Every year, more than a million Americans are struck down by a heart attack or stroke. For many, sudden death will be their first—and last—symptom of undetected vascular disease. Those lucky enough to survive often face invasive procedures like angioplasty and coronary bypass surgery, followed by a lifetime of curtailed physical activity and costly heart medications.

If you trust your vascular health to mainstream doctors, you may be gambling with your life. Although cardiovascular disease remains the nation’s number-one killer, American medicine prioritizes heart disease treatment rather than prevention. Sadly, it has become far more profitable to treat heart disease than to prevent it.

Fortunately, natural strategies that can help avert life-threatening heart attacks and strokes are readily available today. One of the most promising heart-protective agents to emerge in recent years is *pomegranate*. Packed with unique antioxidants that guard the body’s endothelial cells against free-radical assault, pomegranate has been shown to prevent—and even reverse—cardiovascular disease.

Research also shows that pomegranate can stop the progression of deadly prostate cancer. And scientists are now exploring pomegranate’s potential in averting ailments ranging from diabetes to Alzheimer’s disease, as well as its role in supporting skin, joint, dental, and liver health.

In this article, we examine the growing volume of research that attests to pomegranate’s myriad health-promoting properties—particularly its role in safeguarding the delicate endothelial cells that line blood vessels and are so critical to preserving optimal vascular function in aging adults. > > >
POMEGRANATE: POWERFUL SUPPORT FOR CARDIOVASCULAR HEALTH

Approximately 71 million Americans suffer from cardiovascular diseases such as hypertension (high blood pressure), coronary artery disease, a history of stroke, or peripheral vascular disease (impaired blood flow to the extremities). Atherosclerosis—a disease of the blood vessels, characterized by inflammation, vascular endothelial cell dysfunction, and impaired nitric oxide production—is a major component of cardiovascular disease.

In both laboratory and clinical studies, pomegranate shows great promise in averting the numerous pathological changes associated with cardiovascular disease. Scientists believe pomegranate works through several mechanisms to fight cardiovascular disease by:

- reducing oxidative stress
- supporting the synthesis and activity of nitric oxide
- inhibiting the oxidation of potentially harmful LDL (low-density lipoprotein).

Reducing oxidative stress and inflammatory damage in blood vessels is a well-documented way to lower the risk of cardiovascular disease, both known and undetected. Mounting evidence suggests that compounds in pomegranate known as punicalagins are cardioprotective by virtue of their powerful antioxidant and anti-inflammatory effects.

In one study, for example, pomegranate juice outperformed numerous other potent antioxidants—grape juice, blueberry juice, red wine, vitamin C, and vitamin E, among others—in "quenching" the damaging effects of free radicals on cell membranes. While all the antioxidant nutrients tested effectively prevented the overgrowth of undesirable muscle cells in blood vessel walls—a factor contributing to elevated blood pressure—pomegranate juice was by far the most effective of all.

Supporting the action of nitric oxide is another way to protect the cardiovascular system. Nitric oxide exerts many essential antioxidant and anti-inflammatory effects in the body, including scavenging certain reactive oxygen species, preventing LDL oxidation, deterring the adhesion and aggregation of blood cells and platelets along the endothelial cell lining, and inhibiting the proliferation of vascular smooth muscle cells. Together, these effects help retard the progression of atherosclerosis. When scientists tested pomegranate against other antioxidants, they found that it helped enhance the biological actions of nitric oxide, thus conferring significant cardioprotection.

Preventing dangerous LDL oxidation is also crucial to protecting the blood vessels of the heart. Oxidized LDL can severely damage cardiovascular health by injuring cells that line the coronary arteries, leading to inflammation and narrowing that can precipitate a heart attack. LDL oxidation also reduces the activity of enzymes that produce nitric oxide in those blood vessels, thus preventing them from responding normally to changing demands for blood flow. When scientists treated human coronary artery cells with pomegranate juice, they discovered a dramatic correction in levels of nitric oxide production. This correction is likely to be beneficial in preventing complications of blood vessel disease, including heart attacks.

