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October 2023

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A large, glossy, three-dimensional red heart is centered on the page. The heart has a slight shadow beneath it, giving it a sense of depth. The text "The LDL Cholesterol DEBATE" is printed in white, bold, sans-serif font across the center of the heart.

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1. *Med Res Rev.* 2019;39(5):1851-1891.
2. *ACS Omega.* 2022 Apr 19;7(15):12835-45.



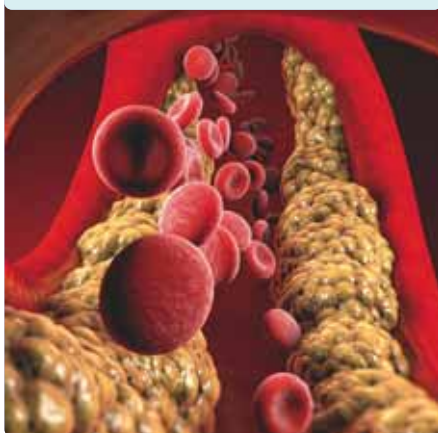
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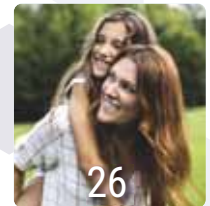
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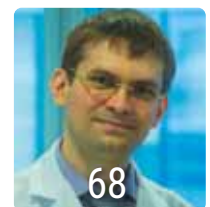
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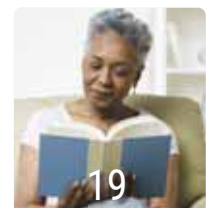
Dr. Alex Zhavoronkov uses *deep neural network* artificial intelligence to analyze, understand, and mitigate human **aging**.



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Omega-3s benefit polycystic ovary syndrome; supplements reverse measure of brain aging; higher vitamin D levels help overactive bladder; pain relieving property of PEA.



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* Br J Pharmacol. 2004 Mar;141(5):825-30.

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The LDL Cholesterol Debate



WILLIAM FALOON

One of the great controversies in recent decades is what level of **LDL cholesterol** is associated with the lowest risk of occlusive **arterial disease** (atherosclerosis).¹

Those with a **genetic** propensity to over-produce **cholesterol** suffer premature **atherosclerosis** and increased **cardiovascular disease** incidence.^{2,3}

This undisputed fact has been used to help support the importance of lowering very **high** LDL cholesterol.

The **debate** centers around what constitutes “**optimal**” LDL blood levels for normal and high-risk individuals.

With age, **LDL** often elevates to ranges that cause or contribute to **arterial blockages**.^{4,5}

This is concerning because **atherosclerosis** remains the leading cause of disease, disability, and death in the United States.⁶

I am aware of different positions that well-informed people take on the “**LDL Cholesterol Debate**.”

The data presented in this editorial reflect views of those who argue for lower **LDL** blood levels to reduce **atherosclerotic-induced** disorders.

Options for achieving safer **LDL** blood levels are provided.



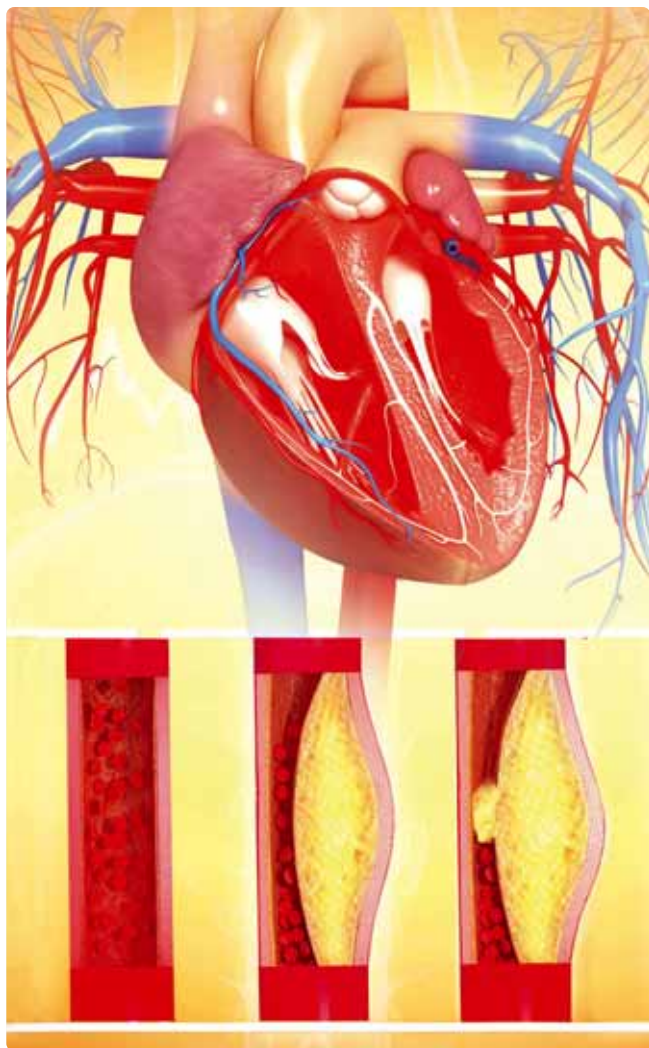
Differences in opinion about “optimal” **LDL cholesterol** values have caused fierce debate for many decades.

While clear consensus remains elusive, a recent review paper argues that based upon *all* current evidence, the **LDL** level to prevent **atherosclerosis** should be lower than commonly advocated.⁷

The authors of the review suggest targeting **LDL** to as low as **40 mg/dL** for patients at *highest* risk. This is similar to the **LDL level** of newborn infants.

These authors acknowledge that these low LDL levels will be challenging to achieve and may not be feasible for all patients without use of LDL-reducing drugs.

For patients with no significant additional risk factors for cardiovascular disease, the authors suggest that keeping **LDL** below 85 mg/dL from birth throughout life would likely **delay** onset of **atherosclerosis** complications until **age 100 years** or more.⁷



This conflicts with what some in the alternative and conventional medical communities recommend. Yet there are data to argue that **LDL** is a “**vascular toxin**.”⁷

The authors point to mathematical modeling of observational data that suggests **atherosclerosis risk** is lowest at an **LDL** level of around **38 mg/dL**.

Current LDL cholesterol guidelines vary between European and American experts, as well as among different expert working groups within different countries.

The current consensus generally suggests **LDL** blood levels should be below **100 mg/dL** in healthy individuals and below **70 mg/dL** in people at high coronary risk.

I’ll describe how the new “*lower*” LDL recommendations apply later in this article.

Modern-Day Achilles Tendon

Cardiovascular diseases are the greatest threats to our healthy longevity.

We at **Life Extension**® have long advocated that more needs to be done in order to prevent and treat **atherosclerosis**.

Arterial/vascular disease not only causes **heart attacks** and ischemic **strokes**, but also contributes to:

- Several types of dementia⁸⁻¹⁰
- Peripheral arterial disease¹¹⁻¹³
- Heart failure¹³⁻¹⁵
- Renal artery stenosis^{11,16,17}
- Carotid artery stenosis and embolization¹⁸
- Kidney failure¹⁹
- Hypertension²⁰
- Aortic calcification/stenosis^{21,45}
- Mesenteric artery disease²²
- Erectile dysfunction²³⁻²⁵
- Frailty^{26,27}
- Accelerated aging²⁸

Arterial disease represents our greatest vulnerability. It’s an **Achilles tendon** to our continued existence.



Treating Atherosclerosis More Aggressively!

A review article published **December 2022** in the *American Journal of Preventive Cardiology* made provocative arguments for achieving very low LDL blood levels.⁷

For those who don't want to read this full-text document, I summarize the following salient points:⁷

- **Atherosclerosis** is a **preventable** disease.
- Elevated **LDL** is a necessary factor for atherogenesis induction.
- Observational data from retrospective analyses, prospective longitudinal data, and interventional randomized clinical trials support **LDL** as a significant **risk factor** for **atherosclerosis**.
- The percentage of (high- and very high-risk) patients who achieve **optimized LDL** target reductions is low and has remained low for the last 30 years.

- The majority of patients at **atherosclerotic risk** are inadequately treated, leaving them vulnerable to disease progression, acute cardiovascular events, and poor aging.
- The relationship between **LDL cholesterol** and risk for **atherosclerotic cardiovascular disease** is one of the most *highly* established/ investigated issues in the entirety of modern medicine.

The above bullet points may enlighten some of you, while causing disagreement amongst others.

I next describe the most controversial aspect of this **December 2022** published review.⁷

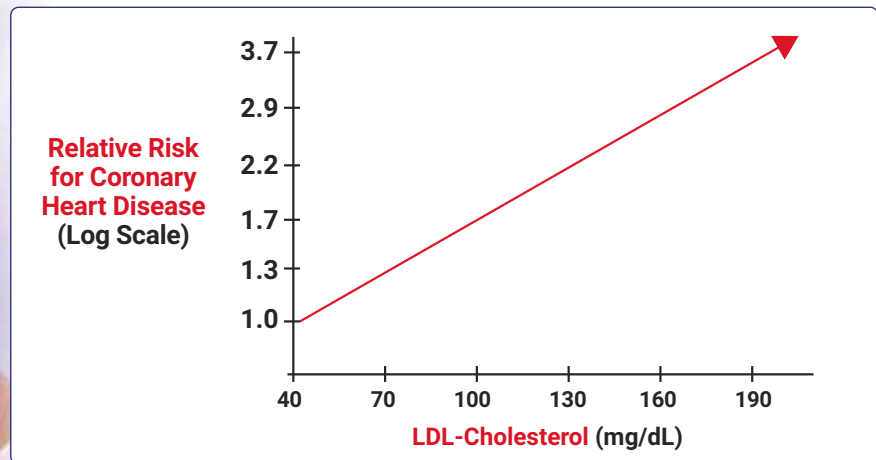
Optimal LDL Blood Levels: "20-40 mg/dL"?

The authors of this **2022 review** argue that the optimal **LDL** appears to be the level present at birth (**20–40 mg/dL**). They also recognize that this range is probably not necessary for everyone nor practical to attain widely.



