LE Magazine July 2007

REPORT

Reversing Atherosclerosis Naturally

By Dale Kiefer

Scientists have discovered a natural ingredient derived from a species of melon that has been shown to reverse signs of atherosclerosis in aging blood vessel walls. This nutritional supplement is able to boost levels of the body's most powerful antioxidant defense enzyme, superoxide dismutase (SOD).

A comparison of two recently-published clinical trials shows that this natural supplement not only reversed signs of atherosclerosis in human blood vessel walls, but that it did so better than a leading multibillion dollar prescription statin drug. Just eight months ago, Life Extension members were enlightened to the ability of pomegranate to reverse signs of atherosclerosis. This specialized melon extract, together with pomegranate, offers aging humans a powerful new weapon in the battle to reduce the risk of heart attack and stroke by restoring healthy function to aging arteries.

ATHEROSCLEROSIS: THE SILENT ENEMY

Even people who have no symptoms of cardiovascular disease may be developing silent, progressive atherosclerosis as they grow older. Derived from Greek words meaning "hard paste", atherosclerosis is a chronic inflammatory condition affecting the interior of the arteries, which become stiff, clogged, and dysfunctional. Consisting of cholesterol, cellular debris, and other components, atherosclerotic plaque blocks the flow of vital oxygen and nutrients to tissues throughout the body.

Atherosclerosis is believed to begin when the delicate inner arterial lining—the endothelium—is damaged and becomes dysfunctional; possibly beginning as early as childhood.[1] Sticky, fatty substances, such as low-density lipoprotein (LDL), fibrinogen, and triglycerides adhere to the endothelial lining and begin to trap other components, including calcium. The plaque may cause a rupture in the arterial wall, allowing a blood clot to form. Clots can block local blood flow completely, or they may break free and cause dangerous blockages elsewhere. When such blockages occur in the vessels supplying the heart, for instance, a heart attack occurs. Deprived of oxygen, cardiac muscle dies quickly; when a blockage affects the blood supply to the brain, a stroke may result.

THE SUPEROXIDE RADICAL AND ENDOTHELIAL DYSFUNCTION: DANGER TO AGING ARTERIES

Damage to cells that line our arteries is a critical initiating event in atherosclerosis, a leading cause of heart attack and stroke. As the delicate endothelium (inner arterial wall) becomes weakened, toxic substances circulating in the blood pass through the endothelial cell layer and become oxidized. This oxidation induces chronic inflammation that leads to thickening of the blood vessel wall and subsequent atherosclerosis. Depending on a person's individual risk factors (such as poor diet, lack of exercise, high homocysteine, high levels of inflammation, smoking, high blood pressure, and the aging process itself), oxidized lipids continue to accumulate in the endothelium, and the atherosclerotic process accelerates.

Scientists know that oxidative stress is a crucial, causal factor in endothelial dysfunction, which itself is a key initiating event for abnormal blood vessel wall thickening and atherosclerosis. Cutting-edge research shows that superoxide dismutase, the body's most important antioxidant defense enzyme, plays an important role in maintaining healthy endothelial function by quenching dangerous superoxide radicals.

The superoxide radical inactivates the crucial vasodilator nitric oxide and compromises endothelial function.[2,3] Furthermore, rapid improvement in endothelial function and regression of atherosclerosis is associated with reduction of the dangerous superoxide radical in the arterial wall.[4] New research shows that the superoxide radical plays a role in hypertension associated with kidney disease, oxidative vascular stress associated with accelerated atherosclerosis in diabetes, and heart failure in humans.[5-8]

STATIN DRUGS AND ATHEROSCLEROSIS

In the past, numerous studies have examined the effects of cholesterol-lowering statin drugs on atherosclerosis using proven ultrasound technology that measures for pathological thickening (intima-media thickness, or IMT) of the aging blood vessel wall. Interestingly, most large statin drug trials show only slowing of progression, rather than regression of atherosclerosis, as measured with this highly-respected technology.

For example, the 1998 REGRESS study showed slowing of progression of atherosclerosis, but not regression, with the statin drug pravastatin (Pravachol®).[16] The 1995 KAPS study also showed that

pravastatin produced a significant slowing of progression of atherosclerosis, but not regression.[17] Although the ASTEROID study showed evidence of regression of atherosclerosis in high-risk patients, this study used the very potent statin drug, rosuvastatin (Crestor®).[18] Another head-to-head comparative study (ARBITER) showed slight regression of IMT with a high dose of the potent drug atorvastatin (Lipitor®).[19] However, many "in the know" unbiased medical experts have raised questions about the results of this study, commenting on data handling and methodological issues used by the Pfizer-sponsored investigators.