Just as water flowing rapidly down a canyon gradually erodes the canyon walls and stirs up residues, blood flowing under high pressure or disturbed by narrowed arteries can damage blood vessel walls, increasing oxidative damage and worsening atherosclerosis. A recent Italian study found that pomegranate juice concentrate reduced oxidant-related cellular changes in blood vessel cells exposed to high shear stresses, such as those produced by disturbed blood flow.
flow. The juice also increased nitric oxide production, further protecting the cells. After demonstrating these effects in cell cultures, the scientists administered pomegranate juice to mice with elevated cholesterol levels, and found that they could markedly impede the progression of atherosclerosis. These exciting findings suggest that the dangerous effects induced by perturbed shear stress can be reversed by chronic administration of pomegranate juice.

**POMEGRANATE MAY REVERSE ATHEROSCLEROSIS**

Human studies of pomegranate juice have demonstrated even more dramatic effects, showing that pomegranate may actually reverse atherosclerosis. Israeli scientists studied patients with narrowing of their carotid arteries as a result of atherosclerosis. The carotid arteries in the neck are responsible for more than 80% of blood flow to the brain, and narrowing of these major vessels is a major risk factor for stroke. Among patients given daily pomegranate juice supplements (providing 78 mg of punicalagins) for one year, atherosclerotic lesions in the common carotid artery decreased by 35% in size, while actually growing by 9% in a control group. Thus, pomegranate reversed existing atherosclerosis, which continued to worsen in those who did not consume pomegranate. Blood analysis showed that total antioxidant activity increased 130% in the pomegranate juice group, compared to before-treatment values. Finally, the participants' systolic blood pressure fell by an impressive 21% after one year of pomegranate juice supplementation.

The same Israeli scientists showed that this blood pressure reduction from drinking as little as 2 ounces of pomegranate juice daily (providing 78 mg of punicalagins) was due to decreased activity of angiotensin converting enzyme (ACE). This is a tremendously important finding, since drugs that inhibit ACE activity are commonly used to treat hypertension. Further, the study raises the possibility that pomegranate juice may help patients avoid having to take such drugs.

A study from the California-based Preventive Medicine Research Institute examined the effects of pomegranate juice in human patients with established coronary heart disease. Forty-five patients with coronary heart disease and cardiac ischemia (insufficient blood flow to the heart muscle) were randomly assigned to drink 8 ounces of pomegranate juice or a placebo beverage daily. At the onset and conclusion of the three-month study, scientists measured the participants' blood flow to the heart muscle, both at rest and during stress. Before administration of pomegranate juice, both groups showed the same amount of stress-induced ischemia. At the end of three months, however, the pomegranate group demonstrated a significant improvement in stress-related ischemia, indicating more optimal blood flow to the heart muscle. By contrast, stress-related ischemia worsened in the placebo group. Because these effects could not be attributed to changes in the patients' weight, blood sugar, or cardiac medications, it appears that daily consumption of pomegranate juice alone improved stress-induced ischemia in these patients.

Its effects in supporting healthy blood pressure, ensuring optimal blood flow, and preventing and reversing atherosclerosis make pomegranate an essential nutrient in every heart health program.

### POMEGRANATE COUNTERS DIABETES AND METABOLIC SYNDROME

In addition to its diverse cardio-protective effects, pomegranate may have profound benefit for people with diabetes and the pre-diabetic condition known as metabolic syndrome.

To start with, pomegranate components appear to lower blood sugar levels immediately following a meal, according to research from Australia. Scientists there who studied obese rats with type II diabetes-induced damage. Pomegranate helps lower after-meal blood sugar levels and protects the cardiovascular system from diabetes-induced damage.