Correlation Between LDL and Heart Disease Risk

The graph below shows that as LDL **blood levels** rise, there is an observed, progressive *increase* in **coronary heart disease** risk.⁵⁰



CREDIT: Grundy SM, Cleeman JI, Merz CN, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. *Circulation*. 2004 Jul 13;110(2):227-39.

Data Supporting Lower LDL Levels

The authors of the **December 2022** review cite the following data to argue that today's LDL reference ranges are too high:

- Animals and humans who maintain low cholesterol levels early in life have very little **atherosclerosis**.
- Very low **LDL** levels are observed among hunter-gatherer populations who have less evidence of atherosclerotic disease.
- The **LDL** level where there is no excess risk of atherosclerotic cardiovascular disease is approximately **38 mg/dL**. (This is strikingly low by most current standards.)
- Over a **26.5- year** follow-up, even baseline **LDL under 100 mg/dL** resulted in a continuous rise in risk for coronary **heart disease mortality**. (This suggests the importance of targeting **LDL lower** than current standards.)^{30,31}
- The average LDL level of men presenting with an **acute coronary syndrome** is approximately **150 mg/dL**.³² (This **LDL** level was viewed as "normal" in the 1980s when heart attack rates were *higher*.)
- These lower **LDL** levels are difficult to achieve in a modern society and may not be necessary for people not at high cardiovascular disease risk.
- Unfortunately, **aging** itself is the *greatest* coronary artery disease risk factor.³³
- In addition, most of us have had exposure to **secondhand tobacco** smoke and less than ideal **dietary** practices in our early years. This inflicts **arterial damage** that can manifest as **cardiovascular disease** in later life.
- One way to reduce **cardiovascular risk** is to target **LDL** to lower ranges depending on individual circumstances.

These authors suggest that **LDL below 40 mg/dL** seems the most effective goal for patients in the category of more advanced **atherosclerosis**. This means **vascular disease** patients at *highest* risk.

Recall that the current target advocated by many lipid authorities, but not all, for those at **high cardiovascular risk** is **LDL below 70 mg/dL**.

What you've read so far represents quite a difference of opinion! Especially when today's general recommended **LDL** reference range is somewhere below **100 mg/dL**.

To put this in historic perspective, in the **1980s** the upper limit for **LDL** readings was around **160 mg/dL**,²⁹ which is considered **high** by today's standards.

We at **Life Extension®** argued back then that **LDL** blood levels should be below 100 mg/dL. Subsequent research helped validate this, yet there is now published data to suggest even lower LDL targets.

LDL-Lowering Strategies

Decreasing intake of **saturated fat** (meat, butter, cheese, and full-fat dairy) to less than **7%** of daily calorie intake can reduce LDL by **8% to 10%**.³⁴

The problem is that a typical aging person's **LDL** is far above 120 mg/dL.

Even if they stick with a rigid diet, a **10% decrease** translates into an **LDL level of 108 mg/dL**, which may be twice as **high** as ideal for many individuals.

Statin drugs have been attacked by alternative medicine for decades. Yet the **side-effect** risks of modest statin drug dosing may be trivial compared to the **deadly** impact of elevated **LDL** and related proteins like **apolipoprotein B (ApoB)**.^{35,36}

Dangerously high levels of **ApoB** occur commonly in people with high **LDL**.³⁷ The statin drug **rosuvastatin** was shown to reduce **ApoB** levels by **36%-45%**, which was better than other statin drugs tested.³⁸



Life Extension® Magazine published an article in 2003 showing that every *other* day dosing of a modest **statin (10 mg/atorvastatin)** yielded significant benefits with zero side effects. And for some of you, a modest statin dose taken every *other* day might push your **LDL** down to an ideal range.³⁹

Those with **higher LDL** levels may take a **modest** dose statin combined with another drug (ezetimibe) that blocks intestinal reabsorption of cholesterol.⁴⁰ Others need a **higher** dose statin drug to achieve **LDL below 40-70/mg/dL** depending on their **cardiovascular risk** factors.

An expensive class of drugs (PCSK-9 inhibitors) such as **Repatha®** can slash **LDL** to below **30 mg/dL**. Insurance companies often refuse to pay the high price of this drug.^{41,42}

I am aware of the concerns raised about statin drug side effects. Overlooked by many, however, is the ability of statin drugs to **lower** elevated **LDL** and **ApoB**.

There has been a multi-decade debate about what **optimal LDL** blood levels should be. As it relates to the dangers of **elevated ApoB**, there is virtual unanimity, i.e., keep your **ApoB** levels in **low** ranges to **reduce atherosclerotic** risks.

A Non-Drug Approach!

An article on page 36 of this month's issue describes a **botanical extract** that has demonstrated **LDL-lowering** effects.

The latest **human** study showed a **21.8%** **decline** in **LDL**. The **placebo** arm of this study had a **3.83%** **LDL increase**.⁴³

In addition to reduced **LDL**, this **plant extract** was shown to lower **total cholesterol**, **triglycerides**, and **C-reactive protein*** while boosting beneficial **HDL**.

These favorable blood changes were accompanied by improved **endothelial function**, a measure of arterial health.

For many readers of **Life Extension® Magazine**, a **21%** **reduction** in **LDL** will achieve desired levels. Others might need a **statin drug** in addition to this **plant extract** to achieve optimal **LDL** ranges.

* **C-reactive protein** is a marker of **chronic inflammation**. Elevated C-reactive protein has been shown in some studies to be a greater cardiovascular risk factor than high LDL cholesterol.⁴⁴

Interesting Maps

The maps copied on the next page show an association of **high cholesterol** prevalence and **increased** incidence of **stroke** and **lower** life expectancy.

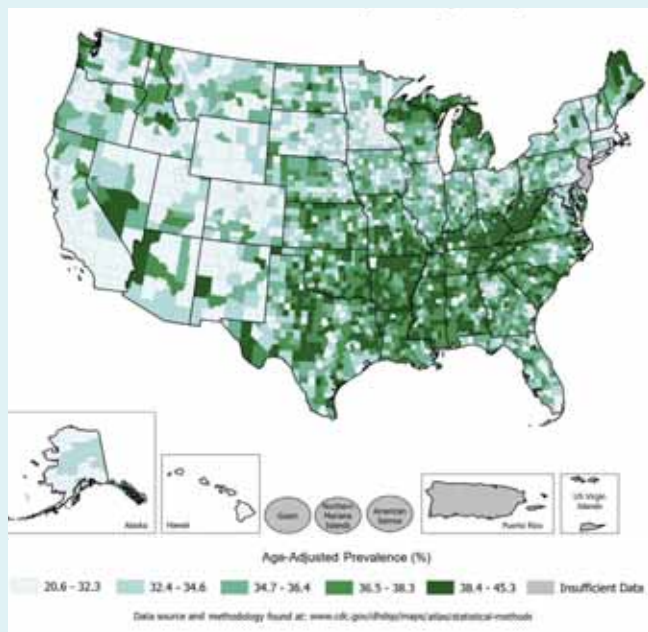
While these maps show correlation and not causation, they depict shorter lifespans in areas where most people **fail** to take care of their health.

Map A shows that concentrations of counties with the **highest cholesterol prevalence**—meaning the top quintile—are located primarily in Mississippi, Louisiana, Arkansas, Oklahoma, Texas, Kentucky, Tennessee, Michigan, Maine, South Carolina, and Kansas.⁴⁶



A

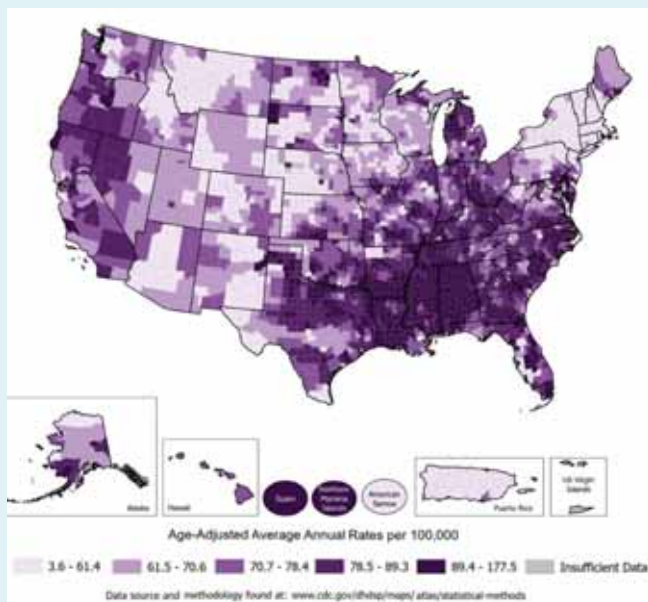
High Cholesterol Prevalence, 2018-2020 Adults Screened, 18+, by County



Source: CDC.
<https://www.cdc.gov/cholesterol/facts.htm>

C

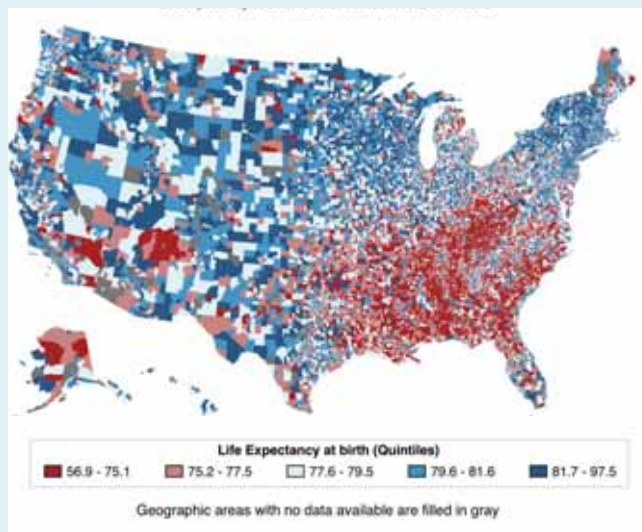
Stroke Death Rates, 2018-2020 Adults, Ages 35+, by County⁴⁸



Source: CDC.
<https://www.cdc.gov/stroke/facts.htm>

B

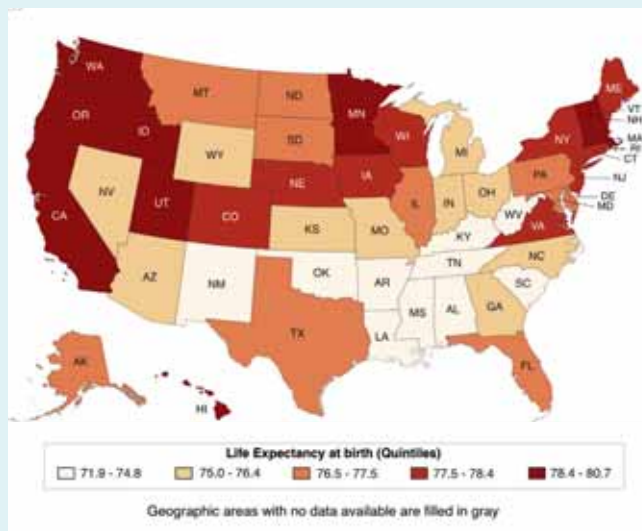
Life Expectancy at Birth for U.S. States and Census Tracts, 2010-2015⁴⁷



Source: CDC.
<https://www.cdc.gov/surveillance/blogs-stories/life-expectancy.html>

D

Life Expectancy in the U.S. in 2020⁴⁹ **Nine-Year Disparity in Human Longevity** (Note lighter colors below reflect reduced life expectancy.)