Recently, a clinical trial published in the influential Journal of the American Medical Association indicated that the cholesterol-lowering statin drug, Crestor® (rosuvastatin), is capable of slowing the progression of silent subclinical atherosclerosis. As expected, over the course of two years, a high dose (40 mg) of the very potent statin drug Crestor® significantly lowered harmful lipid levels. But it merely slowed or halted atherosclerosis progression—it did not produce regression. In the investigators' own words: "***Rosuvastatin [Crestor®] did not induce disease regression."***[20]

In sharp contrast, a nutritional supplement derived from a unique species of melon was shown recently to not only halt IMT progression in apparently healthy adults, but to significantly reverse its progression over the course of two years.[21]

CONVENTIONAL APPROACHES TO ATHEROSCLEROSIS

A variety of genetic and environmental factors play key roles in the development of atherosclerosis, but the understanding of this complex process is still evolving in mainstream medicine. There's no question, however, about a number of all-too-common risk factors. These include: obesity, inactivity, diabetes, high blood pressure, insulin resistance, high lipid levels, low HDL, elevated C-reactive protein, smoking, and a family history of heart disease.

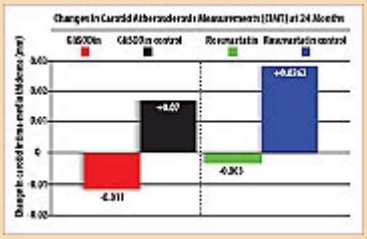
Mainstream medicine is just beginning to recognize atherosclerosis-associated chronic inflammation, perpetuated by oxidative stress and detectable by biochemical markers that indicate ongoing inflammation and oxidative damage.[9,10]

Age alone is a major risk factor for atherosclerosis.[11] This should come as no surprise, since aging is associated with increasing inflammation, and inflammation is associated with atherosclerosis development.[12-14] Efforts to fight inflammatory and oxidative processes have been shown to reverse some of the early damage that sets the stage for atherosclerosis. Life Extension advocates a comprehensive approach to averting cardiovascular disease that includes addressing the many implicated triggers of endothelial dysfunction and atherosclerosis, such as high homocysteine, low levels of omega-3 fatty acids, and elevated fibrinogen levels.[15]

Current mainstream medical treatments for atherosclerosis generally focus on controlling only a few of the multiple identified causes of atherosclerosis. Life Extension advocates that members aggressively monitor and treat ALL the known causes of endothelial dysfunction and atherosclerosis as part of a comprehensive strategy to minimize the risk of developing our nation's number one killer, cardiovascular disease.

ORAL SOD REVERSES IMT

Impressive new research indicates that a patented form of the natural antioxidant superoxide dismutase (SOD) significantly reverses the IMT thickening process, long before atherosclerosis becomes life-threatening.[21] Known as the "enzyme of life" when it was first discovered in the late 1960s, SOD is considered the body's most important antioxidant defense enzyme. Its powerful benefits include the ability to activate and regenerate other key native antioxidants, such as glutathione peroxidase and catalase. By itself, SOD disarms the extraordinarily reactive superoxide radical. It accomplishes this feat with lightning speed, thus preventing superoxide from wreaking havoc with important biological tissues, including the delicate vascular endothelium.



Comparison of two years of treatment with bioavailable SOD (GliSODin®) versus rosuvastatin (Crestor®) on carotid artery atherosclerosis in two separate studies. Carotid artery intima-media thickness decreased significantly in those who received GliSODin®. Rosuvastatin halted

atherosclerosis progression, but did not produce a statistically significant reversal of disease.

Both studies showed that control patients (receiving neither GliSODin® or rosuvastatin)

experienced serious progression of atherosclerosis at two years.[20,21]

Scientists have long sought a way to boost levels of SOD as a natural means of combating the oxidative damage that lies at the root of so many degenerative disease processes, including atherosclerosis.[21] Noting that certain varieties of cantaloupe had an exceptionly long shelf life, food scientists found that these melons provided an exceptionally rich source of SOD. Still, this SOD remained stubbornly unavailable to the body when consumed orally. Until, that is, French researchers pioneered a method to "cloak" a natural melon-derived SOD molecule with gliadin (a simple protein derived from wheat), protecting it from the harsh acidic environment of the stomach and intestines long enough for the bioactive SOD enzyme to be absorbed intact into the bloodstream.[22,23]Dubbed GliSODin®, this compound has been thoroughly documented to be a particularly potent orally bioavailable form of SOD. Many competing products purporting to contain SOD are simply ineffective. Without the protection of the gliadin molecule, most SOD supplements are destroyed by the digestive tract long before they can benefit the body, rendering them ineffective as oral supplements.

