Major Advance in Intestinal Health

Slash Risk of Deep Vein Thrombosis

Kill Harmful Bacteria in Your Intestinal Tract

Plant Polyphenols That Protect Against Cancer

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Boost Efficacy of Your Probiotic

Metformin Cuts Glaucoma Risk
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<tr>
<th>Product</th>
<th>Retail Price</th>
<th>SUPER SALE Discount Price Per Bottle</th>
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<tr>
<td>Advanced Bio-Curcumin®</td>
<td>$30</td>
<td>$18.23 (four-bottle purchase)</td>
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<tr>
<td>Absorbs up to 7-times better, with added benefits of ginger and turmeric extracts.</td>
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<tr>
<td>Extend-Release Magnesium</td>
<td>$13</td>
<td>$7.88 (four-bottle purchase)</td>
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<td>Provides immediate-release magnesium citrate along with a 6-hour extended-release magnesium for optimal benefits.</td>
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<tr>
<td>AMPK Activator</td>
<td>$48</td>
<td>$29.70 (four-bottle purchase)</td>
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<tr>
<td>Activating AMPK “turns off” many of the destructive factors of aging, enabling cells to return to their youthful vitality. Research shows that the two plant extracts contained in this formula promote AMPK activation.</td>
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<tr>
<td>Super K with Advanced K2 Complex</td>
<td>$30</td>
<td>$18.23 (four-bottle purchase)</td>
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<tr>
<td>Provides two forms of vitamin K2 (1,000 mcg of immediate-release MK-4 and 200 mcg of long acting MK-7), along with 1,500 mcg of K1.</td>
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<tr>
<td>Super Omega-3 EPA/DHA</td>
<td>$32</td>
<td>$15.35 (ten-bottle purchase)</td>
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<tr>
<td>A highly purified Alaskan fish-oil blend plus sesame lignans and olive extract provide essential omega-3 fatty acids and components of a Mediterranean diet.</td>
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<tr>
<td>Two-Per-Day Multinutrient Formula</td>
<td>$22</td>
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<tr>
<td>Compared to formulas like Centrum®, Two-Per-Day has up to 50 times higher potency, unique botanical ingredients plus biologically active B-vitamins and natural vitamin E. Each bottle provides a two month supply—as little as $6.75 a month!</td>
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<tr>
<td>Memory Protect</td>
<td>$24</td>
<td>$14.40 (four-box purchase)</td>
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<td>This new product contains microdoses of lithium and proline-rich polypeptide, which have been found to arrest and (in the case of proline-rich polypeptide) even reverse cognitive decline.</td>
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<tr>
<td>Ultra Natural Prostate</td>
<td>$38</td>
<td>$21.60 (ten-bottle purchase)</td>
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<td>Comprehensive support for an aging prostate gland utilizing extracts from pygeum, nettle, beta-sitosterol, flower pollen, and saw palmetto plus boron and lycopene.</td>
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Customers traditionally take advantage of the SUPER SALE to stock up on a year’s supply of their favorite supplements. To place your order, call 1-800-544-4440 or visit www.LifeExtension.com (SUPER SALE pricing available only to customers in the US, Canada, and England.)

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REPORTS

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Probiotics have become enormously popular supplements. When bacteria-killing phages were added to probiotics in the animal model, there was a 40-100-fold increase in beneficial intestinal flora with huge reductions pathogenic E.coli. Combining probiotics with phages may represent a new standard of intestinal balance.

48 CANCER PROTECTIVE VEGETABLE EXTRACT
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58 ACHIEVING OPTIMAL SELENIUM STATUS
Selenium has long demonstrated cancer prevention potential, but controversy exists over what are ideal forms of this mineral. A continuous stream of data reveals how different selenium compounds exert their own unique effects in impeding malignant transformation.

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PQQ, or pyrroloquinoline quinone, can improve heart and brain health, and possibly slow the progression of aging. Researchers have found that PQQ has potential to decelerate the deterioration of joints in rheumatoid arthritis and osteoarthritis, exerting a protective effect in the joints.

86 METFORMIN REDUCES THE INCIDENCE OF OPEN-ANGLE GLAUCOMA
Glaucoma is the second leading cause of blindness in the world. Scientists have discovered persuasive data that the AMPK-activating drug metformin may help protect against glaucoma. Life Extension encourages those at risk to speak to their doctor about these new findings.

DEPARTMENTS

7 AS WE SEE IT: GREATEST THREAT TO LONGEVITY
According to the Surgeon General, deep vein thrombosis may cause up to 180,000 deaths each year. Those who spend time sitting are at the highest risk. Researchers have developed a nondrug approach for the prevention of deep vein thrombosis, utilizing two natural compounds that drastically reduce platelet aggregation-and fibrin-induced clots.

19 IN THE NEWS
Vitamin D shortens hospital stays; omega-3 reverses heart damage; drug doubles melanoma survival time; and taurine and magnesium inhibit cardiovascular disease.
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Editorial
Editor-in-Chief • Philip Smith
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Michael D. Ozner, MD, FACC • Jonathan V. Wright, MD, Xiaoxi Wei, PhD

Contributors
Michael Downey • Rita Haven • Garry Messick • Sonia Whitman
Jessica G. Shanta, MD • T.R. Shanta, MD, PhD, FACA

Adverting
Vice President of Marketing • Rey Searles • rsearles@lifeextension.com
National Advertising Manager • Leslie Stockton • 404-347-1755

Vice President of Sales and Business Development
Ron Antriasian • rantriasian@lifeextension.com • 781-271-0089

Circulation & Distribution
Life Extension • 3600 West Commercial Blvd., Fort Lauderdale, FL 33309
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Customer Service: 800-678-8989
Email: customerservice@LifeExtension.com
Wellness specialists: 800-226-2370 • Wellness email: wellness@LifeExtension.com

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John DeLuca, MD, operates the Life Extension Clinic in Caracas, Venezuela. He is the first physician in Caracas to specialize in anti-aging medicine.

Ricardo Bernales, MD, is a board-certified pediatrician and general practitioner in Chicago, IL, focusing on allergies, bronchial asthma, and immunodeficiency.

Mark S. Bezzek, MD, FACR, FAARM, FAAAEM, is board-certified in internal medicine, emergency medicine, and anti-aging/regenerative medicine. He is the director of Med-Link Consulting, which specializes in bioidentical hormone replacement therapy, natural alternatives, anti-aging, and degenerative diseases. He holds US patents for a multivitamin/mineral supplement, an Alzheimer’s/dementia compilation, and a diabetic regimen.

Anna M. Cabeca, DO, FACC, ABAARM, is a board-certified plastic surgeon, was medical director of the microsurgical successful menopause and age-management medicine.

John M. Catz, MD, DO, FACOG, ABAM, is a board-certified plastic surgeon, was medical director of the microsurgical research and training lab at Southern Baptist Hospital in New Orleans, LA, and currently practices in Sun Valley, ID.

William Davis, MD, is a preventive cardiologist and author of Wheat Belly: Lose the Wheat, Lose the Weight and Find Your Path Back to Health. He is also medical director of the online heart disease prevention and reversal program, Track Your Plaque (www.trackyourplaque.com).

Martin Dayton, MD, DO, practices at the Sunny Isles Medical Center in North Miami Beach, FL. His focus is on nutrition, aging, chelation therapy, holistic medicine, and oxidative medicine.

John DeLuca, MD, DC, is a 2005 graduate of St. George’s University School of Medicine. He completed his internal medicine residency at Monmouth Medical Center in Long Branch, NJ, in 2008 and is board-certified by the American Board of Internal Medicine. Dr. DeLuca is a Diplomate of the American Academy of Anti-Aging Medicine and has obtained certifications in hyperbaric medicine, pain management, nutrition, strength and conditioning, and manipulation under anesthesia.

Ronald L. Shuler, BS, DDS, CCN, LN, is involved in immunoncology for the prevention and treatment of cancer, human growth hormone secretagogues, and osteoporosis. He is board-certified in anti-aging medicine.

Paul Wand, MD, Fort Lauderdale, FL, is a clinical neu-rologist with special expertise in treating and reversing diabetic peripheral neuropathy and brain injuries from various causes.
Anti-Aging Center. She is double board-certified in Anderson Cancer Center, focusing on screening models John Boik, PhD, consultant at the Urologische Klinik Castringius, Planegg, effects in animals and humans.

of Technology (MIT). He has specialized in human medicine. She is a faculty member of the new University Deborah F. Harding, MD, is medical director of the Tahoma Clinic in Tukwila, WA. He received his MD from and reduce mechanical icing.

world’s highest-impact peer-reviewed journal focused on intervention in aging. He received his BA and PhD from Aubrey de Grey, PhD, is a biomedical gerontologist and Editor-in-Chief of Rejuvenation Research, the world’s University of Cambridge in 1985 and 2000 respectively. Dr. de Grey is a Fellow of both the Gerontological Society of America and the American Aging Association and sits on the editorial and scientific advisory boards of numerous journals and organizations.

a urologist specializing in prostate cancer for 10 years. He has a private practice in Bad Reichenhall, Germany, and is prostate cancer consultant at the Urologische Klinik Castringius, Planegg, Munich. In his integrative approach to prostate cancer he works together with an international network of experts to improve treatment outcomes for prostate cancer patients with a special focus on natural and translational medicine.

is founder of the Harding Anti-Aging Center. She is double board-certified in internal medicine and sleep disorder medicine. She also earned the Cenegenics certification in age management medicine. She is a faculty member of the new University of Central Florida Medical School.

is president and director of research at Critical Care Research, a company that grew out of 21st Century Medicine in Rancho Cucamonga, CA. Dr. Harris participates in groundbreaking hypothermia, cryothermia, and ischemia research. His research interests include antioxidant and dietary-restriction effects in animals and humans.

Peter H. Langsjoen, MD, FACC, is a cardiologist specializing in congestive heart failure, primary and statin-induced diastolic dysfunction, and other heart diseases. A leading authority on coenzyme Q10, Dr. Langsjoen has been involved with its clinical application since 1983. He is a founding member of the executive committee of the International Coenzyme Q10 Association, a fellow of the American College of Cardiology, and a member of numerous other medical associations.

Dipnarine Maharaj MD, MB, ChB, FRCP (Glasgow), FRCP (Edinburgh), FRCPath., FACP Dr. Dipnarine Maharaj is the Medical Director of the South Florida Bone Marrow Stem Cell Transplant Institute and is regarded as one of the world’s foremost experts on adult stem cells. He received his medical degree in 1978 from the University of Glasgow Medical School, Scotland. He completed his internship and residency in Internal Medicine and Hematology at the University's Royal Infirmary.

Michael D. Ozner, MD, FACC, FAHA, is a board-certified cardiologist who specializes in cardiovascular disease prevention. He serves as medical director for the Cardiovascular Prevention Institute of South Florida and is a noted national speaker on heart disease prevention. Dr. Ozner is also author of The Great American Heart Hoax, The Complete Mediterranean Diet and Heart Attack Proof. For more information visit www.drozner.com.

Jonathan V. Wright, MD, is medical director of the Tahoma Clinic in Tukwila, WA. He received his MD from the University of Michigan and has taught natural biochemical medical treatments since 1983. Dr. Wright pioneered the use of bioidentical estrogens and DHEA in daily medical practice. He has authored or co-authored 14 books, selling over 1.5 million copies.

Xiaoxi Wei, PhD, is a chemist expert in supramolecular assembly and development of synthetic transmembrane nanopores with distinguished selectivity via biomimetic nanoscience. She has expertise in ion channel function and characterization. She founded X-Therma Inc., a company developing a radical new highway towards non-toxic, hyper-effective antifreeze agents to fight unwanted ice formation in regenerative medicine and reduce mechanical icing.
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Twenty years ago I was leaving a medical conference when one of our ardent supporters rushed up and handed me a huge textbook. She begged I take it home to read. She was adamant that Life Extension® make a greater effort to enlighten its readers about the underlying cause of most disability and death in persons over age 50.

The threat described in the textbook occurs when an abnormal blood clot forms inside an artery or vein. The medical term is thrombosis.

Two disorders involving arterial thrombosis are:

- Heart Attack
- Ischemic Stroke

Two disorders involving venous thrombosis are:

- Deep Vein Thrombosis (DVT)
- Pulmonary Embolism

Those stricken with cancer are particularly susceptible to venous thrombosis. Chemotherapy patients are up to 6-times more vulnerable.

One reason we’ve recommended low-dose aspirin since 1983 is its ability to inhibit platelet aggregation, a major factor involved in arterial thrombosis, leading to a heart attack or ischemic stroke.

Recent studies show that arterial thrombosis occurs more frequently than previously thought. Minor thrombotic events seldom display outward symptoms and, over time, predispose us to a host of degenerative illnesses including mind-robbing mini-strokes.

Many of the nutrients you take have diverse antiplatelet effects. This is important in protecting against arterial thrombosis, but far less so for venous thrombosis.

The Surgeon General published a report showing that deep vein thrombosis (and subsequent pulmonary embolism) may cause 100,000-180,000 deaths each year in the US. To put this in perspective, pancreatic cancer is estimated to kill more than 41,000 Americans in 2016. Pancreatic cancer has a decidedly deadly reputation, yet the public is largely unaware that deep vein thrombosis (and subsequent pulmonary embolism) poses a greater overall health risk.

The Surgeon General was highly critical of mainstream medicine for not recognizing patients at risk for deep vein thrombosis and taking appropriate preventive measures.

Longtime readers of this magazine should be comforted with the knowledge that they are already taking steps to reduce their arterial thrombotic risk.

This issue describes startling new data about deep vein thrombosis, and what can be done to help prevent it.
As We See It

People often take for granted that blood effortlessly flows through their arteries and veins like water moves through a hose.

The reality is that blood flow is highly dependent upon a complex interplay of different mechanisms, including coagulation factors that regulate the tendency of blood to form a clot.

For example, platelets play an important role in "plugging" holes in our circulatory system, helping to reduce bleeding in conjunction with other clotting factors.

Conversely, when platelets abnormally aggregate (clot) inside a blood vessel in response to arterial plaque and/or endothelial damage, the result is stoppage of blood flow to the affected part of the anatomy. An abnormal blood clot in a cerebral artery can lead to ischemic stroke, whereas a thrombus (clot) that forms in a coronary artery can result in a heart attack.

As humans age, mini-thrombotic events can occur to small arteries in the brain. This includes transient ischemic attacks (TIAs) in the brain that, over time, can cause damage to our cognitive abilities.

Preventing the development of these minor and major thrombotic episodes is critical for healthy longevity. The good news is that we know a lot about what causes pathologic blood clotting inside arteries and veins, and how to prevent it.

Role of Inflammation in Both Arterial and Venous Thrombosis

Inflammation sets in motion a sequence of events that can lead to arterial and venous thrombosis. Normal aging results in increasing levels of vascular inflammation, often without outward symptoms.

Readily obtainable blood markers that can reveal systemic inflammation are homocysteine, C-reactive protein, and fibrinogen. Heightened levels of these inflammatory biomarkers are correlated with arterial thrombosis and subsequent risk of cardiovascular disease.

Fish oil, vitamin D, curcumin, and other plant extracts inhibit many underlying inflammatory factors that increase C-reactive protein. The biologically active form of folic acid (5-MTHF) along with vitamins B12 and B6 can slash elevated homocysteine through two distinct detoxification pathways.

In contrast to the association between risk of arterial thrombosis and C-reactive protein elevation, C-reactive protein is not very useful in predicting future venous thrombosis or pulmonary embolism. Recent evidence does point to the role of proinflammatory cytokines like IL-8 and tumor necrosis factor-alpha in venous thrombosis risk.

Nattokinase is an enzyme extracted from a Japanese food (natto) prepared from fermented soybeans. Venous inflammation tends to raise fibrinogen levels, and fibrinogen is an important factor involved in inflammation as well as venous thrombosis formation.

Nattokinase has been shown to decrease levels of fibrinogen along with clotting factors VII and VIII, which are involved in the formation of venous thrombosis.

Epidemic of Deep Vein Thrombosis

Deep venous thrombosis and pulmonary embolism are major causes of disability and death. Each year, as many as 900,000 Americans may be affected by venous thromboembolism. Of those diagnosed, up to 30% will die within one month, and the first symptom will be sudden death in about 25% of those who have a pulmonary embolism.

Venous thrombosis is the formation of a blood clot inside a vein that can obstruct flow in the localized affected part of the venous circulatory system. When a venous blood clot dislodges from its primary location and travels to block circulation in another body part, this is referred to as a venous thromboembolism. When a deep vein thrombosis dislodges and travels to the lungs, this worrisome and potentially life-threatening condition is called a pulmonary embolism.
A variety of factors are implicated in the formation of venous thrombosis. Two major, related risks for the development of deep vein thrombosis are:

- **Hemostasis** (reduction/stagnation of blood flow)
- **Hypercoagulability** (propensity of blood to clot inside veins due to lifestyle, cancer or genetics)

The good news is that steps can be taken to reduce the risk of deep vein thrombosis, as well as thrombotic risks throughout the circulatory system. This means that strategies to protect against deep vein thrombosis may also confer protection against stroke and heart attack.

**What Causes Blood Vessel Clots in Arteries?**

To sustain life, blood must remain in a fluid state so that it can freely circulate, while simultaneously being able to properly clot at the site of a vascular injury.

Any event that activates platelets can cause them to aggregate to form an occlusive thrombus.

As it relates to aspirin, fish oil and certain plant polyphenols, you'll often read about their “anti-platelet” properties. What this describes is their ability to interfere with platelet activity, adhesion, and aggregation, thereby reducing arterial thrombotic risk.

Antiplatelet therapies, however, can be sabotaged by dysfunction of our endothelium (inner arterial lining). A healthy endothelium produces substances that stabilize platelets and impede their unwanted adhesion.

When the endothelial lining is lost, platelets are exposed to parts of the arterial wall that cause them to aggregate. Protecting against endothelial dysfunction is thus essential to maintain vascular health as we age. This is where pomegranate and other plant polyphenols play a critical role.

Antiplatelet strategies employed today, utilizing certain medications and nutrients, can greatly mitigate these arterial thrombotic factors.

---

**Conventional Arterial Thrombotic Risk Factors**

LDL cholesterol is a common factor involved in development of atherosclerotic plaque in arteries. Elevated LDL contributes to deposits of plaque that cause arterial pathways to gradually narrow until normal blood flow is disrupted. When this happens, there is a greater propensity for arterial clot formation (arterial thrombosis).

**Hypertension** increases the velocity at which blood is thrust through the arterial system. As blood pressure elevates, platelets become more likely to aggregate and create a thrombotic event.

Conventional cardiovascular and arterial thrombosis risk factors are diabetes, smoking, abdominal obesity, and hyperlipidemia (elevated LDL and triglycerides). Some of these same factors are also associated with increased risk of deadly venous thrombotic events.

The encouraging news is that proven methods exist to control underlying causes of thrombosis and the vascular diseases that can develop acutely or chronically.
As We See It

How Arterial and Venous Clots Differ

There are distinctions between the processes that cause arterial and venous thrombosis.

Arterial thrombosis largely involves platelet aggregation forming around clogged/jagged points in the arterial system, or in response to irregular heart beat (atrial fibrillation) or an artificial heart valve.

Deep vein thrombosis typically occurs due to hemostasis (reduction in venous blood flow) and hypercoagulability (tendency of the blood in veins to clot due to genetic, cancer or lifestyle factors).

One major cause of reduction in venous blood flow is chronic venous insufficiency. This frequently occurs from obesity, lack of physical activity/sitting with the legs in a dependent position, and previous deep vein thrombosis, which injures or destroys one or more of the valves that are located in the deep veins of the leg.

In order to efficiently return blood to the heart when a person is sitting or standing, veins contain tiny valves that open and close. Properly functioning valves prevent blood from flowing backward while muscles surrounding the veins compress them, helping pump venous blood back to the heart.

Veins contain valves while arteries do not. When veins are damaged by prior venous clot, or physical inactivity leads to pooling of blood in the deep veins of the legs, venous blood flow decreases, setting the stage for venous thrombosis.

In contrast with the venous system, platelets in the arterial system are adversely activated as they bump into buildups of plaque along the arterial walls and interact with a dysfunctional endothelium. In this scenario, platelets begin to clump together, causing a cascade that can lead to blood flow being cut off to vital tissue (such as a portion of the heart muscle).

In the venous system, normal blood flow can slow, and if left to stagnate too long, the blood within these veins begins to coagulate (clot). The problem of deep vein thrombosis, however, extends beyond mere stagnating pools of blood in the lower legs.

How Arterial and Venous Clots Differ

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Symptoms of Deep Vein Thrombosis

A blood clot in one of the deep veins can include the following symptoms:

- Mild to severe pain in the affected arm or leg
- Swelling of an arm or leg
- Redness or color change
- Warmth of the skin

A venous blood clot that has traveled to the lung (called a pulmonary embolism) has symptoms that include:

- Chest pain
- Shortness of breath
- Fast heartbeat

Nutrients that Help Protect Against Arterial Thrombosis

- Green tea
- Fish oil
- Olive polyphenols
- Quercetin
- Resveratrol
- Grape seed extract
- French maritime pine bark extract
- Lycopene
- Pomegranate
- Garlic
- Flax seed oil
- Ginger
- Curcumin
Nattokinase has been shown to decrease fibrinogen levels and help dissolve fibrin clots that obstruct blood flow.32,87

The flow chart on this page shows a simplified version of the complex process of coagulation involved in thrombosis formation. The fibrinogen/fibrin-dissolving effects of nattokinase can help stop this coagulation cascade at several checkpoints.