Source: CDC.
https://www.cdc.gov/nchs/pressroom/sosmap/life_expectancy/life_expectancy.htm

Your Blood Test Results Are What Matter!

The objective of a **lipid-lowering** program is to achieve blood levels that have been shown to reduce **cardiovascular risks**.

Low-cost **blood tests** provide readings of artery-clogging lipids including LDL, ApoB, and triglycerides.

Current guidelines generally suggest **LDL** readings over **99 mg/dL** are potentially dangerous.

In recent years, those with cardiovascular risks have been advised to drop their LDL to below **70 mg/dL**.

A **2022** published review provides evidence that those patients at *highest* cardiovascular risk may benefit from targeting LDL below **40 mg/dL**.⁷

If a blood test reveals *higher* than **optimal LDL** or other vascular risk factors, initiate the appropriate corrective action(s). Then retest in a few months to check how the approach works for you.

Assess Your Cardiovascular Risks

The time to lower atherogenic risks is before one suffers a **heart attack** or ischemic **stroke**.

I continue to be surprised when asking educated people what their **LDL**, **triglyceride**, and **C-reactive protein (CRP)** levels are. Most respond by saying they have no idea.

I am aware of the different positions that informed people take on the “**LDL Cholesterol Debate**.”

The data presented in this editorial reflect the views of those who argue for lower **LDL** levels to reduce cardiovascular risks.

The blood test panel on the next page costs **hundreds of dollars** at commercial labs but is available to **Life Extension®** readers at a steeply discounted price.

The **Cardio Core Essentials Panel** costs only **\$68** (item # LC100086) if you order by December 31, 2023.

You can obtain this blood test panel by calling (24-Hours) **1-800-208-3444** or visit: **www.LifeExtension.com/CORETEST**

For longer life,



William Faloon, Co-Founder
Life Extension®

Scientific references for this editorial can be found on page 16.



CARDIOVASCULAR RISK Blood Testing

The build-up of fatty plaque inside arteries occurs long before coronary heart disease or ischemic stroke strike.

Blood tests can identify correctable risks before atherosclerotic disease outwardly manifests.

The cost of comprehensive blood testing impedes most people from identifying their cardiovascular vulnerabilities.



This special **Cardio Core Essentials Panel** (Item # **LC100086**) provides the following measures of **atherosclerotic risk** for only **\$68**:

➔ **C-REACTIVE PROTEIN (CRP)**

The C-reactive protein (CRP) blood test measures the level of systemic inflammation, that can indicate the status of your heart health and how at-risk you are for developing cardiovascular problems. Factors that contribute to atherosclerosis include chronic inflammation, and elevated lipids.¹ The result is higher levels of CRP in patients with atherosclerosis than in those without atherosclerosis.

➔ **APOLIPOPROTEIN B (APOB)**

Apolipoprotein B (ApoB) is the main protein constituent of all non-HDL cholesterol in your blood. This test measures potential plaque-forming particles in your blood. The higher your ApoB the higher your risk of future cardiovascular events.²

➔ **KIDNEY FUNCTION:**

• Uric acid • BUN (blood urea nitrogen) • Creatinine
• BUN/creatinine ratio • eGFR (estimated glomerular filtration rate)

➔ **BLOOD SUGAR:** Fasting glucose

➔ **LIPID PROFILE:**

• Total cholesterol • Triglycerides • HDL cholesterol
• LDL cholesterol (calc.) • VLDL cholesterol (calc.)
• Total cholesterol/HDL ratio (Estimated Coronary Heart Disease risk)

➔ **ELECTROLYTES AND MINERALS:**

• Sodium • Potassium • Chloride • Calcium • Phosphorus
• Iron • Carbon dioxide (CO₂)

➔ **LIVER FUNCTION:**

• Alkaline phosphatase • LDH (lactate dehydrogenase)
• AST (aspartate aminotransferase) • ALT (alanine transaminase) • Total protein • Albumin • Globulin
• Albumin/globulin ratio • Bilirubin

➔ **COMPLETE BLOOD COUNT:**

• Red blood cell count • Hemoglobin • Hematocrit
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Blood test services are available only in the continental United States and Anchorage, AK. Not available in Maryland. Restrictions apply for residents of MA, NY, NJ, RI, and PA.

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In the News



Brain Aging Measure Reversed by 2.8 Years

Biological brain aging was reversed among participants who were in a nutritional supplement program for an average of 13 months, a clinical study in *Brain Science* reported.*

The study included 47 people who were assigned lifestyle changes and 42 who were assigned an individually tailored program of supplements that included, but was not limited to, vitamins **A, B complex, C and D, alpha-lipoic acid, CoQ10, magnesium, omega-3 fatty acids, zinc, and *Bifidobacterium* and *Lactobacillus*** probiotics.

Brain biological age was estimated before and after the intervention using a quantitative electroencephalogram.

Participants who consumed the supplements had a brain biological age that averaged **2.83 years younger** than the age measured at the beginning of the intervention. Those in the lifestyle group had a brain age that averaged only **0.02** years younger than it was at the start of the study.

Editor's Note: "...brain biological age *deceleration*, and even *reversal*, with accompanying improvements in mental-physical health comorbidities, is possible in humans using accessible interventions, such as lifestyle changes or nutraceutical supplementation, within a practical time frame," the authors concluded.

* *Brain Sci.* 2023 Mar 21;13(3):520.

Meta-Analysis Affirms Pain-Relieving Property of PEA

A systematic review and meta-analysis of clinical trials affirmed the association between supplementing with palmitoylethanolamide (PEA), a naturally occurring fatty acid amide, and improvements in **chronic pain**, **functional status**, and **quality of life**.*

The research team selected 11 double-blind randomized controlled clinical trials that included 774 men and women with **chronic pain**.

The conditions responsible for their chronic pain included gynecologic disorders, neurologic diseases, temporomandibular joint arthritis, knee arthritis, irritable bowel syndrome, and others.

The studies evaluated the effects of oral PEA in doses of **300–1,200 mg** per day administered in one or two doses. Treatment periods ranged from 10 days to 12 months.

Pooled analysis of the studies found a reduction in **pain intensity** among participants who received PEA compared to the control group. No major side effects were attributed to PEA in any study.

Editor's Note: "PEA is a well-tolerated approach for chronic pain," the researchers stated.

* *Nutrients*. 2023 Mar 10;15(6):1350.





Overactive Bladder Improvement Linked to Higher Vitamin D Levels

A systematic review and meta-analysis showed an association between *higher* vitamin D levels and a *lower* risk of overactive bladder or urinary incontinence. A decreased risk of incontinence was also revealed among people who used vitamin D supplements.*

The investigation included four randomized controlled trials, three cohort studies, three cross-sectional studies and three case-control studies that examined the relationship between vitamin D levels and overactive bladder or urinary incontinence. Vitamin D levels were lower in participants with either condition in comparison with control groups.

Participants who were vitamin D deficient had over **four times** the odds of overactive bladder, and a **30%** greater risk of incontinence compared with those who were not deficient. Analysis of articles that reported the effects of vitamin D supplementation found a **66%** lower risk of incontinence among supplemented participants.

Editor's Note: "Vitamin D deficiency increases the risk of overactive bladder and urinary incontinence, and vitamin D supplementation reduces the risk of urinary incontinence," the authors concluded.

* *Nutr Rev.* 2023 May 17;nuad049.

Omega-3s and Polycystic Ovary Syndrome

Improvements in insulin resistance and lipids were shown among women with polycystic ovary syndrome (PCOS) in association with omega-3 supplementation, according to a meta-analysis published in the *Journal of Ovarian Research*.*

PCOS is a hormonal and metabolic condition that can include ovarian cysts, menstrual irregularities, infertility, and other conditions.

The meta-analysis of 11 clinical trials included 816 women with PCOS. The trials studied changes in metabolic status associated with omega-3 supplementation or with the consumption of foods that provided at least **1,000 mg** per day of omega-3 for at least eight weeks.

Compared with the control group, women who received omega-3 supplements experienced reductions in waist circumference, fasting plasma insulin, fasting glucose, insulin resistance, triglycerides, total cholesterol, and LDL cholesterol.

In the omega-3 group there were also increases in levels of adiponectin, a hormone involved in regulation of glucose levels, fatty acid metabolism, and **insulin sensitivity**.

Editor's Note: "Omega-3 fatty acids may be an effective intervention for alleviating metabolic status in PCOS," the authors concluded.

* *J Ovarian Res.* 2023 Mar 17;16(1):54.



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Who We Are

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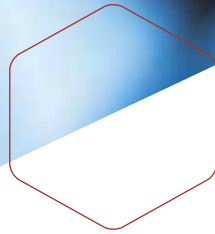
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ASTAXANTHIN and Aging Skin





BY MICHAEL DOWNEY



Astaxanthin has long been associated with eye,¹ brain,² and heart health.³

Scientists have also demonstrated that this **carotenoid** protects the health of the **skin**.

It does so by inhibiting drivers of **skin damage**, helping to maintain skin function and structural integrity.^{4,5}

Aging skin is more than a cosmetic issue. Loss of skin integrity and functionality can impair overall health.⁶

Clinical trials show that oral **astaxanthin** can help protect skin against sun damage, loss of moisture, and development of wrinkles, while improving skin health.