CLINICAL STUDY CONFIRMS EFFICACY OF GLISODIN® FOR REGRESSION OF ATHEROSCLEROSIS

In a groundbreaking new study, investigators led by Professor Maurice Cloarec from the French National Association for Medical Prevention showed that oral supplementation with GliSODin® was associated with regression of atherosclerosis in middle-aged adults (ages 30-60), as determined by ultrasonography. This finding is especially exciting, in that atherosclerosis progression was not slowed, nor halted, but rather that it was actually reversed.

The scientists began this study by recruiting adults with risk factors for atherosclerosis, including a family history of stroke, elevated blood pressure, elevated blood lipids and blood sugar, and a height-to-weight ratio above normal. Subjects received instruction in following a standardized, heart-healthy, Mediterranean-type diet, and were given counseling regarding lifestyle modifications.

A baseline IMT reading was performed, and assessments were also made of individuals' antioxidant status and blood lipid levels, among other health parameters. All subjects first adhered to a new, healthier diet for one year. At the end of the first year, the scientists documented "minor improvements" in blood pressure, body mass index (BMI), and LDL levels among all subjects. These improvements were attributed to the healthier diet and lifestyle modifications. Subjects' antioxidant status, however, remained poor. Furthermore, subjects' IMT values remained unchanged. Investigators noted that the IMT numbers were, "too high…considering the age of these subjects".[21]

At this point, a total of 34 subjects were randomly divided into two groups. One group continued with the amended diet, while a second group continued the diet while also taking 500 IU of GliSODin® daily. Subjects' progress was then monitored for two additional years. During this phase, parameters such as blood pressure, BMI, and LDL levels remained largely unchanged among all subjects. But about nine months after beginning GliSODin® treatment, significant improvements in antioxidant status were documented in the treatment group. Antioxidants monitored included blood SOD levels and blood glutathione peroxidase levels. Levels of malondialdehyde (a biomarker for oxidative stress[24]) were also documented. The antioxidant status of control subjects, who were not taking the supplement, remained essentially unchanged.

REVERSING ATHEROSCLEROSIS: WHAT YOU NEED TO KNOW

- Atherosclerosis is the major component of cardiovascular disease, the leading killer of Americans.
- Even before clinical signs of atherosclerosis become apparent, it is possible to detect silent disease and monitor disease progression using advanced ultrasound measurement of the intima-media thickness (IMT) of the carotid (neck) arteries. This well-documented measure of atherosclerosis is associated with general vascular health, and aberrant values help preduct the likelihood of heart attack and stroke.
- An orally bioavailable form of super-oxide dismutase (SOD) has been found to reverse atherosclerosis, as documented by decreased IMT measurements. This bioavailable form of SOD further helps offset atherosclerosis by boosting levels of essential antioxidants in the body.
- Pomegranate juice extract has also demonstrated efficacy as a powerful source of antioxidants. When consumed daily by adults with advanced atherosclerosis, pomegranate juice helped reverse intima-media thickness.

- By including orally bioavaialble SOD with pomegranate juice extract in your daily program, you may help prevent or even reverse the accumulation of deadly atherosclerotic plaque in your arteries.

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ATHEROSCLEROSIS IS REVERSED

About a year and a half after commencing daily supplementation with GliSODin®, measurable decreases in subjects' IMT were detected. Approximately two years after starting GliSODin® supplementation, decreases in IMT values became statistically significant. In dramatic contrast, control subjects not receiving GliSODin® experienced increased IMT values over the same period.[21] There were no reported side effects in either group.

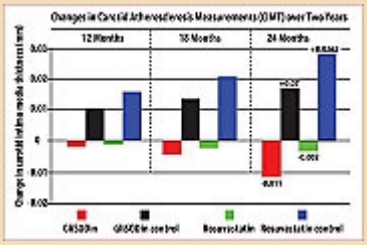
This remarkable study demonstrated that reversal of atherosclerosis in adults with multiple risk factors for future cardiovascular disease is possible through a combination of healthy diet and daily intake of GliSODin® (orally bioavailable superoxide dismutase). These findings were confirmed by monitoring of clinical and biological health parameters, and measurements of carotid IMT. The GliSODin® regimen, "improves, significantly, the anti-oxidant status," noted investigators, *"and diminishes, remarkably, carotid artery IMT."*[21]

It should be noted that these findings echo those of other researchers, who, in previous and subsequent studies, have convincingly demonstrated GliSODin®'s ability to reduce oxidative damage in human volunteers and animal models.[25-27]

POMEGRANATE FIGHTS OXIDATIVE DAMAGE, REVERSES ATHEROSCLEROSIS

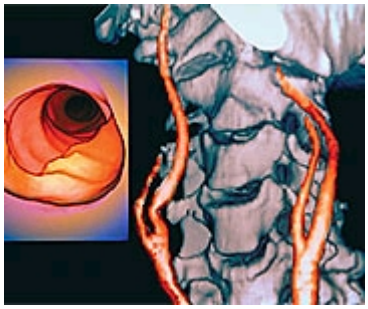
Scientists have recently shown that pomegranate juice offers cardiac health benefits that complement those of GliSODin®. In the past seven years alone, the amount of published research on pomegranate has increased seven-fold over all preceding years in the medical and scientific literature.[40] That's almost certainly because each new study underscores the potential of this fruit to fight cancer and to combat oxidative stress. The latter is of particular importance for atherosclerosis prevention.