Impressive Human Data!

A recent study highlighted the risk of deep vein thrombosis in response to conditions that predispose to stagnation of venous blood in the lower extremities (legs)—specifically, air travel.96

Many people are not aware that air travel, and associated pooling of venous blood in the legs due to inactivity during flight, is a major risk factor for deep vein thrombosis and potentially life-threatening pulmonary embolism.97,98

Using ultrasound imaging, the presence of venous thrombosis was detected in a startling 5%-7% of passengers of flights lasting 7-8 hours.96 These passengers were asymptomatic, meaning they did not know they had developed a venous blood clot!

When a nondrug approach for prevention of deep vein thrombosis was studied in this group of passengers, no lower leg venous clots were detected and lower leg edema (swelling) was drastically reduced.

Beyond “Antiplatelet” Strategies

Inflammation and some other factors that contribute to arterial thrombosis (such as excess homocysteine) also are linked with an increased risk of deep vein thrombosis.84,85 Several of these dynamics, however, play a larger role in the venous system than in arteries.

What happens with deep vein thrombosis is that fibrinogen, also a proinflammatory regulator, excessively converts to a fibrin mesh that traps red blood cells. In deep vein thrombosis, formation of fibrin is also linked with excess inflammation in veins.86 This helps explain the limited efficacy of antiplatelet drugs (aspirin and Plavix®) in venous thrombosis, i.e., they don’t stop the initiating phase of proinflammatory fibrinogen converting to red blood cell-trapping fibrin.

There are multiple underlying coagulation factors that can initiate a deep venous thrombosis. Some require preventive treatment using anticoagulant drugs (warfarin, Pradaxa®, Eliquis®, Xarelto®). There is a common venous thrombotic mechanism, however, that can be impeded with a low-cost nutrient.

Cancer-Related Thromboembolism

Cancer is associated with a 4.1-fold increased risk of venous thromboembolism.88

Poor mobility, venous obstruction, and ongoing chemotherapy further increase risk of recurrence.89,90 Venous thromboembolism is associated with advanced and more aggressive cancers.91,92

Cancer patients with venous thromboembolism have worse survival than cancer patients free of this complication.91 For example, after a diagnosis of venous thromboembolism, the mortality rate at 6 months for cancer patients on anticoagulant therapy is 40%.92

Cancer patients today are dying prematurely from venous thromboembolism. This is why Life Extension® long ago recommended aspirin and low-molecular weight heparin as adjuvant cancer therapies. Not only do overly-active platelets contribute to thrombosis, but they facilitate metastasis.93-95

What might surprise you is that venous thromboembolisms can be the first clinical manifestation of cancer somewhere in one’s body. About 10% of patients with unprovoked venous thromboembolism are diagnosed with cancer. Of these, more than 75% are diagnosed within the first year after their thrombotic episode.2
Whenever you are faced with long-haul air travel, you should stand up every few hours and take a walk through the plane cabin. Consider obtaining high quality compression stockings to wear whenever you fly to reduce stagnation of blood in lower leg veins.99

As you will read in this month’s issue, ingestion of two nutrients taken two hours before the plane departs and again six hours into the flight drastically reduced detection of venous blood clots and lower leg edema at the end of the flight. These nutrients have a dual effect of inhibiting platelet aggregation and helping to thwart fibrin-induced clots.

The fact that short-term dosing of these two nutrients demonstrated such a profound effect in protecting against deep vein thrombosis implies significant systemic benefits for those who supplement daily.

An intriguing article in this month’s issue describes the robust benefits of these nutrients for reducing deep vein thrombosis risk. The first article unveils a novel way of enhancing the efficacy of your probiotic by selectively killing off harmful intestinal bacteria.

Obtain Nutrient Formulas at Year’s Lowest Prices

This is the time of year when we discount prices on every one of our advanced nutritional formulas. Longtime supporters take advantage of the once-a-year Super Sale to stock up on their favorite nutrient formulas. Those who have engaged in healthy lifestyle choices should find comfort knowing that nutrients they may have been using for decades confer considerable protection against thrombosis, which remains the most prevalent underlying cause of disability and death in persons over age 50.

Surgeon General’s Call to Action

In a report published 8 years ago, the Surgeon General stated:

“DVT [deep vein thrombosis] and PE [pulmonary embolism] are major public health problems in the United States. Much is known about how to reduce their burden, yet this knowledge is not being applied systematically today. Without a concerted effort to stem this public health crisis, the incidence and burden of these diseases will only grow larger as the population ages.”

Sadly, this medical neglect continues as hurried physicians are not doing enough to prevent thrombotic events that not only cause DVT/pulmonary embolism, but many strokes and heart attacks.

Our Commitment

No organization is working harder to accelerate human age reversal research than Life Extension.

Your support enables scientists to engage in biomedical research that would have been inconceivable just a few years ago.

To order nutrients you need today at Super Sale prices, call 1-800-544-4440.

For longer life,

William Falloon

(References may be found on page 14.)
Numerous factors in blood can contribute to abnormal blood clots. Thrombosis is the term used to describe clots that form inside blood vessels.

Rather than wait for an acute stroke, coronary blockage, or deep vein thrombus, one can evaluate common thrombotic risk factors that are measured in the blood.

A new low-cost panel has been designed to detect abnormalities in one’s blood that can be corrected before a disabling or lethal blood vessel clot develops.

One of these clotting factors is fibrinogen which markedly increases risk of thrombosis, especially stroke.

The new Thrombotic Risk Panel provides the following tests at a special introductory price of only $139 (if ordered before January 31, 2017):

Inflammatory/Clotting Markers
- Fibrinogen
- C-reactive protein
- Homocysteine
- PT/PTT/INR

Insulin Resistance Markers
- Glucose
- Insulin
- Hemoglobin A1C

Lipid Markers
- Cholesterol (total)
- LDL
- HDL
- VLDL
- Triglycerides

Blood Cells
- Platelet count
- Red Blood Cell count
- Anemia markers
- White Blood Cell count (includes differentiation)

Liver/Kidney Function and more!

Don’t Delay—Order today, visit www.LifeExtension.com or call one of our knowledgeable Wellness Specialists at 1-866-864-3027.

This offer is good through January 31, 2017.

Fasting Not Required

Conventional protocol says that one should fast for 8-12 hours prior to a blood draw. The fast means no eating or drinking anything except water and taking one’s prescription medications.

Life Extension® will soon make an announcement based on new evidence indicating that more valuable data may be obtained if one is NOT in a fasting state when their blood is drawn.

If you are used to fasting prior to a blood test you may continue this practice, but you now have the option of eating/drinking what you normally do in a typical day.

Just write down the time of your last meal and what it contained. This provides a snapshot of what your blood normally looks like on a typical day as opposed to what may be artificially different levels that occur during a fasting state.

Thrombotic Risk Panel • Item # LC100055
Retail: $259 • Introductory price: $139

Additional Blood Tests for Thrombosis

Unlike arterial thrombosis risk due to elevated LDL-C cholesterol and hs-CRP, as well as elevated arterial and venous thrombosis risk due to fibrinogen and homocysteine, some individuals suffer from other coagulation disorders that require additional blood tests to detect.

Additional tests available from your doctor for coagulation factors to evaluate for venous thrombosis risk include:

- Factor V Leiden (mutation)
- Prothrombin gene G20210A (mutation)
- Antiphospholipid antibodies (e.g. lupus anticoagulant, cardiolipin antibody, beta-2 glycoprotein antibody)
- Protein C antigen and activity
- Protein S antigen and activity
When Anticoagulant Drugs Are Needed

People with artificial heart valves or atrial fibrillation are at high risk for developing a thrombus that breaks loose and travels up a carotid artery, where it can cause an acute ischemia stroke.100,101 There are also inherited conditions in which blood clotting proteins improperly react, either causing blood to overcoagulate or preventing expression of normal clot dissolving factors. Some of these coagulation disorders that result in too much clotting include:

- Factor V Leiden
- Antithrombin III (ATIII) deficiency
- Protein C or protein S deficiency
- Prothrombin (PT) gene mutation
- Antiphospholipid antibody syndrome

Those in a hypercoagulable state are usually prescribed one of the four following anticoagulant drugs:

- Pradaxa®
- Eliquis®
- Xarelto®
- Coumadin® (warfarin)

The major side effect risk of these drugs is unwanted bleeding. These drugs also don’t always prevent a thrombotic event. Those who choose the oldest of these drugs (warfarin) are subjected to severe vitamin K deficiency that rapidly calcifies tissues. This can lead to future degenerative illnesses (such as accelerated atherosclerosis and aortic valve stenosis).

Despite these side effect risks, those at high thrombotic risk should work closely with their physician to use the anticoagulant drug that best meets their individual needs. To review our detailed report on the pros and cons of each of these drugs, log on to: LifeExtension.com/thrombosis

References


The Two-Per-Day multinutrient formula is superior to commercial multivitamins because it provides vastly higher potencies of vitamins, minerals and plant extracts.

Two-Per-Day also provides optimal forms of vital nutrients such as:

- **5-MTHF**: Active form of folate—up to 7 times more bioavailable
- **Natural Vitamin E**: Twice as bioavailable as synthetic vitamin E
- **Selenium**: Three different forms that each have specific properties: selenium-enriched yeast (SelenoExcell®), Se-methyl-selenocysteine, and sodium selenite
- **B-Vitamins**: Enzymatically active forms of B2 and B6
- **Added value**: Alpha lipoic acid and plant extracts like apigenin

The retail price of a 60 day supply of the new Two-Per-Day tablets is $20. (Item # 02115)

Your price during our 26th annual Super Sale is reduced to $13.50. If you buy four bottles, the price is reduced to $12.15 per bottle.

Two-Per-Day capsules (Item # 02114) retail price is $22, but with Super Sale, a 60-day supply is $14.85, or just $13.50 each when you buy four bottles.

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This year’s Super Sale begins November 14, 2016.

To order call 1-800-544-4440 or visit LifeExtension.com

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These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
Super Bio-Curcumin® features a patented extract from turmeric root that absorbs up to 7 times better than standard curcumin. This product is ideal for those seeking to support normal cell-cycle growth and healthy inflammatory response.

Advanced Bio-Curcumin® contains the same optimal potency of curcumin with the added benefits of ginger and additional turmeric extracts.

Suggested dose for either Super Bio-Curcumin® formula is one capsule daily.

To order Super Bio-Curcumin® or Advanced Bio-Curcumin® with Ginger & Turmerones, call 1-800-544-4440 or visit www.LifeExtension.com
Omega-3 Heals the Heart

Results from a trial reported in the journal *Circulation* reveal improved heart function and less scarring in patients given omega-3 fatty acids for six months following a heart attack.*

The trial included 360 heart attack survivors who received fish oil-derived omega-3 or a placebo within a month of the attack. At the beginning and end of the treatment period, blood samples were analyzed for omega-3 levels, inflammation biomarkers and other factors, while magnetic resonance imaging evaluated cardiac structure and tissue characteristics.

At the end of the study, participants whose omega-3 index rose to the top 25% of subjects had a 13% reduction in left ventricular systolic volume index (a marker of heart remodeling) compared to those whose omega-3 levels were among the lowest. Participants who received omega-3 experienced significant reductions in markers of inflammation and heart muscle fibrosis.

Editor’s Note: The findings suggest a role for omega-3 in the prevention of cardiac remodeling, a condition characterized by alterations in heart shape and function that can occur after a heart attack, which is associated with heart failure.

Vitamin D
Associated with Shorter Hospital Stays in Ventilated Patients

A pilot trial reported in the *Journal of Clinical and Translational Endocrinology* found that critically ill patients receiving mechanical ventilation who were given a high-dose vitamin D supplement had a shorter hospital stay in comparison with those who received a placebo.*

Researchers randomized 31 ventilated intensive care unit patients to receive 50,000 IU or 100,000 IU of vitamin D3 daily for five days. Thirteen of the subjects had deficient plasma 25-hydroxyvitamin D levels of less than 20 ng/mL at the beginning of the study. Blood samples were analyzed one and two weeks after the beginning of the treatment period to measure plasma vitamin D and other factors.

Average length of hospital stay was 25 days among those in the 50,000 IU group and 18 days in the 100,000 IU group, in comparison with 36 days in the placebo group. The high-dose vitamin D group thus spent half as much time hospitalized.

High doses were needed because these ICU patients were in acute need to rapidly build up their vitamin D levels.

*Editor’s Note:* “High-dose vitamin D may have multifactorial effects that could contribute directly or indirectly to hospital length of stay, including salutary effects via improved 25-hydroxyvitamin D levels on respiratory or other skeletal muscle function, by modulation of the pro-inflammatory milieu, and by regulation of immune functions, among other contributors,” authors Jenny E. Han and colleagues conclude.

Taurine and Magnesium Decrease Markers of Cardiovascular Disease Progression

The journal *Hypertension Research* reported finding an increase in endothelial progenitor cells and a decrease in free radicals in association with supplementation with taurine and magnesium.*

The body’s endothelial progenitor cells repair the damage to the lining of the arteries that leads to cardiovascular disease. Free radical formation, when unchecked, is a factor involved in cardiovascular disease development.

More than 100 healthy men between the ages of 18 and 25 received 3 grams of taurine, 340 mg of magnesium, or a placebo daily for two weeks. Taurine and magnesium supplementation decreased measures of free radical damage over this two week period.

In comparison with pretreatment levels, endothelial progenitor cell colony-formation numbers, which reflect the vascular repair function of endothelial progenitor cells, significantly increased in study participants supplementing with taurine and magnesium.

**Editor’s Note:** “These findings indicate that the dietary intake of taurine and magnesium may prolong lifespan by facilitating the repair of impaired endothelial functions and thereby prevent the progression of cardiovascular diseases,” the authors observe.

Progenitor cells come from stem cells and serve many functions in repairing and maintaining tissues throughout our bodies. Regenerating the endothelial lining of our arteries has huge potential in reducing atherosclerosis incidence. Taurine and magnesium are ultra-low cost nutrients.

*Hypertens Res. 2016 Jul 14.*
Drug More Than Doubles Chances of Five-Year Survival Rate

According to a study presented at the annual meeting of the American Association for Cancer Research in New Orleans, patients with advanced melanoma who were treated with the immune-oncology drug Opdivo® had far higher survival rates. After 5 years, 34% of patients receiving Opdivo were alive compared to 16% of melanoma patients receiving conventional treatment methods.*

Significantly, oncologists say the results indicate that patients who survive for about four years are highly unlikely to relapse because their immune systems have eradicated or controlled their tumors.

Opdivo® is an immune checkpoint inhibitor. This type of drug blocks certain proteins made by some types of immune system cells, such as T cells, and some cancer cells. These proteins suppress immune responses and can keep T cells from killing cancer cells. When these proteins are blocked, the “brakes” on the immune system are released and T cells are able to better kill cancer cells.

Editor’s Note: The first checkpoint inhibitor to reach the market was Yervoy®. It targets a brake known as CTLA-4 and in a previous analysis was shown to result in long-term survival in about 17% of melanoma patients. A report on checkpoint inhibitor drugs was published in the June 2016 issue of Life Extension Magazine®. Oncology experts working with Life Extension® report favorable outcomes when checkpoint inhibitors are used against other malignancies.

As a man ages, maintaining a healthy prostate is key. We created Ultra Natural Prostate to help you maintain prostate health, so you can focus on what’s important. With over a dozen natural ingredients, this supplement promotes healthy prostate function, supports easier urination, inhibits inflammatory factors, and encourages natural division of prostate cells. Ultra Natural Prostate. The most comprehensive prostate health supplement.
BOOST AND PROTECT YOUR
VASCULAR HEALTH

Optimal heart health depends on many factors including proper functioning of the endothelium—the thin layer of cells lining the interior of the entire circulatory system.

TRIPLE-ACTION PROTECTION

Endothelial Defense™ with Pomegranate Complete and CORDIART™ contains three unique ingredients shown to improve endothelial health.

1. Pomegranate Complete provides potent polyphenols clinically shown to support healthy blood flow.

2. CORDIART™ (extract from sweet orange peels) activates endothelial production of nitric oxide, which supports healthy circulation.

3. Superoxide dismutase (SOD) supports healthy arterial function and boosts the body’s protective enzymes.

To order Endothelial Defense™ with Pomegranate Complete and CORDIART™, call 1-800-544-4440 or visit www.LifeExtension.com

Caution: Do not take this product if you are allergic to wheat or gluten.

Endothelial Defense™ with Pomegranate Complete and CORDIART™
Item #01997 • 60 softgels

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Non-GMO
Contains wheat

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
The new Extend-Release Magnesium provides an immediate release of magnesium citrate to the stomach and a slow 6-hour release of magnesium oxide for optimal intestinal absorption.

According to data from the National Health and Nutrition Examination Survey of 2005-2006, most Americans fail to consume the estimated average requirement of magnesium from food alone.*

Each capsule of the new Extend-Release Magnesium supplies 250 mg of elemental magnesium designed for sustainable absorption into your bloodstream over a 6-hour period.

Those taking a multinutrient supplement that provides at least 100 mg of elemental magnesium may need only one Extend-Release Magnesium capsule daily.

Reference

Non-GMO
ZumXR is a registered trademark and protected by patents.

Caution: If taken in high doses, magnesium may have a laxative effect. If this occurs, divide dosing, reduce intake, or discontinue product.
Probiotics are emerging as enormously popular health supplements.

When one ingests a probiotic, they add bacteria to their digestive tract that produce benefits ranging from alleviating intestinal distress to strengthening immunity.

Another virtue of probiotics is that they can slowly crowd out harmful bacteria strains in the intestines.

In a significant advance, a natural method of selectively killing undesirable bacteria has been developed.

When combined with a probiotic in the animal model, there was an exponential increase in beneficial bacteria with a parallel decrease in unfriendly flora like E. coli.\textsuperscript{1,3}

This article describes a novel way of optimizing probiotic efficacy.
Most people in the United States have likely never heard of **phage therapy**. It was discovered in pre-World War I Eastern Europe, and for much of the pre-World War II era, it was thought to be a promising approach to controlling bacterial illnesses.4,6

In the 1940s, industrial giants like Eli Lily and L’Oréal developed bacteriophage “cocktails” aimed at treating a variety of bacterial infections. But the advent of antibiotics quickly cost phages the spotlight, though their effectiveness has never been in question.7

Phage therapy uses **bacteriophages**, which are sub-microscopic packages of DNA or RNA enclosed in a protein envelope that selectively target harmful bacteria. The name **bacteriophage** literally means “**bacteria eating**.” A bacteriophage attaches itself to a bacterial cell wall and then destroys the host bacteria.

Bacteriophages are ubiquitous in nature, meaning they can be found almost everywhere—from soil, hot springs and the ocean depths to the animal and human body.8

**The name bacteriophage literally means “bacteria eating.”**

Phages are a common and important component of gut flora and are found in various other parts of the human body such as the mouth and skin.8,9 Phages are currently used in the food industry to control disease-causing organisms.10-12

Numerous phages are classed as GRAS—or “generally recognized as safe”—and are commonly used for a variety of different applications, from controlling Listeria in cheese and E. coli in meat and on food-contact surfaces, to Salmonella in food.

With the targeted use of bacteriophages, it is possible to seek out and effectively reduce specific populations of unhealthy organisms that have taken over the **intestinal microbiome**.

The use of bacteriophages allows an exceptionally specific approach to eliminating detrimental bacteria. This is in direct contrast to antibiotics, which employ a mass-killing technique that eliminates healthy and detrimental bacteria, leaving us vulnerable to attack by other organisms.13

By removing common pathogenic bacteria in one’s gut, bacteriophages enable beneficial **probiotic** bacteria to thrive, allowing them to more effectively rebalance the microbiome.

When phages are combined with probiotics in animal models there are huge reductions in the targeted harmful bacteria with a simultaneous increase in beneficial bacteria.
Giving Probiotics a Boost

Many people live in a state of dysbiosis or imbalance that not only threatens their long-term health, but may also contribute to sleep disorders, to a sense of malaise or “fogginess,” and to a range of stomach distress issues that cannot be explained by a specific disease. Fortunately, many studies have shown that positively changing the microbiome—shifting it toward a healthy profile and away from dysbiosis—can also change symptoms and disease risk.14,35,36

One important way of improving the intestinal microbiome is through the use of probiotic bacteria. Probiotics are a great additive therapy that increase the abundance of organisms that can rebalance an ailing microbiome. In some cases, however, probiotics by themselves have difficulty competing with the more aggressive microbes that contribute to dysbiosis in the first place.

A more comprehensive approach is to use probiotics in combination with another therapy, one that selectively targets and reduces the troublesome bacteria that are taking over the microbiome. This approach of targeting harmful bacteria while replenishing beneficial bacteria can make way for probiotics to better help restore the microbiome to a healthy, balanced state. That is how phage therapy works.