Importance of Skin Health

The **skin** serves many functions, including:⁷

- Acting as a barrier against **infection**,
- Helping maintain the body's **hydration** and temperature, and
- Serving as the frontline of **immune** protection against environmental toxins.

Wrinkles and dry, damaged skin are signs of deterioration with age.⁶

When skin structure starts to deteriorate, it can weaken its essential **barrier** function against the external environment.

Age isn't the only factor behind skin **damage**. Skin integrity is also degraded by **ultraviolet (UV) radiation** from the sun.^{8,9}

The damage inflicted results in reduced **firmness** and **elasticity**.

This may lead to deeper wrinkles, mottled pigmentation, roughness, drying, scaling, sagging, photoaging, precancerous lesions, and even skin cancers.⁹

Astaxanthin has been shown to help protect the appearance *and* function of the skin.

How Astaxanthin Reduces Skin Damage

Astaxanthin is a red carotenoid found at high concentrations in certain microalgae.^{1,2}

It is a powerful **antioxidant** and **anti-inflammatory** that provides a wide range of health benefits.¹ In the last several years, researchers have discovered the role it plays in protecting the **skin**.

Evidence shows that astaxanthin combats the negative effects of two underlying causes of skin aging: environmental pollutants and UV light exposure.

Preclinical and clinical data demonstrate that **astaxanthin** can:

- Reduce the secretion of a protein-degrading enzyme called **MMP-1**.^{4,10} MMP-1 *increases* when skin is exposed to air pollution¹¹ and breaks down youthful structure of skin.^{4,11-13}
- Suppress the production of harmful inflammatory cytokines that follows exposure to UV rays.^{4,10,14}

Furthermore, by reducing **MMP-1**, astaxanthin may be able to fight **wrinkles** from multiple other causes.

Protection Against Skin Aging

Researchers investigated astaxanthin's ability to protect the skin against the effects of **pollutants** and **aging**. Studies showed that **astaxanthin**:

- Improved skin wrinkles, elasticity, and texture,^{15,16}
- Boosted skin moisture content while reducing skin water loss,^{15,16}
- Inhibited the **underlying processes** that produce wrinkles and age spots,¹⁵⁻¹⁸ and
- Enhanced **collagen** production in skin cells, which helps maintain or restore skin's youthful plumpness and firmness.¹⁹

These findings show that **astaxanthin** can help prevent the **visible** signs of skin aging and pollutants—*and* protect some of its critical barrier functions, such as water retention.

Defense Against UV Damage

UV radiation is the most powerful driving force behind skin deterioration.

Studies suggest that astaxanthin provides **targeted UV protection**. Astaxanthin has been shown in a clinical and multiple preclinical settings, to:

- Prevent UV-induced loss of the body's antioxidant **glutathione**,²⁰
- Restore UV-diminished levels of the body's antioxidant **superoxide dismutase (SOD)**,²⁰
- Fight UV-induced increases in numerous enzymes that damage skin and promote wrinkles,^{4,21} and
- Reduce UV-induced expression of pro-inflammatory **cytokines** that damage skin integrity.^{18,21}

One study showed that giving **astaxanthin** to mice exposed to UV radiation **suppressed** the harmful molecular responses seen in UV-exposed mice that were *not* given astaxanthin.

The damaging responses **prevented** by astaxanthin included:⁵

- Water loss across the skin barrier,
- Accelerated formation of wrinkles,
- Increased expression in the top layer of skin (epidermis) of **enzymes** that cause skin cells to break down, and
- Increases in the bottom layer of skin (the dermis) of the **MMP-13 enzyme** (MMP-1 alternate in rodents), a contributor to loss of skin tone and elasticity.

This study demonstrated that, preclinically, astaxanthin taken **orally** makes its way to multiple layers of skin,⁵ where it can inhibit or reverse the destructive effects of **UV radiation**.

Real-World Clinical Trial

In one clinical study, **astaxanthin** was “real-world tested” on 65 healthy Japanese women who went about their daily lives between August and December.⁴ Skin damage during these months is generally at its *highest* in Japan because of environmental factors such as UV light and low humidity.

Subjects took either a **placebo** or **astaxanthin** in **6 mg** or **12 mg** doses daily.

In just **16 weeks**, the **placebo** group had:⁴

- Significant worsening of **wrinkles**,
- Reduced **moisture** content, and
- Increased skin markers of **inflammation**.

Women taking either dose of **astaxanthin** showed no **significant skin deterioration** and no increase in **inflammatory** markers.

UV Protection

Another clinical (human) trial was conducted in a lab, where volunteers were exposed to controlled levels of UV rays.²²

For nine weeks, subjects took either a placebo or **4 mg** of astaxanthin daily, after which they were tested with UV exposure.

WHAT
YOU
NEED
TO
KNOW



Maintain Skin Health

- **Astaxanthin** is a carotenoid that supports eye, brain, and heart health. It now shows promise for maintaining **skin** integrity and function as well.
- Studies demonstrate that oral astaxanthin safely slows skin deterioration caused by **age**, **pollution**, and **sun** exposure.
- In clinical studies, astaxanthin helps prevent skin wrinkles, moisture loss, and UV-induced burning, improving skin appearance and health.
- Taking astaxanthin combined with **phospholipids** makes it more bioavailable (absorbable).

Compared with the placebo group, those taking **astaxanthin** had:²²

- *Increased* time before UV exposure caused burning,
- *Reduced* loss of skin moisture in the UV-exposed area, and
- Significant *improvement* of skin roughness and texture in **non-irradiated** areas.

That means both UV-exposed *and* non-UV-exposed skin health was **improved** by astaxanthin.

In addition, a 2021 **meta-analysis** of studies concluded that **astaxanthin** improves moisture content and elasticity, and reduces **wrinkles**,²³ adding clear evidence that astaxanthin may be used to maintain skin health and fight skin damage.²⁴

Summary

Studies have demonstrated that the carotenoid **astaxanthin** inhibits key skin-damaging factors.

These effects have been clinically validated to **reduce** and **reverse** aspects of **skin aging** caused by pollutants and sun exposure, while improving outward appearance and skin health. •

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

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"I'm a big fan of it."

Sue

VERIFIED CUSTOMER REVIEW

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NT2 Collagen™ standardized cartilage providing Total Collagen	40 mg
Boron (calcium fructoborate as patented FruiteX-B® OsteoBoron®)	1.5 mg

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^Δ 3-O-acetyl-11-ketoB-boswellic acid.

Item #02238 • 60 capsules
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4 bottles \$22 each



For full product description and to order **ArthroMax® Advanced with NT2 Collagen™ & AprèsFlex®** call 1-800-544-4440 or visit www.LifeExtension.com

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Maintain Endothelial
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ARTERIAL PROTECT can help stabilize endothelial plaque and promote healthy blood flow throughout the body.*

Just one capsule a day provides the patented French Maritime **pine bark extract** used in clinical studies along with **Gotu Kola**.

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* *Int Angiol.* 2014 Feb;33(1):20-6.

Item #02004
30 vegetarian capsules
1 bottle **\$33**
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"I like what I see when I look in my mirror!"

Nancy

VERIFIED CUSTOMER REVIEW

The quickest way to betray your age is with a tired appearance ...

Revive Hair, Skin, and Nails from Within

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Working from the inside out, **Hair, Skin & Nails Collagen Plus Formula** is an oral supplement with nutrients shown to benefit the hair, skin, and nails to keep them looking vibrant and healthy. Rejuvenating nutrients include:

- **VERISOL® Bioactive Collagen Peptides®**—Stimulates the formation of new collagen and elastin to promote skin suppleness and elasticity¹
- **Cynatine® HNS Plus**—Provides solubilized keratin, zinc, B vitamins, biotin, and copper to boost production of keratin for strong hair, skin, and nails
- **Biotin**—Supports nail strength and integrity²
- **Silicon**—For the formation of collagen and keratin molecules³



Item #02322 • 120 tablets

1 bottle **\$24.75**

4 bottles \$22.50 each

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Michael
VERIFIED CUSTOMER
REVIEW

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HIGHLY ABSORBABLE

ASTAXANTHIN

Supports Liver Health

"I take this every morning and what a difference it makes!"

Kathryn

VERIFIED CUSTOMER REVIEW

ASTAXANTHIN is a carotenoid that benefits the liver, heart, skin, and immune system. Research suggests that astaxanthin can play a role in promoting cardiovascular health.¹

Found naturally in seafood and algae, as little as **50%** of **astaxanthin** is normally **absorbed** in the bloodstream.^{2,3}

Life Extension® combines **4 mg** of **astaxanthin** with a blend of four different **phospholipids**, which has been shown to enhance carotenoid **absorption** by **several-fold**.⁴

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For full product description and to order **ASTAXANTHIN 4 mg with Phospholipids**, call 1-800-544-4440 or visit www.LifeExtension.com



Item #01923
30 softgels

1 bottle **\$12**

4 bottles **\$10.50 each**

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AMLA

Reduce Artery-Blocking **LIPIDS** and **INFLAMMATION**

BY MICHAEL DOWNEY

Arterial disease often initiates in youth and rapidly worsens with **age**.¹

As **blood flow** is obstructed, people suffer diminished energy and cognition.

Progressive **arterial blockage** can manifest as coronary **heart disease**, ischemic **stroke**, and other bodily impairments.¹

Factors that contribute to **arterial occlusion** include **chronic inflammation**, **oxidative stress**, and elevated **lipids**.¹

Placebo-controlled human trials have found that a **fruit extract** can lower artery-damaging **lipids**, thus providing a **non-drug** approach to support **cardiovascular health**.^{2,3}



How Occlusive Heart Disease Develops

Coronary artery disease develops as plaque builds up in blood vessels feeding the **heart muscle**.

As coronary blood flow diminishes, the heart becomes oxygen and nutrient deprived. The *first* sign of a problem can be **angina** pain and/or **heart attack**.⁴

Many factors initiate and worsen atherosclerosis. *Prevention* before severe coronary artery obstruction (or aortic stenosis) manifests is considered the most effective strategy.¹

This includes lowering **inflammatory** markers and lipids like **triglycerides**, **apolipoprotein B**, and **LDL** when elevated.

