful choices with whole, nutritious foods. Ideally, swap high-LA vegetable oils with healthy fats instead, such as grass fed butter, ghee, or tallow.

For a detailed explanation of the dangers that LA poses to human health, I encourage you to read my study published in Advances in Redox Research.[5] There, I discuss crucial topics, such as LA's effect on cardiolipin, metabolic function, and gut microbiome.

3. **Get moving with regular exercise —** Make exercise a non-negotiable part of your routine. Whether it's biking, swimming, or lifting weights, regular physical activity significantly reduces inflammation and insulin resistance, improving the flexibility and health of your arteries.

   If you are new to exercise, I recommend you start walking. This simple act, done gradually and steadily, is one of the most effective forms of exercise anyone can do. Best of all, it's an exercise that can't be overdone. For an in-depth look at the benefits of walking, read "**The Benefits of Walking — How to Get More Steps in This Summer**."

4. **Lose excess weight —** In relation to the previous point, excess weight leads to plaque buildup in your arteries, thus restricting blood flow to your heart. Ultimately, this affects your other organs, too, as they won't get enough blood. To help you tackle the root cause of obesity, read "**Study Challenges the Current Definition of Obesity**."

5. **Boost your vitamin K2 intake —** This nutrient serves as your body's master regulator for calcium distribution, ensuring that it supports important functions instead of calcifying your arteries. That said, I recommend boosting your K2 intake via fermented foods, such as natto and homemade fermented veggies. Certain cheeses, such as Munster, Gouda, and Brie, are also rich in vitamin K2.

Frequently Asked Questions (FAQs) About Fisetin and Vascular Calcification

Q: What is vascular calcification, and why is it harmful?

A: Vascular calcification occurs when calcium builds up in artery walls, making them stiff and less flexible. This condition increases the risk of hypertension, heart attacks, and strokes, especially prevalent among adults over age 60.

Q: How can fisetin help prevent vascular calcification?

A: Fisetin, a naturally occurring flavonol found in strawberries, apples, and onions, prevents artery calcification by activating the enzyme DUSP1. This enzyme inhibits harmful signals (specifically the p38 MAPK pathway) that otherwise lead to hardened arteries.

Q: Who would benefit most from increasing fisetin intake?

A: Individuals with conditions like kidney disease, diabetes, or those experiencing excessive vitamin D intake can gain cardiovascular benefits by regularly consuming fisetin-rich foods or supplements.

Q: Beyond cardiovascular health, what other health benefits does fisetin provide?

A: Fisetin supports overall health by improving cholesterol and triglyceride levels, enhancing insulin sensitivity, lowering blood pressure, reducing oxidative stress, and exerting anticancer effects by activating the p53 tumor suppressor pathway.

Q: What dietary and lifestyle changes can I make to improve cardiovascular health?

A: To protect your heart and arteries, incorporate more fisetin-rich foods (like strawberries, onions, apples), eliminate ultraprocessed foods, increase physical activity, manage body weight, and consume vitamin K2-rich foods like fermented vegetables and specific cheeses (Gouda, Brie, and Munster).

Sources and References

- [1] StatPearls, Coronary Artery Calcification, November 8, 2024
- [2] Aging, 2025, Vol. 17, No. 4 (Archived)
- [3, 4] Acta Scientific Nutritional Health 9.4 (2025): 84-103
- [5] Advances in Redox Research Volume 15, June 2025, 100128