Phage therapy reduces potentially troublesome organisms that are overabundant in the microbiome, allowing beneficial organisms to flourish. This helps restore the microbiome to a healthy, balanced state.37

Combating E. coli Bacteria

Escherichia coli (E. coli) is a bacterium that normally lives in our intestines. Most types of E. coli are harmless, but some can cause disease.

A troublesome strain of E. coli called H10407 causes abdominal cramps, diarrhea, and gas.38,39 This pathologic E. coli strain also suppresses growth of beneficial bacteria and produces a state of dysbiosis.40

In an effort to help restore a balanced and healthy microbiome, researchers have developed a cocktail of bacteriophages that target dangerous strains of E. coli.

Unlike typical pre- or probiotics, this phage cocktail is effective within hours, not days, and in very small doses.40 It functions not only in the colon (large intestine), where dysbiosis is a problem, but also in the small intestine, where undesirable bacterial overgrowth occurs. It does not cause flatulence, a constant problem with fiber-containing prebiotics.40

Laboratory studies show that this form of phage therapy removes harmful bacteria, making way for beneficial probiotic bacteria to establish and form a healthy microbiome. This has been demonstrated—with impressive results.

What You Need to Know

The Revival of Phage Therapy

• An imbalance in the intestinal microbiome (dysbiosis) is now associated with many serious age-related disorders. Studies show that it is prevalent in older people, particularly those with sleep disorders, vague abdominal complaints, and malaise.

• Changing the intestinal microbiome towards a state of improved health and function is a desirable solution, but until now options have been limited.

• Bacteriophages selectively target and destroy specific harmful bacteria.

• In combination with a mixture of probiotic bacteria, a cocktail of bacteriophages has been shown to reduce the abundance of undesirable bacteria, while freeing beneficial organisms to thrive and increase in numbers.

• Using this probiotic/bacteriophage mixture shows high promise in relieving the functional changes and tissue damage wrought by dysbiosis, and should be added to the regimen of anyone interested in rebalancing their microbiomes to feel better.
Phage Cocktail Promotes Survival of Probiotic Organisms

In one experiment, culture dishes were prepared with a beneficial bacteria \(\textit{Bifidobacterium longum}\), along with a competitive \(\textit{E. coli}\) bacteria.\(^{40}\) A second set of dishes was prepared to which the \textit{bacteriophage} mixture was added. After just 5 hours, there was a visible difference.

In the dishes without \textit{bacteriophage}, there was little growth of the desirable \(\textit{B. longum}\) organisms, indicating their inability to compete with \(\textit{E. coli}\).

In the dishes with the \textit{bacteriophages}, colonies of \(\textit{B. longum}\) skyrocketed to more than 7,000 times their numbers compared to dishes without the bacteriophage. This study demonstrates that the competitive \(\textit{E. coli}\) had been greatly removed from the picture by the \textit{bacteriophage} (Figure 1).

In a related experiment, a probiotic organism \(\textit{Lactobacillus acidophilus}\) was grown in culture, again in competition with \(\textit{E. coli}\).\(^{40}\) In a very similar fashion, without the \textit{phage cocktail}, the \(\textit{E. coli}\) suppressed growth of the beneficial \(\textit{L. acidophilus}\). However, in the presence of the phage mixture, \(\textit{L. acidophilus}\) thrived, reaching colony counts that were 20-fold higher compared to the culture not receiving the \textit{phages} (Figure 2). In similar experiments, growth of the probiotic organism \(\textit{L. rhamnosus}\) was enhanced 15-fold and the beneficial \(\textit{B. bifidum}\) was enhanced nearly 10-fold when grown in culture with the \textit{phage} cocktail.

These experiments demonstrate the value of the \textit{phage} mixture in promoting the growth and survival of probiotic organisms.

In another Petri dish experiment, the common prebiotic \textit{inulin} was used in an attempt to stimulate the growth of the beneficial probiotic \textit{Lactobacillus paracasei}. When the prebiotic was used alone, it failed to ensure the survival of the desired organisms. But when the \textit{phage} mixture was added, it produced an astonishing nine million-fold increase in growth of the probiotic \textit{Lactobacillus paracasei} (Figure 3).

Phage Cocktail Decreases \textit{E. coli} and Improves Normal Gastrointestinal Function

Moving out of the Petri dish and into the animal model, one group of laboratory mice was given the probiotic \(\textit{B. longum}\) in combination with the disease-causing \textit{E. coli} strain H10407.\(^{41}\) A second group of mice was given the same mixture, but with the addition of the \textit{phage cocktail} that targets \textit{E. coli}.

After 24 hours, compared with the control group, animals in the \textit{phage-treated} group gave powerful evidence of a \textit{reduction} in the disease-causing bacteria as can be seen on the following page:
Safety of Phage Therapy

In 1981, Russian researchers reported the successful use of phage therapy to treat antibiotic-associated dysbiosis—displacement of normal intestinal bacteria with pathogenic bacteria—in 500 low-birth-weight infants.

The subjects had all been given antibiotics for at least two to three weeks to treat sepsis and pneumonia, killing off their gut bacteria. They were then administered both a specific bacteriophage and a probiotic (Bifidobacteria) strain. The infants experienced both depletion of their pathogenic bacteria and replenishment of healthy, intestinal bacteria.42

Bacteriophages were successfully used in numerous human clinical and therapeutic settings and demonstrated an extremely strong safety profile.43-46

The reason for the very safe interaction between phages and human tissue likely results from human exposure to vast numbers of phages over the entire course of evolution. This naturally high human tolerance to phages contrasts sharply with the risks inherent in compounds that are relatively novel in human evolution—such as drugs.5

• About a 10-fold decrease of E. coli in the small intestine
• About a 100-fold decrease of E. coli in the colon (large intestine)
• About a 100-fold decrease of E. coli in fecal matter

At the same time, the phage-treated animals showed remarkable increases in the beneficial (B. longum) bacteria as follows:
• About 100-fold increase of B. longum in the small intestine
• About 100-fold increase of B. longum in the colon
• About 40-fold increase of B. longum in fecal matter

This study also revealed marked differences in the appearance of tissue samples and digestive function across the different groups of mice.

Mice treated with E. coli and B. longum alone were constipated, and intestinal segments showed swelling, redness, and leaks compared with healthy animals. The mice given B. longum and E. coli plus the phage mixture had normal bowel movements, while their intestinal tissues showed no detrimental changes.

Bacteriophage attaching to bacteria.
Summary

In addition to being associated with major age-related disorders, an unbalanced intestinal microbiome (dysbiosis) can also be responsible for general “blah” feelings as well as vague but troubling intestinal symptoms that plague aging individuals.

A novel approach to bringing the gut microbiome back into a healthy balance uses safe bacteriophages to selectively reduce harmful bacteria while encouraging beneficial probiotic organisms to flourish.

Called phage therapy, this technique is harmless to humans, but deadly for specific, troublesome bacteria.

Studies show that when probiotic organisms are accompanied by targeted phage therapy, the beneficial bacteria grow up to thousands of times their baseline rate, thanks to the removal of the more aggressive microbes.

Phage therapy shows real promise in relieving the functional changes and tissue damage wrought by dysbiosis and could be especially valuable for aging individuals experiencing intestinal discomfort, sleep disturbances, or general malaise.

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

How “Phages” Differ from Antibiotics

Antibiotics are considered one of the 20th century’s greatest scientific achievements.

But decades of widespread antibiotic use has created “superbugs” that are not easily killed by current pharmaceuticals. Many believe we have reached the end of the “antibiotic era.”

In severe cases, physicians desperately search for alternatives to save their patients’ lives.

This has prompted excitement about an innovative approach developed more than 100 years ago, but overlooked with the advent of antibiotics.

In fact, long before antibiotics were discovered, Eastern European doctors were successfully neutralizing bacterial infections with phage therapy, a treatment aimed at selectively targeting and destroying harmful bacteria.

With the rise in antibiotic-resistant bacteria, phage therapy is experiencing a revival among the scientific community because of its effectiveness and safety profile. The potential for phage therapy is so great that just last year the National Institutes of Health sponsored a symposium titled:

“Bacteriophage Therapy: An Alternative Strategy to Combat Drug Resistance”

Phage cocktails have been shown to effectively treat common bacterial invaders, including staph, strep, and E. coli.1-3

Phage therapy also beneficially encourages growth of healthy bacteria in the gut microbiome, which can also reduce harmful bacteria.

With so much scientific investigation into the multiple health benefits of a balanced microbiome, phage therapy is rapidly emerging as a new venue to enhance the benefits of probiotics.
Beneficial bacteria called *S. salivarius* K12 sustain throat health. Each FLORASSIST® Throat Health lozenge has 2 billion colony-forming units of *S. salivarius* K12 that:

- Maintain a balanced inflammatory response
- Help provide probiotic balance for throat health
- Maintain overall good health

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Item #01920 • 30 lozenges • Non GMO

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FLORASSIST® GI with Phage Technology combines four types of phages, along with six strains of probiotics that work within hours, not days.

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- *LL5* - Siphoviridae
- *T4D* - Myoviridae
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Natural Approach to Guard Against DEEP VEIN Thrombosis

Long periods spent sitting—behind a desk, in a car, on a long flight, or on a couch—increase the risk of deep vein thrombosis (DVT), a blood clot that forms mainly in a deep vein in the leg, which can lead to a pulmonary embolism, a condition that is often fatal.1,2

Practically anyone can be at risk, and the statistics are frightening. According to the American College of Cardiology, those who sit more than four hours a day have a 48% increased risk of mortality from blood clots that originate in the veins.3

Through a series of well-designed studies, scientists investigating certain natural extracts found that they can block these blood clots from forming and can help break down small clots before they grow.4-7 They also found that these extracts safely restore the natural anti-clotting and clot-reversal processes, making a dangerous clot less likely to form and quicker to resolve if it does.7-10

When tested on humans in a placebo-controlled study, those taking a dual plant extract experienced zero cases of deep vein thrombosis compared to 5.4% afflicted in the control group.6
Veins have valves, which work with the natural pumping action of the leg muscles to prevent backflow of blood into the lower limbs. With age those valves tend to leak. In people who don’t move around much, blood tends to pool in their legs.

According to the Centers for Disease Control and Prevention (CDC), as many as 900,000 Americans could be affected by venous thromboembolisms (blood clots) every year.11 Compare that to epidemics like all forms of cancer, which kill about 570,000 Americans annually.

As sedentary lifestyles become common, the threat of deep vein thrombosis continues to grow and claim an ever larger number of lives.

Research conducted by the American College of Cardiology found that individuals that spent four hours or more a day sitting compared to those who spent less than 2 hours had an approximate 125% increase in risk of cardiovascular events. This association was independent of traditional risk factors like smoking, hypertension, physical activity, and body mass index. Some even consider sitting to be the new smoking!12

Possible Symptoms of Deep Vein Thrombosis

Deep vein thrombosis often occurs without warning symptoms. But if you do notice any of the following indications, call your doctor, especially if they appear suddenly:27

- Swelling in one or both legs
- Tenderness or pain in one or both legs, even if it’s only when standing or walking
- Warm skin on your leg
- Red or discolored skin on your leg
- Veins you can suddenly see
- Tired legs

A natural, dual plant extract formula has been studied based on its ability to simultaneously inhibit venous clot formation and promote venous wall elasticity.

Combating Deep Vein Thrombosis

After searching for natural, deep vein thrombosis-inhibiting interventions, scientists identified two ingredients that demonstrated powerful preventive effects:

1. Nattokinase, an enzyme extracted from soybeans fermented with the bacterium Bacillus natto, and

2. French maritime pine bark, a natural extract rich in polyphenols.

Nattokinase was shown in studies to break down fibrin—long, strand-like molecules that make up the main protein found in clots—and its precursor, fibrinogen, both of which are involved in red blood cell-induced clot formation.8,19,20 Nattokinase decreased levels of other factors in the blood-clotting cascade, while raising levels of factors that prevent clotting. Specifically, nattokinase reduces the activity of two proteins (factor VIII and factor VII) that can produce unwanted clotting when elevated. No adverse effects or undesirable bleeding were reported.4

How Deadly Venous Thromboembolism Occurs

A deep vein thrombosis can occur quickly, often at first with no warning symptoms. But when this clot breaks apart, symptoms occur with a deadly vengeance. Large pieces of the clot travel silently through the circulatory system and eventually block blood flow into the lungs. This sudden event produces a pulmonary embolism, a blockage that can severely reduce, and even entirely stop, critical blood flow to the lungs—an event that is commonly fatal within minutes.

About 30% of those with a venous thromboembolism will die within one month, and about 25% of those fatalities will occur as sudden death. And about 33% of survivors have a recurrence within 10 years.11 Venous thromboembolisms are estimated to kill up to 100,000 Americans annually.11

Lifestyle changes can reduce the risk, such as quitting smoking, regularly exercising, and eating a healthy diet, but these are often insufficient to prevent a deadly catastrophe. Anticlotting drugs involve a risk of undesired bleeding,13,14 and compression stockings have shown limited effectiveness.15,16 The reason that these approaches provide limited protection is that with physical pooling of blood, natural clot-breakdown systems slowly lose pace with the body’s clot-forming systems.17,18

Clearly, a new defensive strategy is needed.
French maritime pine bark extract was demonstrated to reduce platelet aggregation, while increasing the activity of a blood flow-boosting enzyme that generates nitric oxide in blood vessels. Nitric oxide plays a critical role in regulating vascular function, which reduces thrombotic risks.

Nattokinase and pine bark extract were shown to work together to prevent clots as well as to improve the microcirculation of the legs.9,21

French maritime pine bark extract was also found to inhibit the action of “protein-melting” matrix metalloproteinase enzymes. These enzymes would otherwise degrade elastic proteins in the blood vessel walls, making them stiff and reducing blood flow.10,22

Given these observations, scientists recognized that these two extracts could result in significant prevention of deep vein thrombosis by:4,7-10,19-22

1. Inhibiting unwanted clot formation within veins,
2. Improving microcirculation in the veins of the legs, and
3. Promoting elasticity of vessel walls.
4. Inducing breakdown of fibrin clots.

Now let’s look at a more detailed evaluation of these ingredients.

Nattokinase Breaks Down Blood Clots

Before designing human trials, scientists conducted animal studies that clearly demonstrated the beneficial effects of nattokinase.

Studies in dogs showed that nattokinase produces a mild—but steady—increase in the rate of fibrin degradation in the blood. This effect works to prevent clots and to reduce the size and toughness of any existing ones.8

When nattokinase was given to dogs with experimentally-induced blood clots, researchers were literally able to watch the clots break down in real time using a type of X-ray technology called angiography.8

What You Need to Know

Preventing Deep Vein Thrombosis

• Spending long periods sitting can lead to deep vein thrombosis, which can suddenly, and without warning, trigger a pulmonary embolism.
• The medical establishment provides no safe or practical solutions to prevent this deadly risk.
• A formula has been developed from two natural extracts to help prevent deep vein thrombosis by inhibiting unhealthy clotting, promoting microcirculation, and enhancing vessel-wall elasticity.
• A placebo-controlled study on humans has shown that this dual-extract blend safely prevented deep vein thrombosis in all test volunteers, while also decreasing leg swelling.
• Venous thromboembolisms are defined as a deep vein thrombosis, a pulmonary embolism, or both.26
Then, in spontaneously hypertensive rats—a standard model for studies of high blood pressure in humans—nattokinase was demonstrated to break down fibrinogen (the precursor to fibrin) in the blood. And by a related mechanism, nattokinase reduced blood pressure, potentially by preventing conversion of the hormone angiotensin into its active, blood pressure-boosting form.23

A human study evaluating the effects of nattokinase found that it improves markers of coagulation. For this study, researchers recruited volunteers comprised of healthy individuals, cardiovascular disease patients, and dialysis patients. On a daily basis for two months, subjects took two capsules of nattokinase, each containing 2,000 fibrinolytic units.4

The researchers found that all three groups demonstrated significant decreases in procoagulation factors VII and VIII, and fibrinogen compared to baseline, suggesting that nattokinase works equally well in individuals with normal and impaired endothelial and coagulation function.4

No adverse effects were seen in this study,4 and safety tests completed on nattokinase confirmed its low-risk status.30

Preventing Venous Thromboses with French Maritime Pine Bark Extract

Scientists also conducted human studies on French maritime pine bark extract’s effects on the risks of venous thrombosis.

First, they enlisted 198 people at risk for deep or superficial venous thromboses during flights ranging from seven to 12 hours, with an average flight time of 8.25 hours.5 Test subjects were randomly assigned to either the control or test group. The test group took two capsules, each containing 100 mg of French maritime pine bark extract, two to three hours preflight, two more capsules six hours into the flight, and one capsule the day after. The controls took placebos at the same intervals. All subjects underwent ultrasound scans of their leg veins within 90 minutes before and after their flights to detect clots.

The French maritime pine bark extract-treated group showed no blood clots for an event rate of 0.0%. But the placebo group showed four superficial venous thromboses and one deep venous thrombosis, equivalent to an event rate of 5.15%. No adverse events were observed.5 This study presented evidence to support that French maritime pine bark extract can prevent dangerous blood clots during prolonged sitting.5

Guarding against Lower Leg Fluid Accumulation

The same scientific team conducted a similar study to evaluate ankle swelling during long-haul air flights.24 Aside from being uncomfortable, ankle swelling is an excellent indicator of poor blood return up the veins of the legs, making it a great way to assess the risk of deep vein thrombosis.

The team enlisted 169 volunteers at risk of deep vein thrombosis due to remaining seated during a long flight. The same dose of 200 mg of French maritime pine bark extract was given at the same intervals as in the earlier study. Using standard measurements, edema (swelling) was measured before and after flights, as well as the rate of swelling.
Compared to preflight levels, the edema score in placebo subjects was increased by 58.3%. The edema score in the French maritime pine bark extract-supplemented volunteers increased only 17.9%. This dramatic decrease in edema score represented a significantly reduced thrombotic risk.24 Similarly, the ankle swelling rate was increased during the flight by a mean of 91% in controls, while the French maritime pine bark extract recipients showed only a 36% increased ankle swelling rate, a much safer rate.24

These studies showed the capacity of French maritime pine bark extract to reduce the risk of deep vein thrombosis without any of the side effects of anti-clotting drugs. However, the question remained as to whether this extract was superior to compression stockings, which are known to be safe but not necessarily effective in reducing post-thrombotic syndrome. Post-thrombotic syndrome is a common complication of an otherwise localized deep vein thrombosis, in which blood pools in the affected leg because it cannot return to the heart—causing skin swelling, thinning, and discoloration and sometimes, painful, infection-prone leg ulcers.

To settle this issue, scientists conducted a study comparing French maritime pine bark extract to compression stockings in their ability to prevent post-thrombotic syndrome.25 In this study, 156 patients who had experienced a single, major episode of deep vein thrombosis were divided into three groups. For 12 months, one group used the compression stockings, the second group took 50 mg of French maritime pine bark extract three times daily, and the third group used both the stockings and the same daily French maritime pine bark extract regimen.28 The researchers measured edema score, ankle circumference, and volume of the previously deep-vein thrombosis-afflicted leg compared with the other leg.

Their findings soundly confirmed the superior effectiveness of French maritime pine bark extract:25

1. In the compression stocking-only group, two new deep vein thrombosis cases occurred in the first six months, compared with no new deep vein thrombosis cases in either of the pine bark extract groups.

2. After the first six months, French maritime pine bark extract alone proved significantly more effective than compression stockings alone for relieving symptoms of edema (while the combination of both was better still).

3. Leg volume and ankle circumference measurements showed French maritime pine bark extract-plus-stockings to be superior to stockings alone.

4. In the microcirculation (blood flow in the tiniest vessels), French maritime pine bark extract—but not compression stockings—enhanced blood flow, raised oxygen levels in circulating blood, and decreased carbon dioxide levels, demonstrating improved function.

Human Clinical Trial Combining Nattokinase and French Maritime Pine Bark Extract

Scientists set out to test a formulation combining nattokinase and French maritime pine bark extract in a randomized, placebo-controlled human trial.6 All 204 passengers on a New York-to-London flight were instructed in deep vein thrombosis-prevention techniques: isometric exercises, standing and moving for

Risk Factors for Deep Vein Thrombosis

Deep vein thrombosis (DVT) and the deadly pulmonary embolism it can trigger (venous thromboembolism) is often the result of spending long periods sitting or standing. But other factors can put some individuals at an especially high risk. These risk factors include:27

- use of oral contraceptives,
- advanced age,
- smoking,
- pregnancy,
- severe obesity,
- limited mobility,
- recent surgery or trauma,
- sitting on long-haul flights, and
- cancer.
five to ten minutes, and keeping hydrated. Passengers were randomly assigned to receive either capsules of placebo or capsules of the proprietary blend of nattokinase and French maritime pine bark extract. All subjects took the blend two hours predeparture and again six hours later. Ultrasound scans were done before and after the flight to detect clots.

Passengers taking the supplement had zero deep vein thrombosis cases. However, five of the control passengers developed a deep vein thrombosis, and two others developed superficial clots, for a total of seven events—a 5.4% DVT rate among controls, compared to a 0.0% rate among the test subjects. The scientists also measured leg swelling, which was equal between the two groups preflight. Edema increased by 12% in the controls. But edema decreased by 15% in the supplemented passengers.