Comparison of the effects of orally bioavailable SOD (GliSODin®) versus rosuvastatin (Crestor®) on carotid atherosclerosis (CIMT) over the course of two years. GliSODin® significantly reversed carotid atherosclerosis, and the effects were most pronounced at 24 months. Atherosclerosis did not progress in those receiving rosuvastatin, and it showed a statistically insignificant trend toward reversal. Untreated control subjects experienced dramatic progression of atherosclerosis over the course of two years.[20,21]



In 2004, researchers published the findings of a three-year study on the daily consumption of pomegranate juice (50 mL, or 1.7 ounces) by patients with advanced atherosclerosis.[41] These patients were diagnosed with carotid artery stenosis; a serious condition in which the carotid arteries, responsible for supplying blood to the brain, become noticeably narrowed by buildup of atherosclerotic plaques. Such patients are at increased risk of suffering strokes or other "cerebrovascular accidents". In this study, common carotid IMT *increased* by ***9%*** within one year in the non-supplemented control group. Remarkably, patients drinking pomegranate juice experienced a whopping 35% reduction in the IMT score and a 44% improvement in carotid artery blood flow over the same period. Investigators also documented a 21% reduction in systolic blood pressure among the pomegranate juice drinkers. Serum total antioxidant status was increased by an extraordinary 130% after one year of pomegranate supplementation. Additionally, the scientists monitored the status of an enzyme that may protect against the development of atherosclerotic plaque by protecting LDL against oxidative modification. Pomegranate drinkers' levels of this beneficial enzyme increased by 83% after just one year. "For all studied parameters, the maximal effects were observed after one year of consumption," wrote the researchers.[41]

Other researchers from around the globe have obtained similar results when studying pomegranate's ability to rapidly improve volunteers' antioxidant status,[42] to reduce oxidative stress, and to reverse processes that contribute to the promotion and progression of atherosclerosis, including coronary artery narrowing and LDL oxidation.[43-47]



3-D spiral CT scan / angiogram of carotid atherosclerosis.
Plaque attached to the wall of left internal carotid artery, 1cm above the carotidal bifurcation.

CONCLUSION

Atherosclerosis is a serious threat to health. Its progression has been linked to increased risk of heart attack, stroke, atrial fibrillation and dementia, among other potentially fatal conditions. Since it may begin as early as childhood, and aging has been identified as the greatest risk factor for its development, it is vital to combat this arterial-dysfunction disease as early—and as aggressively—as possible. Nature has provided the means to protect ourselves from this insidious threat. By increasing our levels of the natural enzymatic antioxidant, superoxide dismutase (SOD), and by harnessing the potent polyphenol power of pomegranate, scientists have shown that it is now possible to help reverse the course of atherosclerosis—naturally.

INTIMA-MEDIA THICKNESS: ADVANCED DETECTION OF ATHEROSCLEROSIS

For more than a decade, it's been possible to detect atherosclerosis before it becomes clinically apparent. This is especially significant, as it may be difficult to reverse atherosclerosis by the time it becomes symptomatic. And given that atherosclerosis has been associated with everything from an increased risk of early cognitive decline, Alzheimer's disease, and vascular dementia[28,29] to an elevated risk of stroke, metabolic syndrome,[30] abnormal heart rhythm,[31] and heart attack,[32] there is ample reason to identify and thwart this pathological process as early as possible.

Using advanced ultrasound technology, clinicians are able to image structures within the neck's carotid artery to determine the thickness of its "intima-media", or inner/middle layer.[33,34] By measuring initial thickness and any subsequent changes, clinicians can detect the progress of atherosclerosis and map its progression throughout the entire body while it is still "subclinical", or otherwise undetectable.[32,35-37] Carotid intima-media thickness (IMT) is a well-documented and validated measure of atherosclerosis progression, and it is known to be predictive of future cardiovascular health; especially risk of heart attack and stroke.[35,38,39] Common wisdom acknowledges that gorging on bacon double-cheeseburgers can negatively impact this disease process, but as European researchers noted recently, aging itself may be a leading factor influencing carotid intima-media thickness.[21]

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