Pomegranate may help patients avoid having to take such drugs. Pomegranate offers abundant benefits for the cardiovascular system by preventing damage to arterial walls, promoting healthy blood pressure levels, improving blood flow to the heart, and preventing or reversing atherosclerosis. Pomegranate may benefit people with diabetes and those at risk for the disease. Pomegranate helps lower after-meal blood sugar levels and protects the cardiovascular system from diabetes-induced damage.

Pomegranate may fight the degeneration of joint tissue that leads to painful osteoarthritis, and may protect the brain against oxidative stress-induced changes that can lead to Alzheimer's disease. Pomegranate extracts—alone or in combination with the herb gotu kola—help kill the bacteria that contribute to dental plaque, while helping to heal gum disease. Pomegranate also appears to protect the health of the skin and liver.

The health benefits of pomegranate can be conveniently obtained through the use of low-cost, concentrated juices and extracts.
diabetes found that oral administration of pomegranate extract markedly lowered the animals’ blood sugar levels after a meal, while having minimal effect on the blood sugar levels of animals that had not eaten. This exciting finding suggests that pomegranate extracts block the breakdown of sucrose (table sugar) in the intestine by inhibiting alpha-glucosidase, an enzyme that breaks down sugars. This action could help prevent sugars from being absorbed, thus lessening the abrupt after-meal spike in blood sugar that is so damaging to diabetics.

Diabetes is associated with numerous detrimental changes that impair the function of heart tissue. These include increased levels of non-functional fibrous tissues and increased accumulation of triglycerides within the heart muscle itself. Australian researchers recently found that diabetic rats that were given pomegranate extract for six weeks greatly reduced the amount of non-functioning fibrous tissue in their hearts, while long-term pomegranate supplementation helped improve abnormal cardiac lipid metabolism.

Diabetes is associated with increased oxidative stress and the development of atherosclerosis. Pomegranate’s antioxidant power and ability to fight atherosclerosis led Israeli researchers to examine the effects of pomegranate juice on inflammatory cells in diabetic rats. They compared the antioxidant effects of pomegranate juice to those of white grape juice on macrophages, the immune cells that stimulate inflammation in arterial walls as the result of oxidative stress. Just 10 days of pomegranate juice consumption greatly decreased macrophage oxidant levels and increased cellular antioxidant levels, while the animals fed white grape juice demonstrated exactly the opposite effects.

The Israeli researchers then proceeded to examine the effects of pomegranate juice on the blood and macrophages of human diabetics. The subjects received 50 milliliters (1.69 fluid ounces) of pomegranate juice daily (providing 78 mg of punicalagins) for three months, and their blood and macrophage status was compared to that of healthy controls. Not surprisingly, the diabetics had much higher measures of tissue oxidative damage compared to controls. However, dramatic improvement was found at the three-month mark in the pomegranate-treated group, which recorded a 56% reduction in serum lipid peroxides, an indicator of damaging lipid peroxidation. Similarly powerful effects were seen on oxidant levels in the patients’ macrophages—pomegranate helped reduce cellular oxygen radicals by 71%, while increasing cellular antioxidants by 141%! Perhaps of greatest importance to preventing atherosclerosis and heart disease, pomegranate-supplemented subjects had a 39% reduction in their macrophages’ uptake of oxidized LDL—the deadly fat-protein compound that triggers vascular disease.

Iranian researchers took the next logical step, evaluating the effects of pomegranate juice on the mix of blood fats and cholesterol in diabetic patients. Twenty-two diabetics with elevated blood lipids consumed 40 grams (1.41 fluid ounces) per day of concentrated pomegranate juice for eight weeks, when blood lipid levels were measured again. Total cholesterol and LDL levels decreased substantially, demonstrating that pomegranate juice markedly reduces cardiac risk factors in diabetic patients.

Pomegranate thus offers an array of protective benefits for people with diabetes, from preventing aberrantly high blood sugar levels to protecting the heart against the potentially devastating cardiovascular consequences of diabetes.