These findings confirm that this novel dual-extract formula helps prevent deep vein thrombosis in individuals who spend long periods sitting and reduces the risk of sudden death from a resultant pulmonary embolism. No adverse side effects were reported.

Summary

Deep vein thrombosis is a serious risk for anyone who spends long periods sitting and can lead to a deadly pulmonary embolism.

The two novel ingredients described in this article were shown to protect against venous thrombosis.

These extracts inhibit unwanted venous clot formation, improve leg microcirculation, and promote vessel-wall elasticity.

In a placebo-controlled human trial, these two nutrients prevented deep vein thrombosis in all volunteers who supplemented with it and decreased leg swelling.

While the medical establishment provides no safe or practical solutions, these two agents are available to augment the effects of taking frequent breaks from any kind of prolonged sitting.

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

Thromboembolism

This diagram illustrates normal venous blood flow, venous obstruction by a thrombus formation, and the rupture of the thrombus. A blood clot such as this forming in the leg of an individual with deep vein thrombosis (DVT) can break off without warning and lodge in the lungs or other organs, often resulting in death.
To avoid an embolism, study co-author Dr. Hiroyasu Iso recommends that, while watching TV, you get up “after an hour or so” and “stand up, stretch, walk around. Or while you’re watching TV, tense and relax your leg muscles for five minutes.”

References

Too Much TV Can Lead to Pulmonary Embolism

Our parents always used to say that watching too much TV wasn’t good for us. It turns out they may have been more right than they realized. A recent study published in the journal Circulation found that a sedentary, couch-potato lifestyle can lead to fatal blood clots.28

Starting in 1988, researchers from Japan’s Osaka University recruited more than 86,000 subjects and had them keep track of how much television they watched over a two-year period. After 19 years, researchers found that 59 study participants had died of a pulmonary embolism—a blood clot in their lungs. Lack of activity causes a person’s blood flow to slow down, which can lead to a blood clot, usually in the pelvis or leg. The blood clot can then travel to the lungs and become wedged in a small blood vessel in the lungs with fatal results.

The researchers calculated that the study subjects had a 40% increased risk of incurring a pulmonary embolism for every two hours of TV they watched each day beyond a threshold of 2.5 hours. The risk for participants who watched five hours or more was 2.5 times greater than the risk for those who watched under 2.5 hours.

To avoid an embolism, study co-author Dr. Hiroyasu Iso recommends that, while watching TV, you get up “after an hour or so” and “stand up, stretch, walk around. Or while you’re watching TV, tense and relax your leg muscles for five minutes.”

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<td>This glycation-protection formula helps maintain cellular function, protein structural integrity, and mitochondrial biogenesis. It contains high potency carnosine along with R-lipoic acid, PQQ, benfotiamine, luteolin, and taurine. These ingredients cost far more if taken separately.</td>
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<td><strong>Mega Green Tea Extract</strong></td>
<td>725 mg, 100 lightly caffeinated vegetarian capsules</td>
<td>Item #00953</td>
<td></td>
<td>$30</td>
<td>$16.20 (four-bottle purchase)</td>
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<td>A highly concentrated 98% polyphenol extract delivering 45% of the health-promoting catechin EGCG.</td>
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<tr>
<td><strong>Life Extension Mix™</strong></td>
<td>315 tablets, Item #02155</td>
<td></td>
<td>$80</td>
<td>$46.80</td>
<td>$39.38 (four-bottle purchase)</td>
</tr>
<tr>
<td>This high-potency multinutrient now includes apigenin, which has been shown to ease inflammation and support healthy cell growth and differentiation, and SelenoExcell®, a natural selenium source. (Also available in capsule and powder form.)</td>
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<tr>
<td><strong>AMPK Activator</strong></td>
<td>90 vegetarian capsules</td>
<td>Item #01907</td>
<td></td>
<td>$48</td>
<td>$29.70 (four-bottle purchase)</td>
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<td>Activating AMPK &quot;turns off&quot; many of the destructive factors of aging, enabling cells to return to their youthful vitality. Research shows that the two plant extracts contained in this formula promote AMPK activation.</td>
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<td><strong>Cognitex® with Brain Shield®</strong></td>
<td>90 softgels, Item #01896</td>
<td></td>
<td>$60</td>
<td>$35.10</td>
<td>(four-bottle purchase)</td>
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<td>Optimal support for the brain. Includes gastrodin, alpha-glyceryl phosphoryl choline, vinpocetine, phosphatidylserine, uridine-5'-monophosphate, and more. Available with or without pregnenolone.</td>
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<td><strong>Super K with Advanced K2 Complex</strong></td>
<td>90 softgels, Item #01834</td>
<td></td>
<td>$30</td>
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<td>(four-bottle purchase)</td>
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<td>Provides two forms of vitamin K2 (1,000 mcg of immediate-release MK-4 and 200 mcg of long acting MK-7), along with 1,500 mcg of K1.</td>
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<td><strong>Triple Action Thyroid</strong></td>
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<td>Item #02003</td>
<td></td>
<td>$36</td>
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<td>A combination of ashwagandha, guggul, and Korean ginseng extract work in synergy to support healthy thyroid function.</td>
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<td><strong>Memory Protect</strong></td>
<td>36-day supply, Item #02101</td>
<td></td>
<td>$24</td>
<td>$14.40</td>
<td>(four-box purchase)</td>
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<td>This new product contains microdose lithium and proline-rich polypeptide, which have been found to block and (in the case of proline-rich polypeptide) to reverse cognitive decline.</td>
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<td><strong>European Milk Thistle</strong></td>
<td>60 softgels, Item #01922</td>
<td></td>
<td>$28</td>
<td>$16.88</td>
<td>(four-bottle purchase)</td>
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<td>High-absorption phospholipid-enhanced formula delivers nearly 5 times more active components to the bloodstream to support detoxification processes as well as promote liver health and function.</td>
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<td><strong>Skin Restoring Phytoceramides</strong></td>
<td>350 mg, 30 vegetarian capsules</td>
<td>Item #01596</td>
<td></td>
<td>$25</td>
<td>$15.53 (four-bottle purchase)</td>
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<td>Oral phytoceramides derived from wheat can reach the skin’s deepest layers to offset the body’s natural decline with age.</td>
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<td><strong>ArthroMax® Herbal Joint Formula</strong></td>
<td>60 capsules, Item #02108</td>
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<td>$40</td>
<td>$24.30</td>
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<td>Studies have shown that this combination of three natural ingredients (Chinese skullcap, cutch tree and white mulberry) supports healthy joint function.</td>
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<td><strong>Super R-Lipoic Acid</strong></td>
<td>300 mg, 60 vegetarian capsules</td>
<td>Item #01208</td>
<td></td>
<td>$49</td>
<td>$30.38 (four-bottle purchase)</td>
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<td>Superior efficacy compared to alpha-lipoic acid—supplies 240 mg of stabilized R-lipoic acid.</td>
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<td><strong>Advanced Bio-Curcumin® with Ginger and Tumerones</strong></td>
<td>30 softgels, Item #01924</td>
<td></td>
<td>$30</td>
<td>$18.23</td>
<td>(four-bottle purchase)</td>
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<tr>
<td>Absorbs up to 7-times better, with added benefits of ginger and turmeric extracts.</td>
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<td><strong>Extend-Release Magnesium</strong></td>
<td>60 vegetarian capsules</td>
<td>Item #02107</td>
<td></td>
<td>$13</td>
<td>$7.88 (four-bottle purchase)</td>
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<td>Provides immediate-release magnesium citrate along with a 6-hour extended-release magnesium for optimal benefits.</td>
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These statements have not been evaluated by the Food and Drug Administration. These products are not intended to diagnose, treat, cure, or prevent any disease.
How Vegetable Extracts Protect Against Cancer

Apigenin is a polyphenol found in vegetables such as parsley and celery. It is receiving increased attention as a low-cost nutrient to protect against common cancers.

What makes apigenin so fascinating is how it functions to starve cancer cells, promote cancer cell destruction, and protect cellular DNA against environmental toxins (that can result in future malignancies).

Compounds such as indole-3-carbinol (I3C) are found in cruciferous vegetables. These cruciferous compounds have been shown to work in complementary ways with apigenin (non-cruciferous) to combat cancer and other age-related diseases.

According to a study published in the International Journal of Oncology:

“Cancer prevention through diet may be largely achievable by increased consumption of fruits and vegetables. Considerable attention has been devoted to identifying plant-derived dietary agents which could be developed as promising chemopreventives. One such agent is apigenin.”

1
Apigenin Protects Cells from Cancer

Apigenin fights oxidative stress and inflammation—two factors that play a role in cancer development.1-9 Oxidative stress and inflammation generate DNA damage that can lead to uncontrolled proliferation of non-functioning cells, i.e., cancer.10,11 But that’s just one aspect of how apigenin functions.

Unique mechanisms of apigenin have led researchers to intensely evaluate it.12 What they’ve discovered is that apigenin has a host of other anticancer properties:

1. Apigenin Stops Cancer Cells from Replicating

Apigenin attacks cancer at a variety of stages and in different ways. At every step, apigenin seems to aggressively stop cancer’s various pathways. Apigenin has the ability to stop cancer cells from replicating, to reduce their invasiveness, and to slow their growth. Scientists believe this is largely related to its ability to shut down nuclear factor-kappa B (NF-kB).13,14 When activated, NF-kB leads to a flood of proinflammatory molecules that can promote tumor growth and the spread of cancer.15,16

In an animal study of nonmelanoma skin cancer, apigenin inhibited the production of inflammatory signaling molecules known to promote tumor proliferation.17

2. Apigenin Causes Cancer Cells to Die Off

In a cell study of chronic lymphocytic leukemia (a common malignancy in older adults), apigenin prevented the DNA mutations tied to cancer, while promoting the naturally-occurring cell death (apoptosis) that cancer cells otherwise evade.18

Apigenin may promote apoptosis by reactivating an important cancer-suppressor gene called p53.19 Inactivation of p53 is a common feature of cancer cells, which results in the cell’s loss of control over when to replicate and when to die naturally.20 By restoring p53 activity, apigenin essentially allows cancer cells to die a natural death.21

3. Apigenin Cuts off Cancer Cells’ Ability to Grow

In additional to causing cancer cells to die off naturally, studies have also shown that apigenin modulates a host of factors that can give cancer a promotional boost once it gets started.

Apigenin has repeatedly been shown to regulate the insulin-like growth factor signaling pathway known to promote the growth of prostate cancer cells when deregulated. Under the influence of apigenin, those cells quit their explosive growth and proceed to kill themselves off by apoptosis.12

4. Apigenin Starves Cancer Cells

Finally, apigenin appears capable of literally starving cancer cells into submission through several unrelated, but complementary, mechanisms.

First, apigenin suppresses the expression of a protein essential for transporting glucose into cancer cells.22,23

Apigenin further promotes this “energy crisis” by going after cancer cells’ mitochondria, the tiny intracellular power plants that generate energy. When mitochondria from human liver cancer cells were treated with apigenin, their membranes became leaky to the extent that it destroyed affected cancer cells.24

Based on the mechanisms by which apigenin thwarts cancer at every turn, new human studies are needed to further explore this impressive cancer-destroying polyphenol. The underlying mechanisms discussed here have been found to be effective in animal models of leukemia and the following solid tumor malignancies:

- Prostate14,25
- Larynx (voice box)22
- Leukemia18
- Liver (hepatocellular carcinoma)26
- Pancreatic9
- Skin17
- Breast27
Apigenin Protects Brain Cells

Alzheimer’s and Parkinson’s are two common neurodegenerative diseases. Together, they cause untold misery for patients, their families, and their other caregivers. Numerous studies show apigenin’s ability to reduce some of the known contributors to neurodegeneration.

For example, apigenin fights excitotoxicity, the neuronal damage that occurs over a lifetime of intense brain cell stimulation. This is critical since excitotoxicity promotes brain cell death and dysfunction in both Alzheimer’s and Parkinson’s diseases. Apigenin also was shown to protect dopamine-producing cells of deep brain centers affected by Parkinson’s disease. This important action reduces neuroinflammation and the activation of inflammatory cells in the brain.

When applied to brain cells in culture, apigenin protected those cells from toxicity induced by beta amyloid, the toxic “junk” protein found in abundance in the Alzheimer’s brain. Finally, given the importance of elevated blood sugar in the development of Alzheimer’s (it has been called “Type III diabetes” by some researchers), it is interesting to note that apigenin attenuates the cognitive decline seen in adult diabetic rats. Animals treated with apigenin have demonstrated improved learning and memory retention in a mouse model of Alzheimer’s disease.

Health Benefits of Vegetable Extracts

• Vegetable extracts present in broccoli, celery, parsley, kale, Brussels sprouts, and many others—have long been revered for their health-promoting benefits.

• It is now recognized that four compounds, apigenin, I3C, DIM, and BITC, are responsible for the majority of that protection, and in very specific and complementary ways.

• All four have powerful cancer-protective effects, attacking and preventing malignancies through a multitude of overlapping mechanisms.

• Apigenin also has exceptional cardiovascular, metabolic, and neuroprotective properties, while I3C/DIM promote cardiovascular and liver health.

• Consumption of these plant compounds provides broad-spectrum protection against many of the most common symptoms of aging.
Apigenin, I3C, DIM, and BITC are compounds found in vegetables that offer wide-ranging protection against the factors that damage our DNA.

Apigenin Promotes Cardiometabolic Health

Oxidative stress and inflammation are deadly to heart and blood vessel cells. Inflammation/oxidation can also induce the kind of damage in liver and fat tissues that can promote weight gain, diabetes, and other metabolic changes that raise cardiovascular disease risk. Apigenin can contribute substantially to protecting against all of these effects.

At the most fundamental level, apigenin has been shown to prevent new cholesterol molecules from being synthesized in liver cells, which can reduce the amount of cholesterol in circulation.\(^{37}\) In a similar fashion, animal studies show that apigenin lowers blood sugar levels by decreasing insulin resistance, decreasing elevated insulin levels, and decreasing the formation of new glucose in the liver.\(^{38,39}\)

Studies in diabetic rats reveal that apigenin can improve the function of the endothelial cells that line arteries and directly control blood flow and pressure.\(^{39}\)

Preclinical studies show that apigenin helps protect the heart muscle against ischemia/reperfusion injury, the serious damage that occurs in the minutes to hours following a heart attack or stroke, when oxygen-starved (ischemic) tissue is suddenly flooded with oxygen-rich blood as circulation is restored (reperfusion).\(^{40-42}\)

I3C: Complementary Tissue Protection from Cruciferous Vegetables

I3C (indole-3-carbinol) is a major component found in cruciferous vegetables. While I3C has many overlapping activities with apigenin, it also adds a substantial number of unique functions.\(^{43}\) Many of these benefits are also produced by 3,3’-diindolylmethane (DIM), a condensation product of I3C molecules.\(^{44,45}\)

Through these unique functions, I3C and DIM provide complementary protection against cancer, heart disease, and more. Let’s take a look.

I3C/DIM: Unique Protection against Cancer

The most promising of I3C’s cancer-fighting properties has to do with its impact on enzymes that metabolize the sex hormones estrogen and testosterone.\(^{46}\)

For example, I3C and DIM have been found to reduce a carcinogenic form of estrogen called 16-alpha-hydroxyestrone while boosting beneficial 2-hydroxyestrone. A large study of over 10,000 women showed that those with highest amounts of 2-hydroxyestrone compared to 16-alpha-hydroxyestrone had a remarkable 42% lower risk of breast cancer.\(^{47}\) Since hormone-dependent cancers such as breast and ovarian tumors thrive on unhealthy hormone balances, this is an important step in cancer prevention.\(^{48-50}\)

There’s also considerable evidence that I3C modifies the function and expression of estrogen receptors on cells. Studies show that I3C downregulates the expression of estrogen receptor alpha, which...
is known to cause cancer-promoting cellular changes when it is overexpressed.\textsuperscript{50-53} Turning down estrogen receptor alpha allows greater influence for the protective estrogen receptor beta, which further reduces estrogen-dependent cancer risk.\textsuperscript{50}

**I3C/DIM Promote Cardiometabolic Health**

I3C and DIM have multiple antiobesity effects. Obese mice treated with I3C showed decreased body weight, fat accumulation, fat-mediated release of inflammatory cytokines, and fat infiltration by inflammatory cells—all of which produce obesity-associated health risks.\textsuperscript{54-57}

I3C and DIM also reduce blood sugar, insulin, and markers of sugar-induced protein damage in mice on high-fat diets. These are effects that contribute to reduced atherosclerosis and cardiovascular disease risks.\textsuperscript{58,59}

**I3C/DIM Provide Wide-Ranging Liver Protection**

I3C and DIM also have impressive liver-protective properties. These are partly due to their ability to suppress oxidative stress, in part through their activation of AMPK, and in part through their anti-inflammatory properties.\textsuperscript{60-62}

These mechanisms of action protect the liver against fat accumulation, inflammatory changes, malignancies, and even fibrosis, the scarring and toughening that precedes liver failure.\textsuperscript{63}

In fact, animal studies show that I3C and DIM can prevent fatty liver disease caused both by alcohol and a high-fat diet.\textsuperscript{60,61}

**BITC Offers Complementary Cancer Protection**

Benzyl isothiocyanate (BITC) is another compound found in cruciferous vegetables that provides cancer protection that complements those of other cruciferous compounds.

One of its most startling properties is its ability to inhibit cancer stem cells. Many malignancies recur or fail to respond to treatment because of just a few cancer stem cells that can “hide out” and emerge after treatment is complete.

Both lab and animal studies show that BITC inhibits breast cancer stem cells, while also suppressing cell signaling molecules that contribute to the “stemness” of such cells.\textsuperscript{64-66} As a result, BITC has been found to be effective against numerous types of cancer.

For example, an animal study demonstrated that BITC reduced the number of prostate cancers in cancer-prone mice.\textsuperscript{67} BITC also prevents the stimulation of breast cancer growth induced by high-fat diets, prevents invasion and new blood vessel formation in brain and head and neck cancers, and induces cell death by apoptosis in lung cancers.\textsuperscript{68-71}

**Summary**

Apigenin, I3C, DIM, and BITC are compounds found in vegetables that offer wide-ranging protection against the factors that damage our DNA.

These compounds work in a complementary way to protect our bodies against cancer, cardiovascular and metabolic diseases, neurodegeneration, and even liver disease.

Together, these botanical compounds represent the virtues of consuming more healthy vegetables in one’s everyday diet.

For those who cannot consistently eat large amounts of celery, parsley and other vegetables, apigenin is available in low-cost multinutrient formulas that provide a wide variety of beneficial plant extracts.

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.
References


Support Your Aging Immune System

Life Extension® researchers have developed an innovative formula with three natural extracts—**Pu-erh Tea**, **Cistanche**, and **Reishi Mushroom**—that supports a more youthful immune system.

**Pu-erh tea**
- Supports decreases in inflammatory IL-6 while boosting natural killer cells and naïve T cells.¹

**Cistanche**
- Supports longer life span in animals.²
  - Optimizes the ratio of CD4 to CD8 cells, indicative of a more youthful immune system.²

**Reishi**
- Helps reduce biomarkers of immune senescence.³

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**Immune Senescence Protection Formula™**
Item #02005 • 60 vegetarian tablets

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Non-GMO

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To order Immune Senescence Protection Formula™, call 1-800-544-4440 or visit www.LifeExtension.com

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These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.

References
It’s not easy to get in five servings of vegetables a day—and even if you do, cooking can destroy many of the protective compounds found in broccoli, Brussels sprouts, cauliflower, and celery.

**Triple Action Cruciferous Vegetable Extract** combines vital plant extracts that have been shown to protect cellular DNA.

The formula provides optimal potencies of cruciferous extracts like I3C (Indole-3-carbinol) and DIM (di-indolyl-methane) to favorably modulate estrogen metabolism, along with apigenin.

**To order Triple Action Cruciferous Vegetable Extract, call 1-800-544-4440 or visit www.LifeExtension.com**

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**Triple Action Cruciferous Vegetable Extract**
Item #01468 • 60 vegetarian capsules

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**Triple Action Cruciferous Vegetable Extract with Resveratrol**
Item #01469 • 60 vegetarian capsules

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Selenium is a trace mineral critical for human life.

While there are many different forms of selenium, not all of them provide the same health benefits. This article presents data on the unique benefits of selenium-enriched yeast.

While selenium can be found in foods such as Brazil nuts, pinto beans, and beef, the amount of selenium that is obtained from our diet is highly uneven. This is because the amount of natural selenium in the soil fluctuates from region to region.

Many areas of the United States such as Texas, the Southwest, lower Southeast and Northwestern mountain states have selenium deficient soil. Therefore foods grown in these regions will not be rich in selenium.¹

In the past year, two new studies reveal that selenium status is suboptimal in many people in the industrialized world, and that low selenium status raises the risk for colorectal cancers and cancers of the liver and gallbladder.²,³

Ample selenium has been shown to be a relevant factor in protecting against a uniquely male malignancy, prostate cancer.⁴-⁹

But men aren’t the only ones at increased cancer risk when their selenium levels drop, and prostate cancer is far from the only cancer affected by poor selenium status.
Back in 1983, a group of researchers began a human study to examine the effects of selenium-enriched yeast on skin cancer.