The Lipid Link

A contributor to **cardiovascular diseases** is a person's **lipid profile**.

High blood levels of certain **lipids** (fats) promote **atherosclerotic** lesions. Over time, occlusive plaque reduces blood flow and boosts **heart attack/stroke** risk.

For example, elevated levels of oxidized **low-density lipoproteins (ox-LDL)** can damage **endothelial cells**

that line arteries. Endothelial dysfunction is a key factor in the initiation and worsening of atherosclerosis.

High **triglycerides** increase oxidative stress and the production of **pro-inflammatory** biochemicals.⁵ Elevated triglycerides also induce artery-clogging blood clots by increasing production of certain clotting factors.⁶

Excess triglyceride levels are associated with **small-dense LDL** particles, **very-low-density lipoproteins (VLDL)**, and other particles that promote **atherosclerosis**.^{7,8}

Maintaining healthy **lipid** and **inflammatory** levels is a key factor in cardiovascular risk reduction.

Clinical Results

Animal studies found that **amla** fruit reduces **LDL** and **triglycerides**.⁹⁻¹²

To test these findings in people, scientists developed an **amla fruit extract** standardized to a **60%** content of **tannins**.

This standardized tannin concentrate delivers an **amla extract** dose that has a *long-lasting antioxidant* effect.





In a 12-week clinical trial,³ volunteers with metabolic syndrome (a cluster of conditions that increase cardiovascular risk) were divided into three groups:

- One took a **placebo** twice daily,
- Another took **250 mg of amla extract** twice daily, and
- A third group took **500 mg of amla extract** twice daily.

Both of the **amla** doses were shown to be more effective than **placebo** at improving the measured outcomes. But the *higher* dose showed *substantially* greater reductions in cardiovascular disease risk factors.

In the group taking **500 mg** twice daily of amla extract:³

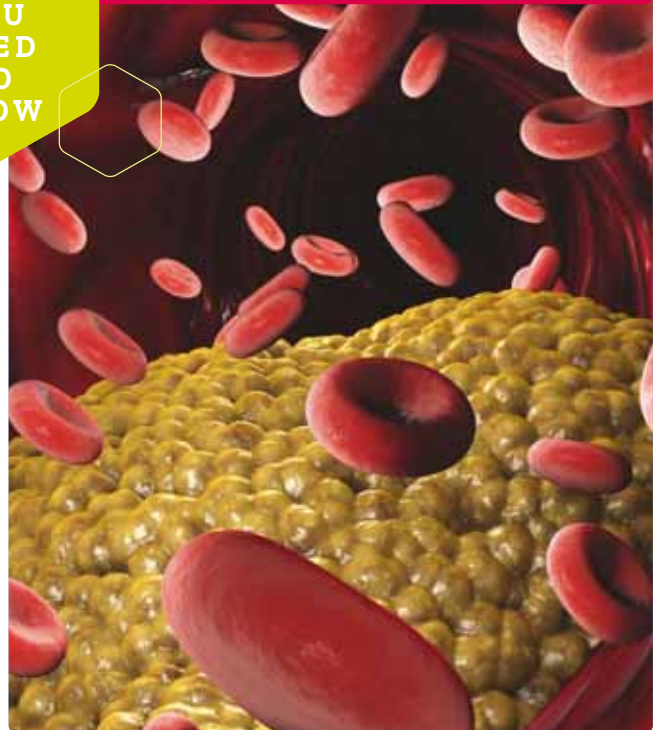
- **LDL cholesterol** *decreased 21.8%*,
- Protective **HDL** *increased 22.2%*,
- **Triglycerides** *decreased 19.2%*,
- **Total cholesterol** *decreased 11.1%*,
- **Endothelial function** was restored to normal range (indicated by improvement in Reflective Index, a validated method to evaluate endothelial function) **>6%**,
- The inflammatory marker **CRP** *decreased 53.8%*, and
- Levels of the body's antioxidant, **glutathione**, *increased 53.2%*.

Each of the above effects have been shown in other studies to reduce cardiovascular risks. There were no serious adverse effects.

Control Lipids and Reduce Heart Disease Risk

- **Cardiovascular disease** is the leading cause of death in America.
- **Amla fruit extract** has been shown in studies to improve lipid levels and other factors that drive cardiovascular disease.
- In a clinical study, taking **500 mg** of amla extract twice daily reduced **LDL** cholesterol by **21.8%**, triglycerides by **19.2%**, and total cholesterol by **11.1%**. It also led to remarkable improvements in endothelial function, inflammation, and oxidative stress.
- The reduction in total cholesterol alone translates to a roughly **30% reduction** in heart disease risk when assessed by conventional standards.

WHAT
YOU
NEED
TO
KNOW



Vascular Risks and Amla Fruit

Elevated lipids are not the only cause of **atherosclerosis**. Other cardiovascular risk factors include:

- **Endothelial dysfunction.** When endothelial cells lining the walls of blood vessels lose normal function, it promotes **atherosclerosis**.^{13,14} Cell and human studies show that **amla extract** enhances production of **nitric oxide**, a compound that signals arterial walls to relax

Optimal Cholesterol Goals

People with a family history or with *modestly* elevated LDL and other atherogenic risk factors may wish to take **amla extract** to reduce dangerous **lipid** and **inflammatory** markers.

Those with high cholesterol who *do* require statins may consult their physician to discuss the option of adding **500 mg** of amla extract twice daily.

If you currently take a prescribed lipid-lowering drug, do not stop taking it, and do not reduce its dosage *until you have consulted your physician*.

The most effective way of measuring individual responses to amla or any lipid-controlling compound is with follow-up **blood testing**.

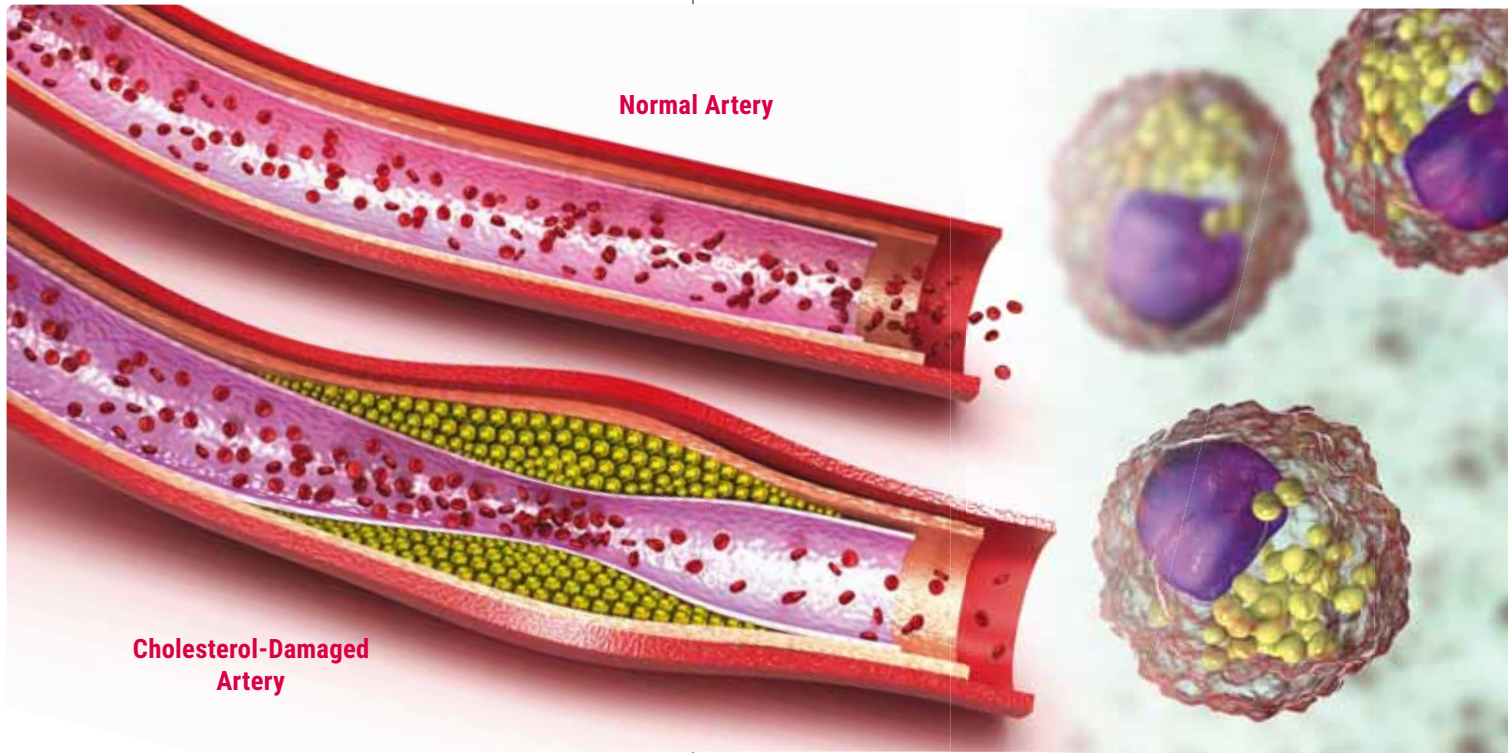
and maintain blood flow.^{2,3,15-17} In a clinical trial of hypertensive patients on medication, amla extract has shown modest improvement in blood pressure in participants receiving amla extract as compared to placebo.²⁵

- **Oxidative Stress.** Clinical and preclinical studies have demonstrated that amla reduces oxidative stress in *three* ways: It inhibits production of free radicals that damage blood vessels, neutralizes existing free radicals, and boosts production of natural cellular antioxidants such as **glutathione**.^{3,18-23,26}
- **Chronic Inflammation.** Inflammation contributes to the formation of atherosclerotic plaque. The inflammatory marker **C-reactive protein (CRP)** is an independent predictor of coronary heart disease.³ In preclinical and clinical studies, **amla** has demonstrated **anti-inflammatory** properties.^{24,25}



CONVENTIONAL CHOLESTEROL TEST RESULT

Test Name	In Range	Out Of Range	Reference Ra
CHOLESTEROL TOTAL	170 mg/dL		100-199 mg/d
HDL CHOLESTEROL	81 mg/dL		>39 mg/dL
TRIGLYCERIDES	76 mg/dL		<150 mg/dL
LDL CHOLESTEROL	86 mg/dL		<100 mg/dL (



Summary

Multiple factors contribute to **cardiovascular disease**. Studies on animals and humans show that **amla fruit extract** reduces many of these risks.