**POMEGRANATE MAY PREVENT AND SLOW PROSTATE CANCER**

Prostate cancer is the most common malignancy and second leading cause of cancer death among American men. Scientists are rapidly learning that the growth of prostate cancer can be prevented by proper dietary supplementation, especially with antioxidant and anti-inflammatory agents. Several of the pure chemical compounds found in pomegranate—including ellagic acid and luteolin—work together synergistically to inhibit cancer cell growth.

Results of a recent laboratory study underscore the dramatic protective effects of antioxidants in pomegranate. When human prostate cancer cells were exposed to pomegranate fruit extract, they immediately began to produce substances that led to their own death. This process of programmed cell death, called apoptosis, is vital to the body’s normal regulation of potentially cancerous tissue. In another experiment, oral administration of pomegranate fruit extract greatly inhibited tumor growth in mice. This correlated with a dramatic decline in blood levels of prostate-specific antigen (PSA), which doctors use to monitor prostate cancer progression. This led the study authors to conclude that pomegranate juice may be useful in preventing prostate cancer, as well as in slowing the progression of existing prostate cancer.

An even more detailed study of the effects of various pomegranate components was conducted by German investigators, who were interested in finding ways to slow or reverse prostate cancer growth. The German scientists studied several different types of prostate cancer, including both those that are dependent on andro-
gens (male hormones) and those that are not. Rates of growth and reproduction were slashed in all prostate cancer cell types tested, regardless of whether the pomegranate extract was derived from the seeds, juice, or oils of the fruit.

Moreover, the researchers determined that the pomegranate extracts worked via several mechanisms simultaneously to slow cancer cell growth—in sharp contrast to chemotherapy drugs, which work through only a single mechanism. Over time, cancer cells can develop resistance to chemotherapy (that is, failure to respond to a previously effective agent), leading some scientists to propose that anti-cancer agents that work by multiple mechanisms may offer greater treatment efficacy.

Finally, the German investigators were able to show that the cell-killing and growth-inhibiting effects of the pomegranate extracts were limited to cancerous cells—normal prostate cells were much less significantly affected. If these findings hold true in men with prostate cancer, pomegranate may help kill cancerous cells while leaving healthy tissues intact. Convincing data from human clinical trials now support pomegranate extract's ability to fight prostate cancer. Doctors at UCLA investigated whether pomegranate could slow the rate of cancer progression in men who had undergone surgery or radiation treatment for prostate cancer. The subjects drank 8 ounces of pomegranate juice daily (providing 280-375 mg of punicalagins), and their PSA doubling times were compared before and after treatment. A short PSA doubling time indicates rapid growth of residual prostate cancer, while a longer doubling time signifies slower tumor growth. Daily intake of pomegranate juice increased mean PSA doubling time from 15 months at baseline to 54 months in 80% of the men post-treatment—a nearly fourfold jump. Even more remarkable, when blood serum from these men was obtained after treatment and applied directly to prostate cancer cells in culture, cell growth rates plummeted and cell death rates soared. The cells also increased their ability to withstand oxidative stress.

In sum, these important findings suggest that pomegranate may help prevent the occurrence of prostate cancer, while slowing the growth and spread of existing prostate cancers.

PROMISING NEW APPLICATIONS FOR POMEGRANATE

Preliminary research findings suggest that, in addition to its potentially lifesaving benefits for heart, diabetes, and cancer patients, pomegranate may confer a multitude of other health-promoting effects in the body, from alleviating the pain and discomfort of arthritis to supporting optimal brain, dental, skin, and liver health.