The researchers found that subjects supplementing with this yeast-based selenium had an approximately 46%-63% reduction in the risk of colorectal, lung, and prostate cancers, with a 50% reduction in the risk of mortality for all cancers. The results were later published in the Journal of the American Medical Association7 and made headline news stories around the world. This generated intense interest in the scientific community in the protective power of selenium. Selenium Lowers Cancer Risk

The association between inadequate selenium status and the risk for many different cancers naturally leads to the question, “Can supplemental selenium reduce cancer risk?”

The answer is that optimal selenium levels through supplementation provide a protective function against the risk of cancer.

Studies going back to the 1970s have generally supported supplemental selenium as a cancer risk-reducing intervention.

As mentioned near the beginning of this article, a randomized, controlled trial published in 1996 demonstrated that 200 mcg of selenium daily from selenium-rich yeast was associated with a 50% reduction in the risk of dying from cancer, a 37% reduction in the risk of developing cancer, and reductions of 58%, 63%, and 46% in the risks for developing colorectal, prostate, and lung cancers, respectively.7

Deeper analysis showed that, among men with baseline normal levels of prostate-specific antigen, or PSA, a marker of cancer risk, those in the treated group showed an overall 74% reduction in their risks of prostate cancer.8

Colon cancer is a selenium-responsive malignancy, as shown in a placebo-controlled 2013 study that supplemented active subjects with 200 mcg of selenium, along with zinc and vitamins A, C, and E over a 5-year period.10

These study subjects consisted of 411 people with polyps removed during screening colonoscopy, indicating their higher risk for colorectal cancers.

In the supplemented group, 38 had a recurrence of polyps, while 62 recurred in the placebo group. This worked out to a 39% reduction in the risk of recurrence in those who supplemented with selenium and vitamins, compared with un-supplemented placebo recipients.

A 2015 study shows that cervical cancer may also be preventable with selenium supplementation.11

In this study, 56 women diagnosed at biopsy with cervical intraepithelial neoplasia (precancerous lesions) were randomly assigned to receive 200 mcg of selenium from yeast or a placebo, daily for 6 months.

The findings showed that 88% of supplemented women had regression of their precancerous lesions, compared with only 56% in the placebo group. This significant difference was accompanied by decreases in fasting blood sugar, insulin, and insulin resistance, all factors associated with increased cancer and metabolic risks.
Some insight into how selenium supplementation works to reduce cancer comes from a study of blood cells from hemodialysis patients, who are at known increased risk for DNA damage, the precursor of new cancers.\(^{12}\)

Forty-two dialysis patients randomly received either selenium-rich yeast or a placebo of standard yeast for 3 months.

The dialysis patients had significantly lower selenium levels than did healthy controls, as expected, but these rose significantly with supplementation.

Markers of DNA damage in circulating white blood cells (a good indicator of damage throughout the body) were three times higher in dialysis patients than in controls at the outset. After 3 months of selenium supplementation, DNA damage markers fell in the dialysis patients, to levels 16\% lower than those in healthy controls.

No similar changes were seen in the placebo recipients.

What You Need to Know

Selenium

- Selenium is a trace element and co-factor for more than 25 key enzymes that can’t function without it.
- Most of those enzymes are involved in systems that protect cells and their DNA from oxidative stress that, unopposed, leads to cancer.
- Studies show that those with lower selenium blood levels are at substantially increased risk for cancers in a variety of organs.
- Selenium supplementation, on the other hand, has been shown effective at reducing cancer incidence and producing protective biochemical shifts that shield cells and DNA from damage.
- No single selenium form, however, provides all of the cancer-preventing benefits available from selenium.
- Instead, a thoughtful regimen that includes multiple forms of selenium is most likely to offer comprehensive cancer-prevention properties.
Not All Selenium is the Same

There are several different forms of selenium and not all of them offer the same health benefits. For example, in a very large and well-publicized 2009 study, researchers from the Selenium and Vitamin E Cancer Prevention Trial (SELECT) reported that, after treating more than 35,000 men with one form of selenium (L-selenomethionine) alone (200 mcg), selenium plus vitamin E, or placebo, they found no significant differences in participants’ risk for prostate cancer in any of the groups compared with placebo.13

Because this was such a large study, it garnered an outsized share of attention, and many scientists and other readers came away with the impression that selenium has no role in cancer prevention. It should be noted that multiple scientific studies dating back to the 1970s show that different forms of selenium provide a spectrum of protection against cancer. Life Extension® long ago discussed the importance of including more than one form of selenium in one’s daily supplement program.

Selenium in a variety of forms has been shown to produce significant reductions in cancer risks.

One form of selenium that has received relatively little attention is selenium-enriched yeast, obtained from high-selenium brewer’s yeast. The study discussed near the beginning of this article, which involved 1,312 patients over a total of 8,271 person-years, found that daily supplementation with selenium-enriched yeast (200 mcg/day), had a 50% reduced risk of dying from cancer, and a 37% decreased risk of developing cancer, compared with placebo recipients.7

Further, with regard to specific cancers, the study found reductions of 46%, 58%, and 63% in the risks of lung, colorectal, and prostate cancers, respectively.7

Selenium Status and Cancer Risks

As of this writing, selenium status has been significantly associated with lower cancer incidence, as shown in the following table:

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<th>Type of Cancer</th>
<th>Impact of Selenium Status</th>
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<tr>
<td>Bladder18</td>
<td>39% reduction with higher selenium levels</td>
</tr>
<tr>
<td>Lung19</td>
<td>90% reduction with higher selenium levels</td>
</tr>
<tr>
<td>Larynx (throat)19</td>
<td>77% lower with higher selenium levels</td>
</tr>
<tr>
<td>Prostate4</td>
<td>71% reduction with higher selenium levels</td>
</tr>
<tr>
<td>Head-and-Neck21</td>
<td>45% reduction with higher selenium levels</td>
</tr>
<tr>
<td>Lung20</td>
<td>140% higher with low selenoprotein levels</td>
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Preventing cancer requires a multifactorial approach. One mechanism involved in cancer development is oxidative stress and the DNA damage that it causes. Selenium is a natural element capable of fighting oxidative stress and has been shown to be effective in preventing cancer and the biochemical changes that precede it.

But because one large study found no significant effects on prostate cancer risks using just one form of selenium (L-selenomethionine), many have turned away from this valuable mineral. The fact is that selenium in its different forms has demonstrated strong cancer-preventive effects. Recent studies amplify the importance of maintaining satisfactory selenium levels. Don’t be fooled by spurious science, often based on flawed studies. Selenium-enriched yeast supplements have demonstrated strong potential for reducing cancer risk. Other forms of selenium contribute to enhanced immunological destruction of early cancers, trigger cancer cell “suicide,” and protect tissues from oxidative stress.

Overall, the evidence points to a daily selenium dose of 200 mcg to reduce cancer risk, which should ideally utilize multiple forms to obtain comprehensive protection.

No single nutrient should be relied on to protect against cancer. This magazine consistently reminds readers of dietary and lifestyle factors that play huge roles in one’s risk of developing malignant disease.

Different Forms of Selenium

The different forms of selenium have been shown to provide various protective properties against cancer, oxidative stress, DNA damage and even shielding against toxic metal poisoning. For this reason, it is recommended that it is best to ingest a 200 mcg “cocktail” daily of various selenium forms to provide broad-spectrum coverage against the diseases of aging.\textsuperscript{14,15}

Here are brief descriptions of well-studied forms, highlighting how each can contribute to selenium-based protection against cancer:

**Sodium selenite** is a simple chemical salt of sodium and selenium. This form of selenium has the ability to ramp up our natural immune system to find and destroy tumor cells.\textsuperscript{16,17}

**Selenium-methyl L-selenocysteine** triggers cancer cell suicide (apoptosis) and also acts on more advanced cancer cells that have lost the fundamental “suicide gene.”\textsuperscript{14}

**Selenium from yeast** provides advanced protection against oxidative stress and resulting DNA damage, to reduce the risks that a cell will undergo transformation into a malignancy.\textsuperscript{6}

Because optimum cancer prevention requires protection from DNA damage, enhanced self-destruction of malignant cells, and a boosted immune system, the benefits of using multiple forms of selenium are obvious.
If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

References

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Warning to Coumadin® (warfarin) Drug Users: Patients prescribed vitamin K-antagonist anticoagulant prescription drugs like warfarin should consult their physician before taking vitamin K supplements like Super K and Super Booster. There is evidence, however, that users of drugs like warfarin could benefit from a consistent low-dose of supplemental K. Ask your doctor if you can take a low dose (45 mcg a day) of vitamin K2 in the long-acting MK-7 form for the purpose of stabilizing your INR levels and also protecting your body against long-term vitamin K deficit. Do not initiate any form of vitamin K supplementation without full cooperation of your treating doctor, as your doctor may need to increase your dose of warfarin to compensate for your vitamin K supplement. Life Extension® provides several forms of low-dose vitamin K for physician consideration.

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Quercetin Protects Against Pesticides’ Damaging Effects

While pesticides kill pests, they also pose danger to humans.

Unprotected human exposure has been linked to cancer, endocrine complications, respiratory disorders, and organ failure.¹

More worrisome are studies showing pesticide exposure can increase risk of neurodegenerative diseases.²-⁴

A number of studies, some published in 2016, indicate that the plant flavonoid quercetin can inhibit the damaging effects of pesticides.
Quercetin Protects Against Pesticides

In various studies conducted on rats, quercetin was shown to provide substantial protection against a number of pesticides.

A June 2016 study in the journal Human & Experimental Toxicology found that quercetin had protective effects against toxicity induced by a mixture of organophosphate pesticides, which were originally developed as biological warfare agents.

The United States Environmental Protection Agency has indicated that organophosphate pesticides are dangerous not only to humans but also to bees and wildlife. The study showed that quercetin can protect against organophosphate pesticide toxicity through the following mechanisms:

- Preserving energy, fatty acid, and sex hormone metabolism
- Inhibiting oxidative stress
- Protecting against DNA damage
- Preserving kidney and liver function

Also, although there is no specific treatment for poisoning by the pesticide paraquat, researchers are investigating quercetin's ability to minimize oxidative stress through its free-radical scavenging properties as a possible therapy.

In a 2016 study, scientists demonstrated that quercetin protects cells against oxidative stress and cellular death caused by dichlorvos, another organophosphate pesticide. In lab cells exposed to this pesticide, pretreatment with quercetin significantly reduced dichlorvos-induced cell death, inhibited ROS (reactive oxygen species) generation, reduced levels of malondialdehyde (a marker of oxidation), and modulated the activities of two primary antioxidants (catalase and superoxide dismutase).

In the same year, another rat study produced very similar findings. Various parameters representing the negative health effects of a mixture of pesticides were ameliorated when quercetin was simultaneously administered.

As the population ages, researchers have increasingly focused on the potentially devastating brain effects of pesticides.

Pesticides are found in our food, air and water. Harmful chemicals are so abundant in our environment that we often absorb them without eating food.

With advances in manufacturing, many pesticides are no longer sprayed on crops. Instead, systemic pesticides are mixed in with fertilizer and absorbed by plants through their vascular system. This makes it impossible for consumers to wash off pesticide residue because it’s within the fruits and vegetables that you eat.

While everyone is vulnerable to the dangers of pesticides, those especially at risk include children, pregnant women, sick persons, and the elderly. Pesticide exposure can result in conditions ranging from learning disabilities to Parkinson’s disease and cancer. Because many different types of pesticides are used by farmers, exposure can overwhelm our efforts to stay healthy. Even everyday lawn chemicals pose risks and can remain in our body for decades.

Quercetin, a flavonol occurring in certain fruits and vegetables, shows promise in animal studies to protect against some of the dangers of pesticides. Until farmers completely stop their use, we are always at risk. But initial studies in the laboratory show that quercetin can provide some measure of cellular protection.
QUERCETIN PROTECTS AGAINST PESTICIDES’ DAMAGING EFFECTS

Recent studies link chronic pesticide exposure to increased prevalence of dementia, including Alzheimer’s disease.

Pesticides Linked to Alzheimer’s Disease

About 5.4 million Americans live with Alzheimer’s disease,¹⁸ the sixth leading cause of death in the US.¹⁹ After age 65, the risk of Alzheimer’s disease or vascular dementia doubles every five years.²⁰

Early-stage Alzheimer’s disease patients are usually anxious, well aware that something is wrong. Short-term memory is poor and patients have difficulty finding ordinary words. Crippling depression sets in with the awareness that something is being lost that will never be regained.

A great deal of Alzheimer’s disease research has gone into finding the genes that increase susceptibility. However, multiple other factors are implicated, including chronic infections, declining hormone levels, inflammation, mitochondrial dysfunction, oxidative stress—and toxic chemicals.²¹-²⁶ Chief among this latter group are the over 1,000 chemicals that comprise pesticides, use of which has quintupled since 1945.²⁷

Recent studies link chronic pesticide exposure to increased prevalence of dementia, including Alzheimer’s disease.²,²⁸ Organophosphate pesticides have been shown to lead to microtubule derangements and tau hyperphosphorylation—a hallmark of Alzheimer’s disease. (Phosphorylation is the addition of a phosphate group to a molecule, which turns a protein enzyme on or off, altering its activity.) This mechanism of action suggests that, at the cellular and molecular level, these pesticides may at least partly account for the neurodegeneration of Alzheimer’s disease.²⁸

What You Need to Know

Quercetin vs. Pesticides

- Although designed to kill pests, pesticide compounds can also trigger negative health effects in humans.
- Excessive or prolonged exposure to pesticides has been linked to cancer, endocrine complications, infertility, respiratory disorders, organ failure, birth defects, mood changes, and Alzheimer’s disease.
- Prominent among the flavonoids produced by plants to protect themselves from destructive forces is the potent compound quercetin, which conveys similar protection to humans.
- Accumulating evidence demonstrates that quercetin protects against many of the biological effects of pesticides.

Scientists evaluating 86 Alzheimer’s disease patients and 79 controls found that serum levels of dichlorodiphenyldichloroethylene (DDE)—a metabolite of the pesticide dichlorodiphenyltrichloroethane (DDT)—were 3.8-fold higher in Alzheimer’s disease patients.²⁹

Although banned in the US in 1972, people still come into contact with DDT through imported foods or by living near farmlands where DDT was formerly sprayed or near industrial sites where manufacturers dumped DDT-containing products.³⁰-³³
Similarly, exposure to the pesticide beta-hexachlorocyclohexane (beta-HCH) was found to be detectable in 76% of Parkinson’s disease patients, compared to 40% of those without the disease. Based on serum levels of this pesticide, researchers could predict a Parkinson’s diagnosis with a high degree of confidence.34

**Quercetin’s Broad Brain-Protective Effects**

Exposure to pesticides can result in a range of very subtle neurological symptoms that are not commonly recognized by the medical community, but that can be devastating to the individual, especially over time. These include loss of memory, poor coordination, reduced stimuli-response speed, decreased vision, altered or uncontrollable moods or other behavior, and impaired motor skills.35

Rapidly accumulating evidence has identified quercetin as a potent neuroprotective nutrient. **Quercetin** protects brain cells from excitotoxicity, the damage done by the repeated excitatory electrical impulses observed in Alzheimer’s and other neurodegenerative diseases.16-39 Its potent antioxidant mechanisms reduce toxicity of beta amyloid proteins that accumulate in the brain, eventually producing memory loss and dementia.40,41 Quercetin has also been found to prevent brain-cell death in animal models of Parkinson’s disease.42

**The Alzheimer’s Disease Risk in Your Home and How to Protect Yourself**

When thinking of pesticides, most people focus on the over 1,000 chemicals used in agriculture today. But these 1,000 chemicals have been formulated into over 20,000 products—a fifth of which are designed for nonagricultural uses—in homes, gardens, schools, playgrounds, offices, golf courses, and hospitals. So microscopic traces of pesticides easily drift into homes. Studies show that detectable levels of these compounds can be found in many people, even newborns.27

Just as they do in pests, pesticides can affect the human nervous system. These common pesticides include:51

- **Organophosphates**, a synaptic poison that damages the junction between two nerve cells,
- **Carbamates**, a synaptic poison,
- **Pyrethroids**, an axonic poison that damages axons that conduct impulses away from the cell,
- **Avermectins**, an axonic poison,
- **Imidacloprid**, a synaptic poison, and
- **Fipronil**, an axonic poison.

**Quercetin** has been shown to inhibit pesticide damage by preserving energy, fatty acid, and sex hormone metabolism, inhibiting oxidative stress, protecting against DNA damage, and preserving kidney and liver function.13

In addition, research findings show that quercetin is associated with improved cardiovascular health, reduced cancer risk, milder allergic responses, and improved resistance to infection after extensive exercise.52 And, a recently published study demonstrated that quercetin enhanced memory recall in a mouse model of early-stage Alzheimer’s disease—as well as in human, early-stage Alzheimer’s disease patients.53
Quercetin’s Potent Neuroprotection

Additional to stimulating cellular defenses against oxidative stress, quercetin activates sirtuins (SIRT1) and induces autophagy (removal of cellular waste debris)—both possible mechanisms for its neuroprotection.49

This same review found that the neurotoxicity of several toxic agents, including polychlorinated biphenyls, MPTP (1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine)—and the insecticide endosulfan—was decreased by quercetin in vivo. Findings showed that “...quercetin ameliorates Alzheimer’s disease pathology and related cognitive deficits in an aged...Alzheimer’s disease mouse model.”49

Quercetin was shown to protect brain mitochondria against endosulfan. This pesticide normally induces oxidative stress in brain mitochondria by significantly lowering levels of catalase, superoxide dismutase (SOD), and glutathione. In rats, the pesticide resulted in swelling of mitochondria and higher levels of the oxidative stress marker malondialdehyde.50

Pretreatment with quercetin was demonstrated to protect the brain mitochondria from oxidative stress, lipid peroxidation, and mitochondria swelling normally induced by endosulfan. The activities of the natural enzymes systems and the mitochondrial content of glutathione and malondialdehyde were all returned to healthy levels. The study author concluded:

“Thus, although endosulfan can have neurotoxic effects in brain[s of] rats, this toxicity can be prevented by quercetin.”50

Summary

Pesticide compounds may increase the risk of diseases most commonly associated with aging, including neurodegenerative disorders.

Plants naturally produce molecules known as flavonoids to allow them to withstand a host of destructive forces, including chemical toxins.

New and accumulating evidence demonstrates that the plant flavonoid quercetin delivers protection—for the body and the mind—against many pathological effects associated with pesticide exposure.

The typical daily supplemental dose of quercetin is 150-400 mg. It is often included in resveratrol formulas because of evidence showing that quercetin and resveratrol provide complementary health benefits when taken together.

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.
QUERCETIN PROTECTS AGAINST PESTICIDES' DAMAGING EFFECTS

References

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Scientists have discovered that quercetin, a compound found in certain foods, can safely remove tired, aging (senescent) cells from the body, thereby making room for younger, more vital cells.

A number of studies suggest that quercetin may slow aging and reduce the risk of age-related factors.¹²³

References

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PQQ Reduces Arthritis Inflammation

Pyrroloquinoline quinone, or PQQ, is a vitamin-like compound that has demonstrated impressive biological effects. It is found in tiny quantities in plant foods.1

PQQ is responsible for creating new mitochondria as well as maintaining existing mitochondria within the cell.2 PQQ’s unique abilities have led many researchers to believe it can slow down the progression of aging.

Past studies have shown that PQQ can improve cardiovascular and brain health.3-8 More recent research has shown that PQQ can inhibit breakdown of healthy bone.

The latest findings indicate that PQQ has the potential to decelerate the deterioration of joints in rheumatoid arthritis and osteoarthritis.10,11

Arthritis is a leading cause of disability in the US.12 An urgent need exists to find treatments to prevent or delay its onset. Recent studies published in the journal Inflammation indicate PQQ may very well exert a protective effect in the joints.10,11
**Rheumatoid Arthritis**

Rheumatoid arthritis occurs when the body’s immune system mistakenly attacks the cells in its joints. This leads to the release of inflammatory cytokines and enzymes that damage not just the cartilage, but also the bone. The disease does not just manifest in the joints. It produces a dangerous amount of inflammation that affects the rest of the body. Rheumatoid arthritis increases the risk of cardiovascular disease. Those with rheumatoid arthritis suffer an approximately 40% increased risk of overall mortality.\(^{13,14}\)

In response to the immune system's attack on joints, cells called fibroblast-like synoviocytes, which are found in the joints’ synovial fluid, release inflammatory molecules.\(^{15}\) Fibroblast-like synoviocytes can circumvent healthy cell turnover and instead release inflammatory molecules via a protein complex called NF-kappaB.\(^{10}\)

In one of the new studies from the journal *Inflammation*, researchers tested human fibroblast-like synoviocytes in vitro, or outside of the body. The scientists used an inflammatory agent to activate the release of cytokines from the fibroblast-like synoviocytes cells. In one of the groups of cells, PQQ was also added.\(^{10}\) The group of cells that did not receive PQQ had increased levels of proinflammatory cytokines. The cells that received the PQQ had a decreased production of the proinflammatory cytokines. In addition, PQQ was also able to halt the activation of NF-kappaB. The researchers also noted that PQQ may be able to attenuate certain enzymes (such as matrix metalloproteinases) that degrade a protein called type-II collagen present in our joints.