In a clinical study, taking **500 mg** of amla extract **twice daily** significantly reduced endothelial dysfunction, inflammation, and oxidative stress, along with elevated **triglycerides** and **LDL**.

Improvement in protective **HDL** levels was also observed.

The most effective way of assessing individual responses to **amla** or *any* lipid-controlling compound is with blood tests that include LDL, HDL, C-reactive protein, and other vascular risk markers. ●

Cardio Core Essentials Panel

To review a blood panel that includes **LDL**,²⁹ **HDL**, **C-reactive protein**,²⁷ **triglycerides** and other lipid risk factors like **apolipoprotein B**,²⁸ turn to page 15.

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

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Dryness and loss of firmness are outward signs of normal aging.

One reason is loss of **ceramides** that are required for skin to retain its **moisture** and youthful suppleness.

Skin Restoring Ceramides contains wheat-derived ceramide lipids in an **oral** capsule that **hydrate** the skin and smooth the appearance of fine lines and wrinkles.

Restore Smoother,
Youthful-Looking
Skin from the
Inside Out



Item #02096

30 liquid vegetarian capsules

1 bottle **\$18.75**

4 bottles \$17.25 each

For full product description and to order **Skin Restoring Ceramides**, call **1-800-544-4440** or visit **www.LifeExtension.com**

Contains wheat. Gluten free.

Ceratiq® is a registered joint-trademark of PLT Health Solutions and Arco, Robertet Group, France.



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Prostate HEALTH

The best way to keep YOU in the picture.

Ultra Prostate Formula was created to help maintain prostate health. It contains a dozen ingredients to:

- Support healthy urination
- Promote healthy prostate function
- Support healthy prostate cell division

Ultra Prostate Formula is our most comprehensive *standardized*-ingredient prostate-health supplement.

Item #02029
 60 softgels
 1 bottle **\$29.25**
 4 bottles \$27 each



For full product description and to order **Ultra Prostate Formula**, call **1-800-544-4440** or visit **www.LifeExtension.com**

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PQQ

for a vibrant YOU



PQQ (pyrroloquinoline quinone) energizes cells and can support the growth of new mitochondria.*

PQQ is available in **20 mg** capsules as shown on this page.

Some people use a combination formula that provides **100 mg** of the superior **ubiquinol** form of **CoQ10** along with shilajit and **10 mg** of **PQQ**.

Popular formulas like **Mitochondrial Energy Optimizer** (#01868) provides **10 mg** of **PQQ**. There are also **10 mg PQQ** capsules (#01500) available.

Optimal daily **PQQ** dose is **10 to 20 mg**.



Item #01647 • 30 vegetarian capsules
1 bottle **\$24** | 4 bottles \$18 each

Item #01733 • 30 softgels

1 bottle **\$38.25** | 4 bottles \$31 each

For full product description and to order **PQQ** or **Super Ubiquinol CoQ10 with PQQ**, call **1-800-544-4440** or visit **www.LifeExtension.com**



* *J Biol Chem.* 2010;285(1):142-52.

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D EFEND YOUR HEALTH

"One of my main daily 'go to' supplements."

Lew

VERIFIED CUSTOMER REVIEW

Vitamin D3

Systemic support for immune function and bone health.



Item #01713

125 mcg (5000 IU) • 60 softgels

1 bottle \$7.50 • 4 bottles \$6.50 each



For full product description and to order Vitamin D3, call 1-800-544-4440 or visit www.LifeExtension.com

CAUTION: Individuals consuming more than 50 mcg (2000 IU)/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 10000 IU per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels.

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.

SUPPORT HEALTHY LIPID LEVELS



FRUIT

Amla

EXTRACT

ADVANCED LIPID CONTROL
CAN HELP SUPPORT
HEART HEALTH.



ADVANCED LIPID CONTROL contains a standardized **500 mg** extract of **amla** in each capsule.

Researchers have discovered that **amla** improves various markers of **cardiovascular** health.

In a **placebo-controlled** clinical trial* **amla extract** supported healthy levels of:

- ▶ **LDL**
- ▶ **HDL**
- ▶ **Triglycerides**
- ▶ **Total cholesterol**
- ▶ **Endothelial function**
- ▶ **CRP (C-reactive protein)**

Item #01828
60 vegetarian capsules
1 bottle **\$22.50**
4 bottles \$20.25 each

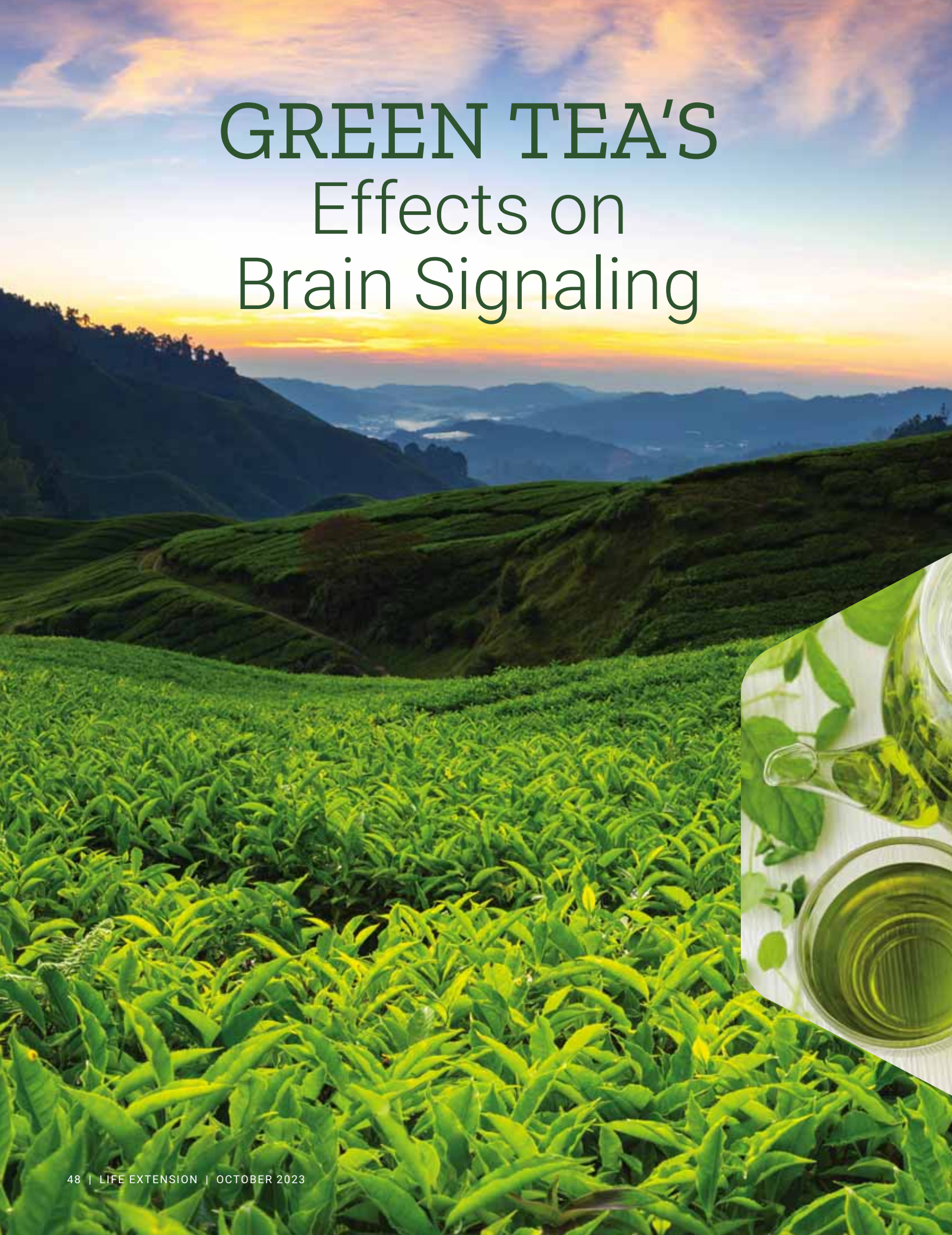
For full product description and to order **Advanced Lipid Control**, call **1-800-544-4440** or visit **www.LifeExtension.com**

* *BMC Complement Altern Med.* 2019;19:97. Capros® is patent protected and a registered trademark of Natreon, Inc.



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GREEN TEA'S Effects on Brain Signaling





BY JAMES RYDER

Green tea contains compounds that have been shown in animal and cell studies to defend **brain function**.^{1,2}

A meta-analysis of 36 observational studies found that **green tea** consumption was associated with lower rates of **cognitive** issues and dementia compared to those who rarely drink it.³

Another meta-analysis found the rate of **cognitive disorders** to be **35% lower** in regular green tea drinkers.⁴

Randomized controlled trials have shown that consuming green tea powder enhanced **cognitive function** in young⁵ and elderly humans.⁶

Green Tea Nutrients

Diet can play a major role in susceptibility to age-related **cognitive decline** and risk for **dementia**.^{7,8}

From preclinical to clinical studies, scientists have identified beneficial effects of **green tea** and its nutrients for the nervous system.^{1,2,9}

Green tea is rapidly dried after picking, which enables it to have *high concentrations* of **polyphenols** known as **catechins**.^{10,11}

In studies that look at various types of tea consumption, the *greatest* benefits to **brain health** have been seen with **green tea**.^{4,12}

Brain and Body Health

The **catechins** in green tea function as **antioxidants** and **anti-inflammatories**.^{13,14} They help reduce major drivers of age-related chronic disease.

That may explain, in part, why the nutrients in green tea have been shown to increase **lifespan** in several animal species, including roundworms,^{15,16} fruit flies,¹⁷ and mice.¹⁸

One preclinical study demonstrated that green tea has additional properties that appear particularly beneficial for the **brain**, including boosting the creation of **new brain cells** and improving the brain's ability to adapt into old age.¹⁹

Two of the most unique ways green tea boosts brain health is through its interactions with the **gut** and its enhancement of **brain signaling**.