PREVENTING OSTEOARTHRITIS

Inflammation destroys joint-cushioning cartilage, inflicting tremendous pain and disability on the estimated 21 million Americans who suffer from osteoarthritis. By severely curtaining physical activity, osteoarthritis can initiate a vicious cycle in which its sufferers become ever more sedentary (and often overweight), triggering additional health problems. Pomegranate's ability to break the cycle of inflammation and tissue damage spurred scientists at Case Western University to explore whether it could protect joint cartilage from inflammation in patients with osteoarthritis. In an in-vitro experiment, they first treated cartilage from osteoarthritis patients with pomegranate fruit extract, and then stimulated the tissue with interleukin-1 beta, a potent inflammatory mediator. The scientists then measured the extent of cartilage destruction and production of inflammatory molecules in the tissue samples.

Pretreatment with pomegranate fruit extract inhibited enzymes that break down cartilage, and sharply reduced the volume of inflammatory products released from the tissue. The researchers concluded that pomegranate fruit extract "may inhibit cartilage degradation in osteoarthritis and may also be a useful nutritive supplement for maintaining joint integrity and function."

AVERTING ALZHEIMER'S

In 2006, scientists at California's Loma Linda University reported groundbreaking research on a potential role for pomegranate juice in averting Alzheimer's disease.

The researchers knew that antioxidant polyphenols from other fruits and vegetables have protected brain cells in various animal models, and that pomegranate juice itself had been shown to limit brain damage in mice that suffered experimentally induced strokes. Since oxidation is thought to produce the Alzheimer's protein known as amyloid beta, the Loma Linda team decided to test their hunch that pomegranate juice could put a stop to amyloid-beta accumulation. They also explored the more radical notion that pomegranate juice alone would have a detectable effect on cognitive abilities, using a "water maze task" that tests animals' ability to accurately and quickly make their way out of a water-filled labyrinth.

The researchers' intuition was rewarded, as mice with Alzheimer's-like disease that were given pomegranate juice from 6 to 13 months...
of age accumulated about 50% less amyloid beta than control mice. The juice-treated animals outperformed control animals, exiting the water maze 35% faster than the control group.\textsuperscript{28} The authors declared their study to be "the first to show beneficial effects (both behavioral and neuropathological) of pomegranate juice in an animal model of Alzheimer's disease."

**Preserving Dental Health**

Emerging research suggests that pomegranate holds promise in promoting optimal dental health.

A recent study indicates that pomegranate fights dental plaque, the yellowish buildup of microorganisms on the teeth that can lead to cavities and gum disease. Scientists found that pomegranate extract helped kill microorganisms isolated from the dental plaque of healthy adults. Additionally, rinsing the mouth for one minute with a mouthwash containing pomegranate effectively reduced the amount of microorganisms cultured from dental plaque.\textsuperscript{23}

Thai researchers studying gum disease discovered that pomegranate extracts, when combined with extracts of another traditional herb called gotu kola (Centella asiatica), enhance gum healing following dental scaling and root planing (deep cleaning between the gums and the teeth down to the roots).\textsuperscript{34} Such procedures are commonly done to restore the vital connection between the gums and tooth roots, in the absence of which bacterial infection, decay, and tooth loss may occur. By simply implanting tiny chips impregnated with pomegranate and gotu kola extracts into the gap between the gum and tooth root, the scientists were able to reduce the size of the gap and increase gum and tooth attachment.\textsuperscript{34} A later study by the same group\textsuperscript{35} showed that treated patients also had less gum bleeding and considerably lower levels of interleukin-1 beta and interleukin-6, two inflammatory cytokines linked to cardiovascular disease.\textsuperscript{30,37}

Maintaining optimal dental health is not only important for preserving the appearance and function of the teeth, but also for protecting against cardiovascular disease. Scientists now know that the chronic inflammation from periodontal disease is closely tied to the worsening of cardiovascular diseases.\textsuperscript{38,39}

**Protecting Skin Health**

New evidence suggests that pomegranate extracts may protect skin against two important factors that degrade its health and appearance over time: accumulating damage inflicted by ultraviolet light, and a decreased ability to regenerate or heal.