In a second part of this study, the researchers tested the effects of PQQ on two groups of mice with an animal model of rheumatoid arthritis. The scientists gave intraperitoneal injections of PQQ to one group of mice but not the other. After 45 days there was a dramatic difference with the PQQ-administered mice showing remarkable protection against inflammatory degeneration. The researchers observed narrowing of space between joints, increased inflammatory cell infiltration, and cartilage damage in the group that did not receive PQQ. Due to these impressive results, the researchers hypothesized that PQQ may be helpful in the treatment of other inflammatory conditions as well.

**Osteoarthritis**

Approximately 33% of Americans 65 and older are affected by osteoarthritis, making it the most common form of arthritis.\(^{18}\) It was believed that osteoarthritis was simply the result of age-related “wear and tear” of the joints, as well as the body failing to produce enough cartilage.\(^{17,18}\) Scientists now understand that the underlying causes of osteoarthritis are similar to that of rheumatoid arthritis.\(^{19,20}\)

A group of researchers conducted a study to test the effects of PQQ for osteoarthritis treatment.\(^{11}\) In this study, human chondrocytes, cells that produce and maintain cartilage, were tested in vitro. The researchers manipulated the environment of the cells to create inflammation and mimic the effects of osteoarthritis. One group of cells received PQQ before the researchers manipulated the environment while the other group did not. The researchers observed increased levels of collagen-degrading enzymes (matrix metalloproteinase) in the group that did not receive PQQ. One of the pivotal biomarkers for inflammation is nitric oxide. Under normal physiological conditions nitric oxide acts as an anti-inflammatory as well as a vasodilator. But in certain circumstances, overproduction can lead to inflammation.\(^{21}\) In the group of cells that received PQQ, there was a significant reduction in joint-degrading enzymes and nitric oxide.
Research Update

Summary

PQQ has been shown to promote mitochondrial biogenesis (creation of new mitochondria), which is essential for older cells to retain youthful energy output. PQQ also protects against mitochondrial damage.  

The two new studies described in this Research Update provide preliminary data to pave the way for human trials in arthritis patients. PQQ was effective at suppressing cartilage-degrading enzymes and inflammatory markers in human cells and in the laboratory mouse model.

These findings open a pathway for clinical studies to evaluate whether PQQ can benefit osteoarthritis and rheumatoid arthritis patients. Those seeking to relieve arthritis symptoms today, without resorting to drugs, have access to a variety of low-cost nutrients with clinically validated effects.

Boswellia has also been shown to inhibit a type of matrix metalloproteinase cartilage-degrading enzyme. An impressive study on osteoarthritis patients showed that daily boswellia supplementation caused a 40.1% reduction on a pain scale compared to placebo in just 30 days.

Curcumin is the most active constituent of the turmeric root. A study tested the effects of curcumin or a nonsteroidal anti-inflammatory drug (NSAID) on 45 humans during a flare-up of rheumatoid arthritis. The researchers tested the patients’ blood for a systemic inflammatory marker called C-reactive protein and their pain score at the beginning of the study and then eight weeks afterwards. The results showed a 52% drop in C-reactive protein in the curcumin group. In the group receiving the NSAID, C-reactive protein increased by 1.5%. The NSAID group had a 42.1% improvement in pain scores, which was similar to the curcumin group, which had a 44.5% improvement (relief) in pain scores.

In addition, the researchers tested the effects of PQQ on mice who underwent a surgical procedure to induce osteoarthritis. Prior to treatment, one group received injections of PQQ with additional injections daily. The other group did not receive any. The group that received PQQ had significantly less severe cartilage damage compared to the group that did not receive PQQ.

Practical Approaches for Arthritis

The studies thus far are laboratory models and not directly relevant to human arthritis patients. PQQ’s most impressive results have been seen in studies showing its support for mitochondrial function, cardiovascular health, and brain health.

For those seeking natural approaches to combat arthritis, there are natural anti-inflammatory compounds in widespread use today including: undenatured type II collagen, boswellia, and curcumin.

Derived from chicken cartilage, undenatured type II collagen has robust data showing reduction in pain and increase in function in dogs, horses, and humans.

Results from one study showed, in just 90 days, a 40% reduction on a pain scale for osteoarthritis patients supplementing daily with undenatured type II collagen.

Boswellia is an Indian plant that has demonstrated potent anti-inflammatory properties. It has been shown to inhibit the pro-inflammatory enzyme 5-lipoxygenase or 5-LOX. This enzyme is responsible for facilitating the production of leukotriene, a pro-inflammatory compound that damages joints and cartilage.


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Metformin and Glaucoma

Glaucoma is the second leading cause of blindness in the world.¹

A medical group submitted a report to Life Extension Magazine® that provides persuasive data that the AMPK-activating drug metformin may be of significant benefit in protecting the eyes against the threat of blindness from open angle glaucoma. This report is written with some technical language that may make it challenging for some of our readers to understand.

We choose to publish it with the caveat that a succinct practical suggestion on how to use metformin to potentially reduce glaucoma risk be made in the introduction.

So here is what the medical group that authored this report recommends:

“This with elevated intraocular pressure (IOP) and/or glaucoma should ask their doctor about prescribing a modest 250 mg-500 mg dose of metformin twice a day after meals as it may have unique beneficial mechanisms in protecting against this blinding disorder.”

We welcome you to read the report beginning on the next page that describes underlying pathologies of open angle glaucoma and how metformin can help to counteract them.
Metformin is a decades-old antidiabetic drug used by millions of type II diabetics all over the world. It is inexpensive, quite commonly prescribed, and its effectiveness in reducing elevated blood glucose is well established.

In addition to its antidiabetic properties, metformin has also been shown to provide a number of other health benefits, including weight reduction, promoting longevity, and reducing cancer incidence, as well as reducing or eliminating chronic pain.\textsuperscript{2-7} It has calorie restriction mimetic cellular effects such as activating the energy enzyme adenosine monophosphate activated protein kinase (AMPK), and it favorably modulates certain genes thought to be involved in aging.\textsuperscript{8,9}

Now, besides all these reported health effects, a new study reports metformin also reduces the development of open angle glaucoma (OAG).\textsuperscript{10}
**Aqueous Humor, Its Functions and Its Relation to Glaucoma Production**

Glaucoma is a disease characterized by the increase of intraocular pressure due to various pathologies related to aqueous humor production, circulation, and drainage. In addition, the disease produces subsequent damage to the retina and atrophy of the optic nerve resulting in reduced visual acuity and ultimately leading to blindness.\(^{11}\)

Aqueous humor is a transparent, watery fluid that provides nutrition to the front part of the eye. It also transports the metabolic debris produced there to the bloodstream, thus maintaining transparency of the lens and cornea so light rays can pass through cleanly and provide clear vision. Most importantly, it keeps the cornea inflated with hydrostatic pressure, like water in a balloon.

There are many varieties of glaucoma, the most common being open angle glaucoma, in which the angle where the cornea and the iris meet is as wide and open as it should be, but the aqueous humor drainage channels become blocked over time and aqueous humor builds up. This raises intraocular pressure.\(^{12,13}\)

As pressure is exerted on the sensitive retina over time, it results in damage to nerve cells and their projection, the optic nerve.\(^{11}\) Once the optic nerve is damaged, it can’t be repaired, even if the raised intraocular pressure is corrected (figure 1).\(^{14,15}\) Abnormally high pressure inside the eye usually causes this retinal and optic nerve damage.

Because open angle glaucoma occurs due to the effects of aging, it may be that the disease is treatable with metformin, because of the drug’s general antiaging properties.

**How Metformin Functions in the Body**

Metformin works to reduce blood sugar in several ways. It decreases the amount of glucose made by the liver, decreases the amount of sugar absorbed into the body, and makes insulin receptors more sensitive. Metformin does not increase insulin levels as many anti-diabetic medications do, which makes it unlikely to cause dangerously low drops in blood sugar.\(^{16,17}\) It’s therefore considered safe for nondiabetics to take.

Let’s examine how metformin works as an antiaging therapeutic agent and extrapolate the findings in terms of its ability to fight glaucoma.

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**AMPK activation helps to mimic the beneficial effects of calorie restriction.**

Metformin enhances the activity of an enzyme found within all our cells called adenosine monophosphate-activated protein kinase, or AMPK for short. AMPK activation helps to mimic the beneficial effects of calorie restriction and exercise, the best documented method of slowing and reversing degenerative aging processes and biomarkers of human aging.\(^{18}\)

The biological effects of increased AMPK activity include inhibition of fat storage, reduced triglyceride synthesis, and increased glucose uptake into muscle for metabolism.\(^{19-27}\) AMPK activation also enhances destruction of diseased or dying cells as well as removal of intracellular metabolic debris—a method to slow and reverse degenerative aging processes of various organs.\(^9\)

Further, experiments have shown that metformin, through AMPK activation, promotes the functional activity of the sirtuin family of genes, which is associated with longevity. Scientists have identified several signaling pathways involved in the regulation of aging processes that promote longevity. One of these signals, named p53, controls cell proliferation and is known as a tumor-suppressor gene. Loss of p53 predisposes normal cells to cancer. Metformin helps protect functional p53 so cells are less likely to become cancerous.\(^{9,28-31}\)

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**Figure 1** shows the production of aqueous humor by ciliary processes and obstruction to its drainage at trabecular meshwork exit channels. This results in raised intraocular pressure (arrows), pressing on the sensitive retina and optic nerve, resulting in glaucoma and ultimately loss of vision.
Metformin’s Inflammation-Reducing Property

_Nuclear factor-kappa B_ (NF-kB) is an internal cell signal that induces _chronic inflammation_ responsible for many diseases, from cancer to heart attack, neurodegenerative diseases and even glaucoma.32-35

NF-kB activation is blamed for many chronic diseases that ravage us as we age. Metformin produces higher _AMPK activity_ which decreases expression of NF-kB.36

By blocking NF-kB, metformin is thought to promote longevity by inhibiting systemic inflammatory processes in the body, which play havoc in all our vital organs including the brain and heart, as well as the eyes.

A recent study has found that metformin relieves neuropathic and other pain by decreasing the activation of microglial cells in the spinal cord that are an integral part of the central nervous system and its proper functioning as discussed below.6

Metformin’s Effects on Nerve Cells (Neurons) and Their Physical Supporter-Glial Cells

Common characteristics for many neurodegenerative diseases include changes in glial cells, progressive neuronal loss, increased inflammation and oxidative stress.37 Thus decreasing the activation of glial cells in the brain is one promising approach to reducing the inflammation in the brain responsible for various neurodegenerative diseases including Parkinson’s and Alzheimer’s disease. This is exactly what a group of researchers found in an animal model of neuropathic

The Benefits of Metformin

- Metformin has been prescribed for decades as an effective treatment against type II diabetes. But studies have shown metformin to have a number of other beneficial effects as well. These include promoting longevity, weight loss, and reduced cancer risk, as well as reducing chronic pain.2,7 The drug also has antiaging effects that mimic calorie restriction, and it favorably modulates genes thought to be involved in aging.8,9

- Now, new research reveals metformin also reduces the development of _open angle glaucoma_, a progressive optic neuropathy and a leading cause of blindness.

- A University of Michigan study has found metformin to be linked with a 25% reduction in the risk of developing open angle glaucoma. Other medications used to treat type II diabetes did not have a similar benefit. Metformin is the only drug that has an intraocular pressure-reduction therapeutic effect.

- Everyone over age 50 would be well-advised to get tested for glaucoma and to ask their physician about possibly taking metformin, which could be preferable to typical antiglaucoma drugs, considering their common side-effects and lack of antiaging properties.
Now let us examine how metformin can help fight glaucoma and age-related neurodegenerative diseases related to glial cell pathology.

Originally marketed as an agent for type II diabetes, metformin has been found to have a number of other uses in clinical practice, including, in one study, the ability to decrease the activation of glial cells in the spinal cord. Researchers reported complete resolution of suffering in some rats with induced neuropathic pain. This study reveals the impact of metformin on the nervous system glial cells, which are believed to be associated with chronic pain. If that is the case, is it possible that metformin can protect other parts of the nervous system, such as the retinal ganglion cells, by inhibiting the activity of glial cells that produce inflammatory cytokines that are toxic to neurons? This would also explain our finding and the findings of other scientists that those on metformin have better cognition with reduction in dementia.

In our practice we routinely prescribe metformin for people over the age of 50 to be taken twice daily after meals to prevent future neurodegenerative diseases and aging.

How Does Metformin Reduce Glaucoma?

A recent study found that metformin reduces the intraocular pressure of primary open angle glaucoma. Open angle glaucoma is a progressive optic neuropathy characterized by loss of retinal ganglion cells and optic nerve atrophy. It's the most common...
form of glaucoma and is often asymptomatic and may even go undetected for a while.\footnote{63} By the time vision is noticeably impaired, the loss is irreversible, because once the nerve cells are dead in the retina with degeneration of the connected nerve fibers, nothing can restore them.

Open angle glaucoma is a manifestation of aging along with other neurodegenerative diseases. Normally, through autophagy, our cells purge themselves of accumulated debris, often called “cellular metabolic junk.” Autophagy is a natural mechanism that disassembles cells’ unnecessary or dysfunctional components as they age and lose their function. But over time, our cells lose this housekeeping ability.\footnote{34,43} Metformin has been shown to promote this process.\footnote{46}

According to a study at the University of Michigan, metformin was associated with a \textbf{25\% reduction in the risk of developing open angle glaucoma}. They also found that other oral antidiabetic medications used to treat type II diabetes did not confer a similar risk reduction. Metformin is the only drug endowed with this \textbf{intraocular pressure-reduction} therapeutic effect.

This retrospective cohort study was based on longitudinal data from more than 150,000 patients with type II diabetes and no preexisting record of open angle glaucoma. Forty percent filled at least one metformin prescription. During the 10-year study period, 5,893 (3.9\%) of the patients of a large health care network developed the disease. The researchers compared users of metformin with nonusers, analyzing the data by means of regression modeling. Each model demonstrated substantial reductions in open angle glaucoma risk among those using metformin. In two years, a diabetic patient taking a daily 2,000 mg dose of metformin would have a \textbf{20.8\%} reduction in open angle glaucoma risk, compared with a diabetic patient who had no metformin exposure.\footnote{10}

Glaucoma is the second leading cause of blindness in the world.\footnote{1} It is estimated that in excess of 2.5 million people have glaucoma in the United States, and that more than 120,000 people are legally blind from the disease.\footnote{42} Many people who have it aren’t aware of it. Blindness from glaucoma is six to eight times more common in African Americans than Caucasians, and, after cataracts, is the leading cause of blindness among them.\footnote{43} We advise all those over the age of 50, especially African Americans and women, to get their eyes tested for glaucoma and ask their physician if it is appropriate to start taking metformin, not as an antidiabetic, but for its antiaging, antiglaucoma properties. Women have longer life expectancy and are more likely than men to develop age-related eye diseases like glaucoma.\footnote{47}

\begin{figure}
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\caption{Metformin was associated with a \textbf{25\% reduction in the risk of developing open angle glaucoma}.}
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\begin{sideways}
\textbf{Autophagy: Cellular House Cleaning}

Christian de Duve, 1974 Nobel Laureate in physiology or medicine, coined the term autophagy (meaning "self-eating") in 1963. This year, biologist Yoshinori Ohsumi, of the Tokyo Institute of Technology, has been awarded the Nobel Prize in physiology or medicine for his discoveries in autophagy, the process whereby a cell recycles part of its own cellular debris (cellular house cleaning).

Scientists had been aware of autophagy for decades, but knew little about how it worked—until Ohsumi’s pioneering experiments in the 1990s. It’s important because autophagy can eliminate invading intracellular bacteria. Disrupted autophagy has been linked to Parkinson’s and Alzheimer’s disease, type II diabetes and other disorders that particularly affect the elderly.

We know that metformin enhances autophagy, which is how it reduces diseases of aging such as Parkinson’s and Alzheimer’s, and may reduce the incidence of glaucoma. This is one more reason to prescribe metformin.
\end{sideways}
There are dozens of drugs available to treat glaucoma.\textsuperscript{48,49} Many of them have systemic complications and lack the antiaging effect of metformin on the rest of the body. Wouldn’t it make sense to prescribe metformin to prevent glaucoma and at the same time delay and/or reverse the ravages of aging?

Researchers at the University of Michigan Kellogg Eye Center have suggested a clinical trial protocol in which newly diagnosed glaucoma patients would be randomized to receive either an IOP (intraocular pressure)-lowering drug plus metformin or a glaucoma drug plus a placebo.\textsuperscript{50} From our point of view, a randomized clinical trial which might take decades may not be needed. Metformin is inexpensive, widely used to treat type II diabetics, and has hardly any adverse effects.

**Summary of How Metformin Wards Off Glaucoma**

Given how aqueous humor is formed, how it circulates and exits the eye, there are numerous possible explanations for how metformin works. It may act to reduce open angle glaucoma risk at multiple levels, which need to be further examined. The possible mechanisms are:

1. Metformin, by inhibiting an inflammatory reaction and its related cytokines, may reduce aqueous humor production by ciliary processes, and bring it to stability.

2. By promoting autophagy, it may prevent exfoliated cells from blocking the aqueous humor drainage channels of the meshwork and the Schlemm’s canal.

3. By AMPK activation, it may reverse the biomarkers of human aging in the uveal aqueous humor production structures and transportation channels of aqueous humor.

4. Due to increased AMPK activation, as the aqueous humor circulates, it comes in contact with trabecular meshwork and may cleanse the glycation around the endothelial cells of the trabecular meshwork, thus allowing the aqueous humor to pass to exits without resistance.

5. Metformin in the aqueous humor may cleanse and open the pores in the Schlemm’s canal and uvea-scleral pathways by activation of AMPK, resulting in autophagy within the disease-afflicted lining cells of trabecular meshwork.

6. By autophagy, it may effectively cleanse the platelet clumps and lipid deposits in the trabecular meshwork and the Schlemm’s canal that facilitates the easy drainage of the aqueous humor without increasing intraocular pressure.

7. Metformin protects the functional p53 gene while repressing and/or blocking the pro-inflammatory NF-kB by reversing or inhibiting inflammatory process in the body, including the eyes.\textsuperscript{29,30,36} By reduction of inflammatory cytokines, it may protect the retina and prevent the degeneration of ganglion cells and optic nerve fibers, thus reducing the chances of blindness.

8. Metformin reduces resistance to insulin, thus helping uptake and metabolism of circulating sugar, and preventing the adverse effects of hyperglycemia such as glycation—the bonding of a protein or lipid molecule with a sugar molecule.\textsuperscript{16,17,51}

9. Loss of ganglion cells in the retina is a leading cause of blindness in open angle glaucoma.\textsuperscript{42} This could be prevented with metformin by decreasing activation of glial cells in the retina and optic nerve.
FDA Approves Human Trials on Metformin Antiaging Effects

Further studies will point out the multiple ways metformin reduces the incidence of open angle glaucoma in older people as it provides antiaging protection in other organs and tissues and possibly even prevents or reduces the incidence of age-related macular degeneration.

Interestingly, the FDA’s approval of the first human trials to see if metformin can protect against diseases of aging was headlined in news media reports. We hope this study includes the drug’s effect on the eyes of the aging population.

For decades, Life Extension has discussed the antiaging effects of metformin. Finally, the FDA has heard their call. This study may take decades to reveal its findings, hence our practice has started advocating for metformin use for people over the age of 50 to promote good health and reverse, inhibit, or stop the ravages of aging.

Although it can cause lactic acidosis if taken in doses that are much larger than required for treatment, metformin is essentially very safe. The public should demand that the FDA approve metformin for use without prescription as an over-the-counter medication, both in oral form and as ophthalmic drops.

This will reduce medical cost and improve the health of many, with reduction in age-related diseases (which cost billions to care for). It will also bestow longevity, with probable reductions of neurodegenerative
diseases such as Parkinson’s and Alzheimer’s, and at the same time provide good eyesight. Until that happens, the best alternative is for patients to ask their physicians to prescribe metformin for them and put it in writing that they, the patients, will not hold their doctors responsible for any untoward effects. Those with elevated intraocular pressure and/or glaucoma should ask their doctor about prescribing a modest 250 mg-500 mg dose of metformin twice a day after meals.

When developed, metformin ophthalmic drops, besides preventing open angle glaucoma, may also prevent or delay the development of age-related macular degeneration and diabetic retinopathy, and restore good vision to the aging population inexpensively. We appeal to the pharmaceutical industry to develop metformin ophthalmic drops with other adjuvant therapeutic agents to treat various eye diseases such as open angle glaucoma, age-related macular degeneration, retinitis pigmentosa, diabetic retinopathy and uveitis.

Jessica G. Shantha, MD, Fellow in Uveal diseases; Proctor Foundation, University of San Francisco, San Francisco California. T. R. Shantha MD, PhD, FACA

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at 1-866-864-3027.