Improving Gut and Brain Health

The relationship between **gut health** and **brain health** is a close one. Signals sent back and forth between the gut and the brain have a profound impact on aging and risk for disease.¹

Intake of green tea helps to ensure a healthy gut by:¹

- **Improving the diversity of bacteria** in the gut. Tea polyphenols have been shown to boost the number of beneficial microorganisms while inhibiting the growth of some potentially harmful strains of bacteria.
- **Protecting the lining of the intestines**. This helps avoid “leaky gut,” which may contribute to the neuroinflammation that drives diseases like Alzheimer’s and Parkinson’s.

Boosting Brain Signaling

Neurotrophic factors are signaling compounds produced in the body that are required to support the optimal health and function of nerve cells.²⁰

Neurotrophic factor *stimulation* helps the brain ward off degenerative disease and fine-tune brain cell function.²⁰

The activity of these **neurotrophic factors** tends to dwindle with age.²¹ And that can contribute to **neurodegeneration**.²⁰⁻²²



The catechins in green tea have been shown to enhance **neurotrophic factor activity**.¹ They do this by:

- Increasing the *production* of **neurotrophic factors**, and
- Enhancing the function of the **receptors** on brain cells that receive signals from them.

Human Studies

Numerous large population studies of green tea's brain benefits have been performed, following **hundreds of thousands** of people.

They consistently find that those who consume the most green tea have **significantly better cognitive performance** and **lower rates of neurodegenerative disorders** than those who consume the least.^{4,12,23-36}

These include lower rates of mild cognitive impairment and dementia.

Summary

Green tea is a source of beneficial compounds known as **catechins**.

In studies, green tea and catechins have been shown to protect the brain into older age.

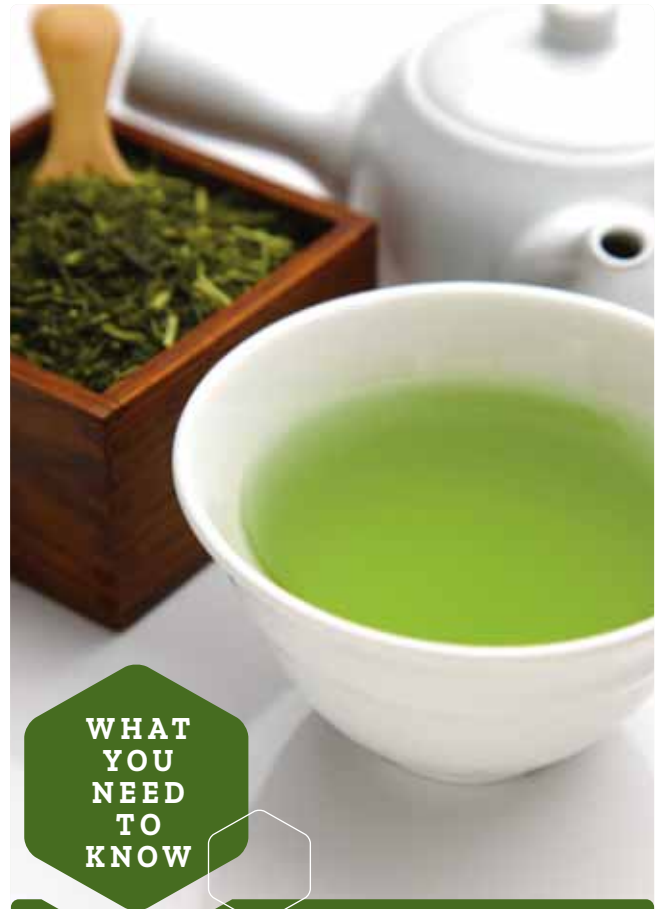
Large observational studies of green tea consumption consistently demonstrate that those who consume the *most* have the *lowest* rates of cognitive impairment and dementia.

Placebo-controlled trials show that consuming **green tea powder** boosts **cognitive function** in old and young human subjects. •

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

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WHAT
YOU
NEED
TO
KNOW

Green Tea's Brain Benefits

- Cognitive impairment and dementia are extremely common with age.
- **Green tea** consumption has been shown in clinical trials to boost cognitive function.
- Large population studies from around the world have consistently demonstrated that those who consume the *most* green tea have better cognitive performance and lower rates of cognitive disorders, including **Alzheimer's disease**.

How Many Cups Do I Need to Drink?

Many of the epidemiological studies that have established the brain benefits of green tea find the best results in those consuming **2-5 cups daily**.^{4,6,9,37}

An alternative is concentrates of **green tea extracts** that are standardized for catechins and other compounds.³⁸



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FLORASSIST® GI

for a Healthy Digestion

Phages target bad intestinal bacteria, allowing beneficial strains to flourish.

FLORASSIST® GI provides a 7-strain blend of **probiotics** in a **dual encapsulation** formula to deliver beneficial bacteria and **phages** where you need them the most.



Dual-Encapsulation Delivery



Item #02125 • 30 liquid vegetarian capsules
1 bottle **\$24.75** • 4 bottles \$22.50 each

For full product description and to order **FLORASSIST® PROBIOTIC GI with Phage Technology**, 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.



Sweet DREAMS

Fast-Acting Liquid Melatonin is a popular way to achieve more rapid sleep onset.

The nice-tasting, citrus-vanilla flavor enables convenient “drop” dosing of **Fast-Acting Liquid Melatonin** each night or when needed.

Life Extension also offers a full range of melatonin in solid forms and a variety of dosages.



Item #02234 • 3 mg per 20 drops, 2 fl. oz

1 bottle \$9 • 4 bottles \$8.25 each



FOR OCCASIONAL SLEEPLESSNESS.

For full product description and to order **Fast-Acting Liquid Melatonin**, call 1-800-544-4440 or visit www.LifeExtension.com

CAUTION: Do not consume alcohol, drive or operate heavy machinery after taking this product.

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MAGNESIUM

CRITICAL FOR
WHOLE-BODY HEALTH

Magnesium is a critically important mineral, yet most Americans do not obtain enough from their diet.

Magnesium helps:^{1,2}

- Keep **heart rhythm** steady.
- Promote normal **blood pressure**.
- Maintain normal **muscle and nerve function**.
- Support a healthy **immune system**.
- Keep **bones strong**.
- Maintain **blood sugar levels** already within normal range.

The suggested intake of magnesium to maintain vascular health from Life Extension is **500 mg** or more a day.



For full product description and to order **Magnesium Caps**, call 1-800-544-4440 or visit www.LifeExtension.com

Item #01459 • 100 vegetarian capsules

1 bottle **\$9** • 4 bottles **\$7.50** each

References

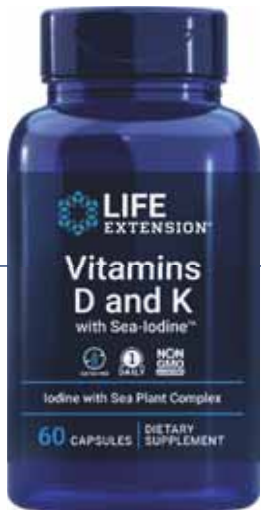
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Caution: If taken in high doses, magnesium may have a laxative effect. If this occurs, divide dosing, reduce intake, or discontinue product.



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EASY WAY TO GET YOUR D AND K (plus Iodine)



Just one capsule daily provides:

Vitamin D3	125 mcg (5,000 IU)
Vitamin K1	1,000 mcg
Vitamin K2 (MK4)	1,000 mcg
Vitamin K2 (MK7)	100 mcg
Iodine	1,000 mcg

Vitamins D and K as well as **Iodine** perform multiple functions for heart, bone and thyroid health.

Life Extension® brings these three nutrients together in one convenient capsule.

Item #02040

60 capsules

1 bottle \$18

4 bottles \$16.50 each



CAUTION: Individuals consuming more than 50 mcg 2,000 IU/day of vitamin D (from diet and supplements) should periodically obtain a serum 25-hydroxy vitamin D measurement. Do not exceed 250 mcg per day unless recommended by your doctor. Vitamin D supplementation is not recommended for individuals with high blood calcium levels. If you have a thyroid condition or are taking antithyroid medications, do not use without consulting your healthcare practitioner. If you are taking a vitamin K antagonist (e.g. warfarin), consult your healthcare practitioner before taking this product.

For full product description and to order Vitamins D and K with Sea-Iodine™, call 1-800-544-4440 or visit www.LifeExtension.com

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"Great product!"

Marcia

VERIFIED CUSTOMER
REVIEW

Oh My *Greenness*

There's a lot of
goodness to green tea.

It supports brain, heart, and cellular health...
and promotes an optimal metabolism.* But,
you'd have to drink several cups a day to get
the benefits of our **Mega Green Tea Extract**.

Each capsule provides **725 mg** of green tea
extract, standardized to **98%** polyphenols—
making it the perfect choice when you don't
have enough time for tea time.

* *Biomed Pharmacother.* 2016(3);78:50-9.

For full product description and to order **Mega Green Tea Extract**,
call **1-800-544-4440** or visit **www.LifeExtension.com**



Item #00953 • 100 vegetarian capsules

1 bottle **\$22.50** | 4 bottles \$18.00 each



Item #00954 • 100 vegetarian capsules

1 bottle **\$22.50** | 4 bottles \$18.00 each



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Pro-Resolving
Mediators:
**An Antidote for
INFLAMMATION**



BY GREGORY E. BIGFORD, PHD MSBA

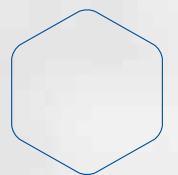
Readers of this magazine know by now that **chronic inflammation** is a major driver of nearly *all* diseases of aging.

Anti-inflammatories can help reduce existing inflammation. But that may not be enough.

To more fully undo the damage that chronic **inflammation** can cause, we need to also **resolve** the inflammation. Resolution **stops** the inflammation at the source *and* helps return inflamed tissues to their healthy, normal state.

Specialized pro-resolving mediators (PRMs) are compounds produced in the body that are *the key players* in the resolution of inflammation.

PRMs may play a vital role in helping to ward off many diseases of aging, including **atherosclerosis** and neurological disorders.



The Dangers of Inflammation

Early **inflammation** in response to an injury or infection is important in healing and protecting the body.

But when that inflammation continues and becomes **chronic** or **unresolved**, it drives the progression of numerous disorders,¹ including:^{2,3}

- Cardiovascular,
- Type II diabetes,
- Alzheimer's,
- Parkinson's,
- Osteoporosis, and
- Arthritis.