Excessive exposure to ultraviolet B (UVB) radiation has numerous adverse health effects on skin, including redness, hyperpigmentation, immune suppression, and photoaging. Research shows that pomegranate extracts protect human skin cells against UVB-induced changes by modulating the biochemical pathways that can provoke cancer and inflammation.\textsuperscript{28}

Pomegranate also protects against ultraviolet A (UVA) radiation, or the damaging, long-wave rays that penetrate deeply into the skin to promote wrinkles and both benign and malignant tumors. This is an important finding, as many

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**Dosing Strategies to Obtain Optimal Benefits from Pomegranate**

Given the wide array of health benefits associated with pomegranate juice and extracts, the question is not whether to supplement with pomegranate, but rather how much offers optimal benefits.

Choosing the ideal dose of pomegranate poses a challenge, as different preparations may contain vastly different amounts of important constituents such as polyphenols—powerful antioxidants that underlie many of the benefits of plant-derived therapies. Many of the clinical studies examining pomegranate's effects in relation to certain disease states (such as cardiovascular disease and prostate cancer) utilized juices and extracts that were not standardized for their polyphenol constituents—making it difficult to ascertain the most efficacious pomegranate formulation and dosage.

Life Extension conducted an extensive review of the scientific literature in order to identify the most beneficial phytochemicals in pomegranate juices and extracts, and the dosages required for maximum efficacy. Punicalagins were identified as the most clinically important pomegranate phytochemicals. Punicalagins are highly bioavailable and possess antioxidant activity that greatly exceeds that of many plant-derived antioxidants.\textsuperscript{45,46} In the most significant clinical studies to date, a daily dose of 78 mg of punicalagins yielded such remarkable benefits as reversing atherosclerosis, reducing high blood pressure, and preventing the adverse cardiovascular consequences of diabetes.\textsuperscript{28,44} Moreover, an important clinical study demonstrated that 280-375 mg of punicalagins per day halted the progression of prostate cancer in men who had failed conventional therapy.\textsuperscript{45} Life Extension thus recommends 78 mg of punicalagins per day for cardiovascular protection, and 280-375 mg of punicalagins daily to promote prostate health.

To provide consumers with the maximum possible health benefit, Life Extension has identified several pomegranate products—including pomegranate juice concentrate and encapsulated pomegranate extract—that are standardized to provide an abundant source of punicalagins.
commercially available sunscreens offer only limited UVA protection. When human skin cells were incubated with pomegranate extracts, they were better able to withstand UVA-induced damage. Scientists believe that pomegranate modulates cellular pathways to confer protection against ultraviolet rays. As skin ages, it often becomes thinner and slower to heal. A promising new study demonstrates that pomegranate extracts may help avert age-related changes in the skin. Investigators applied various pomegranate constituents to skin cells derived from the epidermis (outermost layer) and dermis (layer underneath the epidermis). Pomegranate seed oil extract promoted regeneration and thickening of the skin's epidermis, while an extract of the peel promoted repair of the dermis. Pomegranate extracts may thus help promote healing and regeneration of skin tissues.

ENSURING LIVER HEALTH

As one of the body's most metabolically active organs, the liver is responsible for breaking down and rendering harmless a multitude of chemicals, toxins, drugs, and hormones. Performing this daily task requires a prodigious amount of antioxidants, and new findings suggest that pomegranate is a rich source of liver-protective antioxidants.

In the laboratory, pomegranate extract effectively quenched a variety of dangerous reactive oxygen species, including superoxide, hydrogen peroxide, and hydroxyl radicals. When mice were given pomegranate before exposure to an oxidative stressor that normally causes liver toxicity, they were significantly protected and maintained high levels of crucial liver antioxidants. Pomegranate extract helped protect the animals against pathological changes that accompany liver damage, such as degeneration, fatty changes, and necrosis (tissue death). Pomegranate extract thus confers everyday benefits for liver health.


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