References:


Importance of AMPK

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**References**


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Solla Eiríksdóttir is a celebrity chef in her native Iceland, famed for her TV shows and four restaurants which cater to fans of vegan and vegetarian dishes and raw food. She has published five cookbooks in Iceland, but *Raw: Recipes for a Modern Vegetarian Lifestyle* is her first cookbook in English. Solla, 55, collaborated with her 36-year-old daughter, Hildur, on the new book, and the duo had a specific aim in mind. “What we’re doing is transforming fruit and vegetables into real dishes instead of just making salad all the time,” explains Solla. “We love the freshest raw materials so your taste buds are screaming for more.”

Solla began investigating raw foods just after Hildur was born. She was suffering with a number of allergies at the time, and her doctor wanted to treat her ailments with drugs, but that would have required her to stop breast-feeding her infant daughter. She refused, and instead went to a nutritionist who put her on a vegan diet. Amazingly, Solla’s allergies vanished within six months. From there, she got a job in a vegetarian restaurant, where she began to develop her cooking skills. She subsequently went on to study at the Living Light Culinary Institute in Fort Bragg, California.

Why raw? In the introduction to her new cookbook, the Icelandic chef explains that while most vegetables and fruits are rich in fiber, minerals, vitamins, antioxidants, phytoneutrients, and enzymes, “Some of these compounds are sensitive to heat and a significant amount can be lost in the process of cooking.” Enzymes, in particular, which catalyze digestion, denature with high heat, leading proponents of raw food to usually restrict application of heat in their cooking.

*Raw* features 75 recipes, all equally healthy and delicious. Solla and Hildur helpfully include symbols that denote when a particular dish is gluten-free, dairy-free, nut-free, raw or vegan. The following are four sample recipes from the book. Bon appetit!
Chia and Millet Flake Porridge

Serves 2

- 1 cup almond milk
- 3 tablespoons chia seeds
- 1 cup rolled millet flakes
- 1 teaspoon vanilla powder
- 1 teaspoon ground cinnamon
- ½ teaspoon lemon juice
- A pinch of salt
- ½ banana, thinly sliced for topping

For the raspberry compote:
- 1 pear, peeled, cored, and chopped into small pieces or grated
- 1 cup raspberries (fresh or frozen)
- 1 tablespoon shredded fresh ginger root

Put the almond milk and chia seeds in a clean glass jar, put the lid on, and shake for 2-3 minutes, or until combined. Stir in the millet flakes, vanilla, cinnamon, lemon juice, and salt, then put the lid back on and set aside to rest for 15-30 minutes, or overnight.

For the compote, put the pear, raspberries, and ginger into a medium bowl and mash with a fork until it is the consistency you like. We like it slightly chunky. Alternatively, place the ingredients into a food processor and process using the pulse button.

When ready to serve, pour half the raspberry compote into a bowl or a glass jar, add the chia porridge, and top with a layer of thinly sliced banana. Spoon the remaining raspberry compote on top and eat.

Tofu Scramble with Kale and Avocado

Serves 2-3

- 2 tablespoons olive oil
- ½ onion, finely chopped
- 2 cloves of garlic, chopped
- 4 kale leaves, stems (stalks) removed

For the tofu marinade:
- 2-3 tablespoons almond milk
- 2 tablespoons nutritional yeast flakes
- 1 tablespoon tamari
- 1 tablespoon mustard
- ½ teaspoon ground turmeric
- ¼ teaspoon red pepper (chili) flakes
- A pinch of salt
- 1 cup tofu

To garnish:
- ½ avocado sliced
- Sprouts of your choice (optional)

Start by marinating the tofu. Stir the almond milk, nutritional yeast flakes, tamari, mustard, turmeric, red pepper (chili) flakes, and salt together in a bowl. Before adding the tofu, squeeze out all the liquid. A good way to do this is to wrap the tofu in a clean dish cloth and squeeze it gently so the water comes out through the cloth. Be gentle so the tofu doesn’t become a paste. You may need to use 2 cloths because a lot of liquid is likely to come out. When all the water has been squeezed out, crumble the tofu into a bowl with all the remaining marinade ingredients, and mix to combine.

Heat the olive oil in a saucepan over medium heat. Add the onion and garlic and cook for 3-4 minutes, or until golden brown. Add the kale leaves, stir for 1 minute, then add the tofu and cook for another 4-5 minutes. Serve in a bowl and garnish with sliced avocado and sprouts, if using.
Rainbow Pasta with Pesto

Serves 3-4

1 rutabaga (swede)
1-2 carrots
1 beet (beetroot)
1 small zucchini (courgette)
2 tablespoons lemon juice
1 tablespoon olive oil

For the green pesto:
½ cup cashew nuts
1 handful of basil
2-3 kale leaves, stems (stalks) removed
1-2 tablespoons nutritional yeast flakes
1 large clove garlic
¼–½ teaspoon sea salt flakes
¼–½ teaspoon cold-pressed olive oil

For the pesto, put the cashew nuts in a bowl, pour in enough water to cover, and soak for about 2 hours. Drain and discard the soaking water.

Put the cashew nuts into a food processor with the remaining ingredients, except the olive oil, and blend. The texture of the pesto should be chunky. Transfer the pesto to a bowl and add the olive oil. Stir gently to mix together. Spoon into a clean glass jar and set aside.

Peel the rutabaga (swede), carrots, and beet (beetroot) and use a julienne peeler or spiralizer to shred the vegetables into spaghetti-like strips.

Put your vegetable spaghetti into a bowl and add the lemon juice and olive oil. Stir together, then cover with plastic wrap (Clingfilm) and leave for 15-25 minutes to let the “spaghetti” soften. Serve with green pesto.
Quinoa Pizza Crust

Makes 1 pizza

¾ cup quinoa
½ teaspoon sea salt flakes
1 clove garlic
½ teaspoon freshly ground black pepper
2 teaspoons dried oregano
¼ cup grated vegan cheese
1 tablespoon olive oil

For topping:
Scant ½ cup vegan cream cheese
½ zucchini (courgette), very thinly sliced
2-3 tablespoons pine nuts
3-4 sprigs rosemary
1 tablespoon truffle oil

Put the quinoa into a bowl, pour in enough water to cover, and let soak overnight.

The next day, preheat the oven to 375 degrees and line a baking sheet with parchment (baking) paper.

Drain and rinse the quinoa, then put it into a blender together with ¼ cup water, the salt, garlic, black pepper, and oregano and blend until smooth. Pour the batter into a bowl and mix the cheese and olive oil.

Put a 9 inch tart ring on the prepared baking sheet and pour in the quinoa batter. Bake for 20 minutes, then remove from the oven. Wearing oven mitts, flip the crust over by covering it with another baking sheet, grasping both sides of the 2 baking sheets, and flipping the sheets with the crust between them. Bake on the second sheet for another 5-10 minutes.

Remove the crust from the oven and lower the temperature to 345 degrees. Spread the crust with the cream cheese, top with the zucchini (courgette) slices, and sprinkle with the pine nuts. Bake for another 8 minutes.

Meanwhile, in a small skillet, briefly cook the rosemary sprigs in the truffle oil over medium heat. When the pizza is ready, sprinkle with the fried rosemary and serve.
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Note: Do not change dosing or discontinue cardiovascular medications unless advised to do so by your physician.

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Inositol Caps
Liquid Emulsified Vitamin D3
Liquid Vitamin D3
Low-Dose Vitamin K2
Methylcobalamin
MK-7
Natural Vitamin E
No Flush Niacin
Optimized Folate (L-Methylfolate)
Pantothentic Acid (Vitamin B-5)
Pyridoxal 5'-Phosphate Caps
Super Absorbable Tocotrienols
Super Ascorbate C Capsules
Super Ascorbate C Powder
Super K with Advanced K2 Complex
Vitamin B12
Vitamin B6
Vitamin C with Dihydroquercetin
Vitamin D3 with Sea-Iodine™
Vitamin D3
Vitamins D and K with Sea-Iodine™

Weight Management

7-Keto® DHEA Metabolite
Advanced Anti-Adipocyte Formula
Advanced Natural Appetite Suppress
CalReduce Selective Fat Binder
DHEA Complete
Garcinia HCA
HCActive™ Garcinia Cambogia Extract
Integra-Lean®
Mediterranean Trim with Sinetrol™-XPur
Optimized Irvingia with Phase 3™ Calorie Control Complex
Optimized Saffron with Satiereal®
Super Citrimax®
Super CLA Blend with Guarana and Green Coffee Bean
Super CLA Blend with Sesame Lignans
Waist-Line Control™

Women’s Health

Advanced Natural Sex for Women® 50+
Breast Health Formula
Femmenessence MacaPause®
Natural Estrogen
Progesterone Cream
Super-Absorbable Soy Isoflavones
Ultra Soy Extract
<table>
<thead>
<tr>
<th>ITEM No.</th>
<th>PRODUCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>01524</td>
<td>ACETYL-L-CARNITINE • 500 mg, 100 veg. caps</td>
</tr>
<tr>
<td>01874</td>
<td>ACETYL-L-CARNITINE ARGINATE • 90 veg. caps</td>
</tr>
<tr>
<td>01626</td>
<td>ADRENAL ENERGY FORMULA • 60 veg. caps</td>
</tr>
<tr>
<td>01630</td>
<td>ADRENAL ENERGY FORMULA • 120 veg. caps</td>
</tr>
<tr>
<td>01828</td>
<td>ADVANCED LIPID CONTROL • 60 veg. caps</td>
</tr>
<tr>
<td>00881</td>
<td>AHCC® • 500 mg, 30 caps</td>
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<tr>
<td>29727</td>
<td>AHCC® (KINOKO® GOLD) • 500 mg, 60 veg. caps</td>
</tr>
<tr>
<td>00457</td>
<td>ALPHA-LIPIOIC ACID W/BIOTIN • 250 mg, 60 caps</td>
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<tr>
<td>01907</td>
<td>AMPK ACTIVATOR • 90 veg. caps</td>
</tr>
<tr>
<td>01509</td>
<td>ANTI-ADIPOCYTE FORMULA W/MERATRIM® &amp; INTEGRA LEAN® (Advanced) • 60 veg. caps</td>
</tr>
<tr>
<td>02140</td>
<td>ANTI-ALCOHOL w/HEPATOPRO COMPLEX • 60 caps</td>
</tr>
<tr>
<td>01625</td>
<td>APPLEWISE POLYPHENOL EXTRACT • 600 mg, 30 veg. caps</td>
</tr>
<tr>
<td>01039</td>
<td>ARGININE/ORNITHINE • 500/250, 100 caps</td>
</tr>
<tr>
<td>00038</td>
<td>ARGININE/ORNITHINE POWDER • 150 grams</td>
</tr>
<tr>
<td>01624</td>
<td>(L)-ARGININE CAPS • 700 mg, 200 veg. caps</td>
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<tr>
<td>02040</td>
<td>ARTERIAL PROTECT • 30 veg. caps</td>
</tr>
<tr>
<td>01817</td>
<td>ARTHRIMAX® W/ THEAFLAVINS &amp; APRÉSFLEX® • 120 veg. caps</td>
</tr>
<tr>
<td>01818</td>
<td>ARTHRIMAX® ADVANCED W/UC-II® &amp; APRÉSFLEX® • 60 caps</td>
</tr>
<tr>
<td>02108</td>
<td>ARTHRIMAX® HERBAL JOINT FORMULA • 60 veg. caps</td>
</tr>
<tr>
<td>01404</td>
<td>ARTHR-IMMUNE JOINT SUPPORT • 60 veg. caps</td>
</tr>
<tr>
<td>00919</td>
<td>ARTICHOKE LEAF EXTRACT • 500 mg, 180 veg. caps</td>
</tr>
<tr>
<td>01533</td>
<td>ASCORBYL PALMITATE • 500 mg, 100 veg. caps</td>
</tr>
<tr>
<td>00888</td>
<td>ASHWAGANDHA EXTRACT (Optimized) • 60 caps</td>
</tr>
<tr>
<td>01805</td>
<td>ASIAN ENERGY BOOST • 90 veg. caps</td>
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<tr>
<td>01066</td>
<td>ASPIRIN • 81 mg, 30 enteric coated tablets</td>
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<tr>
<td>01923</td>
<td>ASTAXANTHIN WITH PHOSPHOLIPIDS • 4 mg, 30 softgels</td>
</tr>
<tr>
<td>00929</td>
<td>BENEFOTIAMINE W/ THIAMINE • 100 mg, 120 veg. caps</td>
</tr>
<tr>
<td>00925</td>
<td>BENEFOTIAMINE (Mega) • 250 mg, 120 veg. caps</td>
</tr>
<tr>
<td>01266</td>
<td>BERRY COMPLETE • 30 veg. caps</td>
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<tr>
<td>01496</td>
<td>BERRY COMPLETE W/ACAI (Enhanced) • 60 veg. caps</td>
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<tr>
<td>00664</td>
<td>BETA-CAROTENE • 25,000 IU, 100 softgels</td>
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<tr>
<td>01622</td>
<td>BIFIDO GI BALANCE • 60 veg. caps</td>
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<tr>
<td>01873</td>
<td>BILBERRY EXTRACT • 100 mg, 90 veg. caps</td>
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<tr>
<td>01512</td>
<td>BIO-ACTIVE MILK PEPTIDES • 30 caps</td>
</tr>
<tr>
<td>01631</td>
<td>BIO-COLLAGEN W/PATENTED UC-II® • 40 mg, 60 small caps</td>
</tr>
<tr>
<td>01006</td>
<td>BIOSIL® • 5 mg, 30 veg. caps</td>
</tr>
<tr>
<td>01007</td>
<td>BIOSIL® • 1 fl oz</td>
</tr>
<tr>
<td>00102</td>
<td>BIOTIN • 600 mcg, 100 caps</td>
</tr>
<tr>
<td>01709</td>
<td>BLACK CUMIN SEED OIL • 60 softgels</td>
</tr>
<tr>
<td>01710</td>
<td>BLACK CUMIN SEED OIL W/BIO-CURCUMIN® • 60 softgels</td>
</tr>
<tr>
<td>01008</td>
<td>BLAST® • 600 grams of powder</td>
</tr>
<tr>
<td>02025</td>
<td>BLOOD PRESSURE (Dual Action) • 60 veg. tabs</td>
</tr>
</tbody>
</table>

**SUBTOTAL OF COLUMN 1**

<table>
<thead>
<tr>
<th>ITEM No.</th>
<th>PRODUCT</th>
</tr>
</thead>
<tbody>
<tr>
<td>70000</td>
<td>BLOOD PRESSURE MONITOR (ACCUFIT®) • med/lg cuff</td>
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<tr>
<td>70004</td>
<td>BLOOD PRESSURE MONITOR • Digital wrist cuff</td>
</tr>
<tr>
<td>02024</td>
<td>BLOOD PRESSURE (Triple Action AM/PM) • 60 veg. tabs</td>
</tr>
<tr>
<td>01214</td>
<td>BLUEBERRY EXTRACT • 60 veg. caps</td>
</tr>
<tr>
<td>01438</td>
<td>BLUEBERRY EXTRACT W/ POMEGRANATE • 60 veg. caps</td>
</tr>
<tr>
<td>01506</td>
<td>BONE FORMULA (DR. STRUM’S INTENSIVE) • 300 caps</td>
</tr>
<tr>
<td>01726</td>
<td>BONE RESTORE • 120 caps</td>
</tr>
<tr>
<td>01727</td>
<td>BONE RESTORE W/VITAMIN K2 • 120 caps</td>
</tr>
<tr>
<td>01725</td>
<td>BONE STRENGTH FORMULA W/KOACT® • 120 caps</td>
</tr>
<tr>
<td>00313</td>
<td>BONE-UP® • 240 caps</td>
</tr>
<tr>
<td>01661</td>
<td>BORON • 3 mg, 100 veg. caps</td>
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<tr>
<td>00202</td>
<td>BOSWELLA • 100 caps</td>
</tr>
<tr>
<td>01802</td>
<td>BRAIN SHIELD® GASTROIN • 300 mg, 60 veg. caps</td>
</tr>
<tr>
<td>01253</td>
<td>BRANCHED CHAIN AMINO ACIDS • 90 caps</td>
</tr>
<tr>
<td>01942</td>
<td>BREAST HEALTH FORMULA • 60 caps</td>
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<tr>
<td>00893</td>
<td>BRITE EYES III • 2 vials, 5 ml each</td>
</tr>
<tr>
<td>26576</td>
<td>BROCCO MAX® • 60 veg. caps</td>
</tr>
<tr>
<td>01203</td>
<td>BROMELAIN (Specialty-coated) • 500 mg, 60 enteric coated tablets</td>
</tr>
</tbody>
</table>

**SUBTOTAL OF COLUMN 2**
**OFFER ENDS JANUARY 31, 2017**

**RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS**

**DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE**

<table>
<thead>
<tr>
<th>ITEM No.</th>
<th>PRODUCT</th>
<th>Retail Each</th>
<th>Unit</th>
<th>Each</th>
<th>QTY Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>01659</td>
<td>COGNIZIN® CDP CHOLINE CAPS • 250 mg, 60 veg. caps</td>
<td>36.00</td>
<td>27.00</td>
<td>25.50</td>
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<tr>
<td>01945</td>
<td>COMPLETE B-COMPLEX (BioActive) • 60 veg. caps</td>
<td>12.00</td>
<td>9.00</td>
<td>8.00</td>
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</tr>
<tr>
<td>02996</td>
<td>COMPREHENSIVE NUTRIENT PACKS ADVANCED • 30 packs</td>
<td>90.00</td>
<td>67.50</td>
<td>61.50</td>
<td></td>
</tr>
<tr>
<td>01949</td>
<td>COQ10 w/d-LIMONENE (Super-Absorbable) • 50 mg, 60 softgels</td>
<td>25.00</td>
<td>18.75</td>
<td>16.50</td>
<td>15.00</td>
</tr>
<tr>
<td>01948</td>
<td>COQ10 w/d-LIMONENE (Super-Absorbable) • 100 mg, 60 softgels</td>
<td>46.00</td>
<td>34.50</td>
<td>28.00</td>
<td>26.25</td>
</tr>
<tr>
<td>01928</td>
<td>COQ10 (Super Ubiquinol) • 100 mg, 60 softgels</td>
<td>56.00</td>
<td>42.00</td>
<td>36.00</td>
<td>33.00</td>
</tr>
<tr>
<td>01733</td>
<td>COQ10 w/BIOQ10® (Super Ubiquinol) • 100 mg, 30 softgels</td>
<td>54.00</td>
<td>40.50</td>
<td>33.00</td>
<td>30.00</td>
</tr>
<tr>
<td>01426</td>
<td>COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (Super Ubiquinol) • 50 mg, 60 softgels</td>
<td>62.00</td>
<td>46.50</td>
<td>39.00</td>
<td>36.00</td>
</tr>
<tr>
<td>01425</td>
<td>COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (Super Ubiquinol) • 100 mg, 60 softgels</td>
<td>58.00</td>
<td>43.50</td>
<td>34.50</td>
<td>31.50</td>
</tr>
<tr>
<td>01427</td>
<td>COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (Super Ubiquinol) • 200 mg, 30 softgels</td>
<td>20.00</td>
<td>15.00</td>
<td>12.00</td>
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<tr>
<td>01431</td>
<td>COQ10 w/ENH MITOCHONDRIAL SUPPORT™ (Super Ubiquinol) • 500 mg, 60 softgels</td>
<td>62.00</td>
<td>46.50</td>
<td>39.00</td>
<td>36.00</td>
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<tr>
<td>00862</td>
<td>CRAN-MAX® • 500 mg, 60 veg. caps</td>
<td>17.50</td>
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<td>11.25</td>
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<tr>
<td>01424</td>
<td>CRAN-MAX® WITH ELLIROSETM (Optimized) • 60 veg. caps</td>
<td>18.00</td>
<td>13.50</td>
<td>12.00</td>
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<tr>
<td>01529</td>
<td>CREATINE CAPSULES • 120 veg. caps</td>
<td>10.95</td>
<td>8.21</td>
<td>6.94</td>
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</tr>
<tr>
<td>01746</td>
<td>CREATINE WHEY GLUTAMINE POWDER • 454 grams (vanilla)</td>
<td>30.00</td>
<td>22.50</td>
<td>19.50</td>
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<tr>
<td>01429</td>
<td>CR MICEMETIC LONGEVITY FORMULA • 60 veg. caps</td>
<td>39.00</td>
<td>29.25</td>
<td>27.00</td>
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<tr>
<td>00407</td>
<td>CURCUMIN® (Super Bio) • 400 mg, 60 veg. caps</td>
<td>38.00</td>
<td>28.50</td>
<td>26.25</td>
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</tr>
<tr>
<td>01924</td>
<td>CURCUMIN® W/GINGER &amp; TURMERIC® (Advanced Bio) 30 softgels</td>
<td>30.00</td>
<td>22.50</td>
<td>20.25</td>
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<tr>
<td>01804</td>
<td>CYTOPROTEIN® W/ESC G • 30 veg. caps</td>
<td>30.00</td>
<td>22.50</td>
<td>20.25</td>
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</tbody>
</table>

**SUBTOTAL OF COLUMN 3**

<table>
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<tr>
<th>ITEM No.</th>
<th>PRODUCT</th>
<th>Retail Each</th>
<th>Unit</th>
<th>Each</th>
<th>QTY Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>80157</td>
<td>ADVANCED ANTI-GLYCATION PEPTIDE SERUM • 1 oz</td>
<td>53.00</td>
<td>39.75</td>
<td>34.50</td>
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<tr>
<td>80154</td>
<td>ADVANCED LIGHTENING CREAM • 1 oz</td>
<td>65.00</td>
<td>48.75</td>
<td>42.75</td>
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</tr>
<tr>
<td>80155</td>
<td>ADVANCED PEPTIDE HAND THERAPY • 4 oz</td>
<td>65.00</td>
<td>48.75</td>
<td>42.75</td>
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<tr>
<td>80152</td>
<td>ADVANCED TRIPLE PEPTIDE SERUM • 1 oz</td>
<td>65.00</td>
<td>48.75</td>
<td>42.75</td>
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<tr>
<td>80140</td>
<td>ADVANCED UNDER EYE SERUM W/STEM CELLS • .33 oz</td>
<td>49.00</td>
<td>36.75</td>
<td>31.50</td>
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<tr>
<td>80139</td>
<td>AMBER SELF MICRODERMABRATION • 2 oz</td>
<td>49.00</td>
<td>36.75</td>
<td>31.50</td>
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<tr>
<td>80158</td>
<td>ANTI-AGING FACE OIL • 1 oz</td>
<td>59.00</td>
<td>44.25</td>
<td>39.00</td>
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<tr>
<td>80188</td>
<td>ANTI-AGING MASK • 2 oz</td>
<td>72.00</td>
<td>54.00</td>
<td>47.52</td>
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<tr>
<td>80151</td>
<td>ANTI-AGING REJUVENATING FACE CREAM • 2 oz</td>
<td>65.00</td>
<td>48.75</td>
<td>42.75</td>
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</tr>
<tr>
<td>80153</td>
<td>ANTI-AGING REJUVENATING SCALP SERUM • 2 oz</td>
<td>46.00</td>
<td>34.50</td>
<td>29.25</td>
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</tr>
<tr>
<td>80134</td>
<td>ANTI-GLYCATION SERUM W/BLUEBERRY &amp; POMEGRANATE EXTRACTS • 1 oz</td>
<td>33.00</td>
<td>24.75</td>
<td>23.51</td>
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<tr>
<td>80133</td>
<td>ANTI-OXIDANT FACIAL MIST • 2 oz</td>
<td>32.00</td>
<td>24.00</td>
<td>22.80</td>
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</tr>
<tr>
<td>80127</td>
<td>ANTI-OXIDANT REJUVENATING FOOT CREAM • 2 oz</td>
<td>45.00</td>
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<td>32.10</td>
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<tr>
<td>80128</td>
<td>ANTI-OXIDANT REJUVENATING FOOT SCRUB • 2 oz</td>
<td>59.00</td>
<td>44.25</td>
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<tr>
<td>80117</td>
<td>ANTI-OXIDANT REJUVENATING HAND CREAM • 2 oz</td>
<td>64.00</td>
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<tr>
<td>80105</td>
<td>ANTI-REDNESS &amp; ADULT BLEMISH LOTION • 1 oz</td>
<td>74.50</td>
<td>55.88</td>
<td>48.17</td>
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<tr>
<td>80147</td>
<td>BIOFLAVONOID CREAM • 1 oz</td>
<td>46.00</td>
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<td>29.25</td>
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<tr>
<td>80144</td>
<td>BROCCOLI SPROUT CREAM • 1 oz</td>
<td>46.00</td>
<td>34.50</td>
<td>29.25</td>
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<tr>
<td>80156</td>
<td>COLLAGEN BOOSTING PEPTIDE SERUM • 1 oz</td>
<td>59.00</td>
<td>44.25</td>
<td>39.00</td>
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<tr>
<td>80120</td>
<td>CORRECTIVE CLEARING MASK • 2 oz</td>
<td>64.50</td>
<td>48.88</td>
<td>42.57</td>
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<tr>
<td>80141</td>
<td>DNA REPAIR CREAM • 1 oz</td>
<td>49.00</td>
<td>36.75</td>
<td>31.50</td>
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<tr>
<td>80108</td>
<td>ESSENTIAL PLANT LIPIDS REPARATIVE SERUM • 1 oz</td>
<td>74.95</td>
<td>56.21</td>
<td>49.46</td>
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**SUBTOTAL OF COLUMN 4**
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<tr>
<th>ITEM No.</th>
<th>PRODUCT</th>
<th>YOUR PRICE</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Retail Each</td>
</tr>
<tr>
<td></td>
<td></td>
<td>1 Unit Each</td>
</tr>
<tr>
<td>02021</td>
<td>DIGESTIVE ENZYMES (Enhanced Super) • 60 veg. caps</td>
<td>$22.00</td>
</tr>
<tr>
<td>02022</td>
<td>DIGESTIVE ENZYMES w/PROBIOTICS (Enhanced Super) • 60 veg. caps</td>
<td>$28.00</td>
</tr>
<tr>
<td>01671</td>
<td>D, L-PHENYLALANINE • 500 mg, 100 veg. caps</td>
<td>$18.75</td>
</tr>
<tr>
<td>01540</td>
<td>DMAE BITARTRATE • 150 mg, 200 veg. caps</td>
<td>$18.00</td>
</tr>
<tr>
<td>01570</td>
<td>DNA PROTECTION FORMULA • 60 veg. caps</td>
<td>$34.00</td>
</tr>
<tr>
<td>01931</td>
<td>DOG MIX • 100 grams powder</td>
<td>$18.00</td>
</tr>
<tr>
<td>02006</td>
<td>DOPA-MIND™ • 60 veg. tabs</td>
<td>$48.00</td>
</tr>
<tr>
<td>00321</td>
<td>DR. PROCTOR’S ADVANCED HAIR FORMULA • 2 oz</td>
<td>$39.95</td>
</tr>
<tr>
<td>00320</td>
<td>DR. PROCTOR’S HAIR SHAMPOO • 8 oz</td>
<td>$24.95</td>
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<tr>
<td>01528</td>
<td>ECHINACEA EXTRACT • 250 mg, 60 veg. caps</td>
<td>$14.35</td>
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<tr>
<td>01997</td>
<td>ENDOTHelial DEFENSE™ w/PEOMEGRANATE COMPLETE AND CORDIART™ • 60 softgels</td>
<td>$68.00</td>
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<tr>
<td>00997</td>
<td>ENDOTHelial DEFENSE™ w/GLISODIN™ • 60 veg. caps</td>
<td>$54.00</td>
</tr>
<tr>
<td>01937</td>
<td>EPA/DHA (Mega) • 120 softgels</td>
<td>$20.00</td>
</tr>
<tr>
<td>01737</td>
<td>ESOPHAGEAL GUARDIAN (Berry flavor) • 60 chewable tablets</td>
<td>$36.00</td>
</tr>
<tr>
<td>01042</td>
<td>EUROPEAN LEG SOLE SOLUTION 95 • 600 mg, 30 veg. tabs</td>
<td>$20.00</td>
</tr>
<tr>
<td>01706</td>
<td>EXTRAORDINARY ENZYMES • 60 caps</td>
<td>$26.00</td>
</tr>
<tr>
<td>02008</td>
<td>(CALIFORNIA ESTATE) EXTRA VIRGIN OLIVE OIL • 500 ml (16.9 fl. oz)</td>
<td>$33.00</td>
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<tr>
<td>01514</td>
<td>EYE PRESSURE SUPPORT W/MIRTGENOLE™ • 30 veg. caps</td>
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<td>FACE MASTER® PLATINUM • Facial Toning System</td>
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<td>FAST-ACTING JOINT FORMULA • 30 caps</td>
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<td>FAST-C™ w/DIHYDROQUERCETIN • 120 veg. tabs</td>
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<td>02053</td>
<td>FEM DOPHILUS® • 30 caps</td>
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<td>FEM DOPHILUS® • 60 caps</td>
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<td>01064</td>
<td>FEMENESSENCE MACAPUASE® • 120 veg. caps</td>
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<td>02007</td>
<td>FIBER-IMMUNE SUPPORT (Apple Cinnamon) • 235 grams</td>
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<td>FIBRINOGEN RESIST™ • 30 veg. caps</td>
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<td>01749</td>
<td>FLAX SEED (Organic golden) • 14 oz</td>
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<td>FLORASSIST® GI w/PAGE TECHNOLOGY • 30 liquid veg. caps</td>
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<td>FLORASSIST® HEART HEALTH • 60 veg. caps</td>
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<td>FLORASSIST® ORAL HYGIENE • 30 lozenges</td>
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<td>FLORASSIST® BALANCE • 30 liquid veg. caps</td>
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<td>FLORASSIST® MOOD • 60 caps</td>
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<td>FLORASSIST® THROAT HEALTH • 30 lozenges</td>
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<td>FOLATE HIGH POTENCY (Optimized) • 5,000 mcg. 30 veg. tablets</td>
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<td>FOLATE (Optimized) • 1,000 mcg, 100 veg. tablets</td>
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<td>FOLATE + VITAMIN B12 (BioActive) • 90 veg. caps</td>
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<td>FORSKOLIN • 10 mg, 60 veg. caps</td>
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<td>FUCOIDAN W/MARITECH™ 925 (Optimized) • 60 veg. caps</td>
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<td>GAMMA E MIXED TOCOPHEROL/TOCOTHIENOLS • 60 softgels</td>
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<td>GAMMA E MIXED TOCOPHEROL w/ENHANCED SESAME LIGNANS • 60 softgels</td>
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<td>GARIO (Optimized) • 200 veg. caps</td>
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<td>GASTRO-EASE • 60 veg. caps</td>
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<td><strong>SUBTOTAL OF COLUMN 5</strong></td>
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<td></td>
<td><strong>RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS</strong></td>
</tr>
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</table>

**TO ORDER CALL: 1.954.766.8433 or 1.800.544.4440**

**TO ORDER ONLINE VISIT: www.LifeExtension.com**
<table>
<thead>
<tr>
<th>Item No.</th>
<th>Product Description</th>
<th>Each Retail</th>
<th>Unit of Measure</th>
<th>QTY Total</th>
</tr>
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<td>Liver Efficiency Formula• 30 veg. caps</td>
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<td>01639</td>
<td>5-LOX Inhibitor W/PRÉFLEX®• 100 mg, 60 veg. caps</td>
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<td>L-Lysine• 620 mg, 100 veg. caps</td>
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<td>00455</td>
<td>Lycopen (Mega)• 15 mg, 90 softgels</td>
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<td>MACUGUARD® OCULAR SUPPORT• 60 softgels</td>
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<td>01459</td>
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<td>EXTEND-RELEASE MAGNESIUM• 60 veg. caps</td>
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<td>01908</td>
<td>Mediterranean Trim with Sinepitol®-XPIR 60 veg. caps</td>
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<tr>
<td>01668</td>
<td>Melatonin• 300 mcg, 100 veg. caps</td>
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<tr>
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<td>Melatonin• 500 mcg, 200 veg. caps</td>
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<td>Melatonin• 3 mg, 60 veg. caps</td>
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<td>Melatonin• 10 mg, 60 veg. caps</td>
<td>28.00</td>
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<td>00332</td>
<td>Melatonin• 3 mg, 60 veg. lozenges</td>
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<td>01734</td>
<td>Melatonin (Fast-Acting Liquid)• 2 fl. oz (Citrus- Vanilla)</td>
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<td>01787</td>
<td>Melatonin Timed Release• 300 mcg, 100 veg. tabs</td>
<td>12.00</td>
<td>9.00</td>
<td>8.25</td>
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<td>01788</td>
<td>Melatonin Timed Release• 750 mcg, 60 veg. tablets</td>
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<td>Melatonin Timed Release• 3 mg, 60 veg. tabs</td>
<td>12.00</td>
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<td>02101</td>
<td>Memory Protect• 36 day supply</td>
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<td>01536</td>
<td>Methylcobalamin• 1 mg, 60 veg. lozenges (vanilla)</td>
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<td>Methylcobalamin• 5 mg, 60 veg. lozenges (vanilla)</td>
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<td>00709</td>
<td>Migra-Eeze™ (Buttercup)• 60 softgels</td>
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<td>01522</td>
<td>Milk Thistle (European)• 60 veg. caps</td>
<td>34.00</td>
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<td>01922</td>
<td>Milk Thistle (European)• 60 softgels</td>
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<td>Milk Thistle (European)• 120 softgels</td>
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<td>01940</td>
<td>Miraforte w/STANDARDIZED LIGNANS (Super)• 120 veg caps</td>
<td>62.00</td>
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<td>01669</td>
<td>Mitochondrial Basics W/BIOPOQ®• 30 caps</td>
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<td>01668</td>
<td>Mitochondrial Energy Optimizer w/BIOPOQ®•120 caps</td>
<td>72.00</td>
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<td>MK-7• 90 mcg, 60 softgels</td>
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<td>00451</td>
<td>MSM (Methylsulfonylmethan)• 1,000 mg, 100 caps</td>
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**N**

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<th>Item No.</th>
<th>Product Description</th>
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<th>Unit of Measure</th>
<th>QTY Total</th>
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<td>N-Acetyl-L-Cysteine• 600 mg, 60 veg. caps</td>
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<td>01904</td>
<td>NAD+ CELL REGENERATOR™• 100 mg, 30 veg. caps</td>
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<td>00066</td>
<td>Nattokinase• 60 softgels</td>
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<td>01807</td>
<td>Natural Appetite Suppress (Advanced)• 60 veg. caps</td>
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<td>Natural BP Management• 60 tablets</td>
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<td>01892</td>
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<td>01626</td>
<td>Natural Sex for Women® 50+ (Advanced)• 90 veg. caps</td>
<td>59.00</td>
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<td>01444</td>
<td>Natural Sleep®• 60 veg. caps</td>
<td>13.00</td>
<td>9.75</td>
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</table>

**SUBTOTAL OF COLUMN 7**

RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS

DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE

JANUARY 2017

OFFER ENDS JANUARY 31, 2017

TO ORDER CALL: 1.954.766.8433 or 1.800.544.4440

TO ORDER ONLINE VISIT: www.LifeExtension.com
<table>
<thead>
<tr>
<th>ITEM No.</th>
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<th>YOUR PRICE</th>
<th>QTY Total</th>
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<td>PROSTATEPOLLEN® (120 veg. caps)</td>
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<td>0144</td>
<td>PROTEIN-ISOLATE (Vanilla)</td>
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<td>PROTEIN-ISOLATE (Chocolat)</td>
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<td>0146</td>
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<td>0147</td>
<td>PROTEIN CONCENTRATE (New Zealand)</td>
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<td>PS CAPS (Phosphatidylserine)</td>
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<td>PTEROPURE® Pterostilbene</td>
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<td>PUMPKIN SEED EXTRACT (Water-soluble)</td>
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<td>Pycnogenol® French Maritime Pine Bark Extract</td>
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<td>QUERCETIN (Sophorolysine)</td>
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<td>RED YEAST RICE (Bluebonnet)</td>
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<td>REGIMINT</td>
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<td>REJUVENEX® BODY LOTION</td>
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<td>RESVERATROL W/nicotinamide riboside</td>
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<td>RESVERATROL</td>
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<td>RHODIOLA EXTRACT</td>
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<td>RIBOGEN® French Oak Wood Extract</td>
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<td>200 mg, 30 veg. caps</td>
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<td>(D) RIBOSE POWDER</td>
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<td>0176</td>
<td>(D) RIBOSE TABLETS</td>
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<td>0177</td>
<td>RICH REWARDS® BREAKFAST BLEND GROUND COFFEE</td>
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<td>0181</td>
<td>RICH REWARDS® DECAFFEINATED ROAST GROUND COFFEE</td>
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<td>0182</td>
<td>R-LIPOIC ACID (Super)</td>
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<td>0183</td>
<td>RNA CAPSULES</td>
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**SUBTOTAL OF COLUMN 9**

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<td>SAMe (S-ADENOSYL-METHIONINE)</td>
<td>200 mg, 60 enteric coated tablets</td>
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**SUBTOTAL OF COLUMN 10**

**DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE**

**RECEIVE 25% OFF THE RETAIL PRICE OF ALL PRODUCTS**
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<tr>
<td>01921</td>
<td>URIC ACID CONTROL • 60 veg. caps</td>
<td>24.00</td>
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<tr>
<td>00213</td>
<td>VANADYL SULFATE • 7.5 mg, 100 veg. tablets</td>
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<td>11.25</td>
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<td>02102</td>
<td>VENOFLOW • 30 veg. caps</td>
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<td>00408</td>
<td>VENOTONE • 60 caps</td>
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<td>THE CRAWAY® TO GREAT GLUCOSE CONTROL CD</td>
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<td>33890</td>
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<td>THE BLUE ZONES SOLUTION</td>
<td>26.00</td>
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**SUBTOTAL OF COLUMN 11**

- These products are not 25% off retail price.
- ** Due to license restrictions, this product is not for sale to customers outside of the USA.
- *** Due to license restrictions, this product is not for sale to customers outside of the USA.
- † Due to license restrictions, this product is not for sale to customers outside of the USA and Canada.

**SUBTOTAL OF COLUMN 12**

Not sure exactly which supplements you need?
Talk to a Wellness Specialist toll-free at 1-800-226-2370

receive 25% off the retail price of all products

**DEDUCT AN ADDITIONAL 10% ON ALL PRODUCTS DURING SUPER SALE**
### ORDER SUBTOTALS

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**ORDER TOTALS**

**SUPER SALE DEDUCT 10% (Subtotal X 10%)** ENDS 01/31/17

**POSTAGE & HANDLING** (Any size order, in the U.S., includes Alaska & Hawaii) $5.50

**C.O.D.s (ADD $7 FOR C.O.D. ORDERS)**

**SHIPPING**

**GRAND TOTAL** (MUST BE IN U.S. DOLLARS)

---

**PLEASE MAIL TO:** Life Extension
P.O. Box 407198 • Ft. Lauderdale, Florida 33340-7198
Or Call Toll Free 1-800-544-4440 • Fax: 866-728-1050

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**BILL TO ADDRESS**

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**SHIP TO ADDRESS**

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Prices subject to change without notice. Please notify Life Extension of any address change.
Aging is characterized by inflammation, glycation, mitochondrial decay, and loss of cellular structure/function. Mitochondrial Energy Optimizer provides the following nutrients to help neutralize these changes:

- **Carnosine**: As humans age, proteins in their bodies become damaged by glycation reactions. Glycation can lead to alterations of normal cell function. Carnosine is a powerful anti-glycating agent, and protects neurons against protein carbonyl species associated with normal aging.1-5

- **PQQ**: This micronutrient has been shown to trigger the growth of new mitochondria in aging cells!7 PQQ also activates genes involved in protecting the delicate structures within the mitochondria.8-11

- **Taurine**: Supports whole-body health and boosts new brain cell formation in the area of the brain connected to learning and memory.6

- **Luteolin**: Systemic inflammation is involved in most consequences of aging. Culprits behind inflammatory reactions are pro-inflammatory cytokines, such as interleukin-6 and tumor necrosis factor-alpha. Luteolin is a flavonoid that has been shown to help suppress these inflammatory cytokines.12-16

- **Benfotiamine**: Benfotiamine blocks multiple destructive biochemical pathways, including AGEs’ formation pathway,17-21 which is induced by higher than desirable blood glucose levels.22-23

- **Pyridoxal 5’-phosphate**: Pyridoxal 5’-phosphate is the active form of vitamin B6 that has been shown to protect against both lipid and protein glycation reactions.20-22

- **R-Lipoic Acid**: A microencapsulated Bio-Enhanced® R-lipoic acid facilitates youthful mitochondrial energy output while guarding against free radicals.28-32

To order Mitochondrial Energy Optimizer with BioPQQ®, call 1-800-544-4440 or visit www.LifeExtension.com

These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure, or prevent any disease.
86 METFORMIN REDUCES THE INCIDENCE OF OPEN-ANGLE GLAUCOMA
Scientists have discovered persuasive data that the AMPK-activating drug metformin may help protect against glaucoma. Life Extension encourages those at risk to speak to their doctor about these findings.

7 GREATEST THREAT TO LONGEVITY
The cause of most disability and death in persons over age 50 are abnormal blood clots that block arteries and veins. Fortunately, the healthy practices that readers of this magazine follow reduce risk of these occlusive vascular disorders.

36 PREVENTION OF DEEP VEIN THROMBOSIS
Sitting more than four hours a day increases the risk of potentially lethal blood clots, known as deep vein thrombosis (DVT), by 48%. Researchers have developed two natural compounds that drastically reduce platelet aggregation- and fibrin-induced clots.

58 ACHIEVING OPTIMAL SELENIUM STATUS
Volumes of research reveal how different selenium compounds exert their own unique effects in impeding malignant transformation.

26 KILL HARMFUL BACTERIA IN YOUR INTESTINES
When bacteria-killing phages were added to probiotics, there was a 40-100-fold increase in beneficial intestinal flora with huge reductions of pathogenic E.coli. These findings represent a novel opportunity to achieve optimal intestinal flora balance.

48 CANCER PROTECTIVE VEGETABLE EXTRACT
Data show that apigenin, a polyphenol found in parsley and celery, can effectively starve cancer cells, guard DNA against toxins, and block malignant cell propagation.