Many of these conditions are considered **age-associated diseases**. Because of the role unresolved inflammation plays, the term "**inflammaging**" is sometimes used to describe the hand-in-hand relationship between inflammation and accelerated aging.⁴⁻⁶

Many nutrients exert **anti-inflammatory** effects, which are extremely beneficial.⁷⁻⁹ But to truly counter inflammaging and restore health, the inflammation also needs to be **resolved**.

What Are Pro-Resolving Mediators?

Resolving inflammation is a coordinated and active process guided by specific signaling compounds produced in the body.¹⁰⁻¹²

The compounds that are most responsible for the resolution of inflammation are called **specialized pro-resolving mediators (PRMs)**. PRMs are derived from **EPA** and **DHA**, the omega-3 fatty acids found in fish oil, and from the omega-6 fats found in certain vegetable oils.^{13,14}

In response to inflammation, omega-3s can be converted to several classes of PRMs: **resolvins**, **protectins**, and **maresins**. Omega-6s can be converted to PRMs called **lipoxins**.¹⁵⁻¹⁸

To raise PRM levels in the body high enough to have a significant effect, direct oral intake of PRMs and precursors may be necessary.^{19,20} These include:

- **18-HEPE** (18-hydroxyeicosapentaenoic acid),
- **17-HDHA** (17-hydroxydocosahexaenoic acid), and
- **14-HDHA** (14-hydroxydocosahexaenoic acid).

How PRMs Resolve Inflammation

While each type of PRM has slightly different actions, they complement each other and collectively coordinate the processes involved in **inflammation resolution**.

PRMs resolve inflammation in several important ways. Among others, they:²¹⁻²³

- *Inhibit* the further migration of immune cells that were recruited to damaged tissue during the *acute* inflammatory phase,
- *Inhibit* the release of pro-inflammatory mediators from other immune cells,
- *Help* clear away microorganisms, tissue debris, and dead cells, and
- *Stimulate* cellular regeneration and tissue repair in damaged tissue.

Together, these actions can help counter diseases driven by inflammation.



Metabolic Diseases

Atherosclerosis, the buildup of plaque in artery walls, is driven in part by inflammation *and* by a deficiency of inflammation-resolution signals in the arteries.²⁴ It is the major cause of heart disease, heart attacks, and strokes.

In preclinical studies, specialized **pro-resolving mediators** can help prevent atherosclerosis by initiating the removal of dead cells and cholesterol-rich foam cells in a process called **efferocytosis**. If these cells are not removed, they contribute to plaque progression.^{24,25}

Obesity and **fat tissue** are tied to chronic inflammation. Genetic and dietary studies show that **obesity** is associated with low levels of PRMs in fat tissue.^{17,26}

Non-obese patients with chronic conditions such as **type II diabetes** also show signs of systemic inflammation,¹⁷ and deficiencies in the production of **PRMs** have been associated with defective resolution of inflammation that underlies chronic diabetic wounds.²⁷

In animal models of **obesity** and **diabetes**, administration of **resolvins** was able to improve glucose tolerance, reduce fasting blood sugar, and enhance the clearance of dead and damaged tissue.²⁸ This indicates that PRMs may improve metabolism and wound repair in these conditions.^{27,29}

Preclinical studies show that, in obese animals, taking **omega-3 fatty acids** can increase levels of **resolvins**.²⁶ This is an instance when taking **PRM precursors** may help raise levels more.

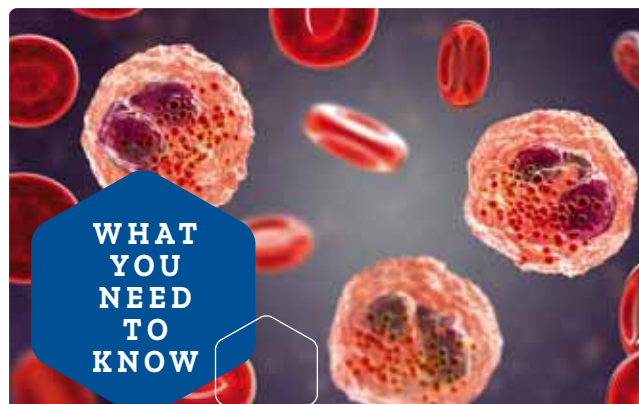
Brain Diseases

Prolonged and unresolved inflammation in the brain contributes to neuronal death in **Alzheimer's disease**. In patients with Alzheimer's, low levels of **lipoxins** (PRMs derived from omega-6s) have been found after death compared to patients without Alzheimer's.³⁰

In addition, animal studies found that treatment with aspirin triggered lipoxin, reduced inflammation, and facilitated the clearance of **beta-amyloid plaques** in the brain,³¹ which are seen in human patients with Alzheimer's disease.

Other preclinical studies show that PRM administration can reduce inflammation and functional deficits in models of age-associated **Parkinson's disease**.^{32,33}

PRMs have been shown in preclinical and experimental models to improve other neurological conditions as well, including postoperative **cognitive impairment**,³⁴ **stroke**,³⁵⁻⁴¹ and **depression**.⁴²



Resolve Inflammation for Better Health

- Compounds called **specialized pro-resolving mediators (PRMs)** help the body resolve inflammation, stopping it in its tracks and returning inflamed tissues to a healthy state.
- *Unresolved* inflammation is tied to many age-related chronic illnesses.
- In preclinical studies, PRMs help prevent **atherosclerosis**, reduce high blood glucose, and aid in diabetic wound healing.
- In animal models, PRMs reduce brain inflammation and help clear away beta-amyloid plaques in the brain, a hallmark of **Alzheimer's disease**. They also improve other neurological conditions, including Parkinson's disease and stroke.
- In a human study, *combining* marine oil enriched with **PRM precursors** with a highly bioavailable **curcumin** improves subjective measures of **pain** and discomfort associated with inflammation.
- The body can convert **omega-3 fatty acids** from fish oil to PRMs. Taking **PRM precursors** can raise levels even higher.

Other Disorders

There is an inflammatory component to many other chronic age-related conditions. For example, PRM production is lower in **osteoarthritis**.⁴³ In a preclinical model of obesity-associated osteoarthritis, treatment with **resolvins** slowed its progression in the knee joint.⁴⁴

Boosting pro-resolving mediators has also been effective in models of inflammatory **liver disease**,^{45,46} and there is evidence that PRMs can reduce **fibrosis** (scarring) in chronic **kidney disease**.⁴⁷

The benefits of PRMs are also being studied in conditions as far-ranging as dry eyes, periodontitis (a serious gum infection), the digestive disease colitis, lung disease, and inflammatory pain,^{16,48,49} highlighting the growing attention to the role these compounds play in resolving inflammation.

Clinical Study

An open-label pilot study published in **2022** demonstrates that taking **PRM precursors** along with bioavailable **curcumin** delivers significant relief of pain and discomfort.¹⁸ The study recruited 29 healthy males and females with mild to moderate pain. Participants received **500 mg** of marine oil enriched with PRM precursors, and **500 mg** of highly bioavailable (absorbable) curcumin. To measure pain, quality of life, and overall health, participants completed three questionnaires.



In just 30 days, the combination significantly reduced:

- **Total** pain,
- Pain **intensity**, and
- Pain **severity**.

An impressive **62%** of participants had an improved **total pain** score at **30 days**, and after 60 days, **79%** of participants had an improvement in **total pain**.

No adverse events were reported.

This suggests that taking **PRM precursors** with a bioavailable form of **curcumin** delivers significant relief of **pain** and discomfort associated with inflammation.

Summary

Without adequate levels of **specialized pro-resolving mediators (PRMs)** in the body, inflammation can persist and do great harm.

Chronic inflammation that underlies so many **age-related** diseases has been associated with lower levels of PRMs in the body.

Adequate intake of **omega-3 fatty acids** from fish oil can increase bodily production of **PRMs**.

Direct oral intake of PRM (pro-resolving mediator) **precursors** can boost levels *higher*.


Emerging evidence suggests that maintaining PRM levels may help fight a variety of inflammatory conditions, from atherosclerosis and degenerative brain diseases to osteoarthritis. •

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

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Fisetin

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Fisetin, a flavonoid found in strawberries and apples, is currently being studied for its effectiveness as a **senolytic** in humans.¹

In preclinical studies, fisetin:

- Mimics effects of **calorie reduction**²
- Targets longevity pathways²⁻⁶
- Extends lifespan of mice by about **10%**⁷
- Removes **senescent** cells through **senolytic** action⁷
- Suppresses excess **mTOR** activation⁸

Fisetin is poorly *absorbed* due to its breakdown in the small intestines.

Bio-Fisetin solves this problem by enclosing **fisetin** with a compound from the fenugreek herb.

A **human** trial showed **bioavailability** of this **fisetin** compound increased up to **25 times** compared to fisetin by itself.⁹

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For full product description and to order **Bio-Fisetin**, call **1-800-544-4440** or visit www.LifeExtension.com

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INSILICO MEDICINE Wages War on Aging and Disease





BY MICHAEL DOWNEY

Scientists relentlessly seek new drugs and nutrients that target chronic diseases and the **aging** process. But progress remains frustratingly slow, as evidenced by:

- It is estimated to take from about seven to over 10 years, and an average of more than \$1 billion, to bring a drug to market,
- Only about **12%** of drugs entering clinical trials gain FDA approval, and
- The cost of drug development *increased* by roughly **8.5% per year** in the past decade.¹

Alex Zhavoronkov, PhD, is on an ambitious mission to **change** all that.

Insilico Medicine, the drug development company that he founded in 2014, has instituted a novel way to dramatically speed up the ability to identify compounds that may not only delay human **aging**, but *simultaneously* treat illnesses such as heart disease, cancer, and diabetes.²

Deep Neural AI

Dr. Zhavoronkov is employing the **deep neural network** form of artificial intelligence to understand human **aging**.³

Neural networks are a type of, or an aspect of, artificial intelligence and machine learning.⁴ These terms are becoming more familiar to us, since they play an increasingly important role in our lives. Neural networks attempt to simulate the way human neurons interact during learning. A neural network is “**deep**” when it contains many layers of simulated neurons.⁵

Insilico has already made gains in using artificial intelligence (AI) and different computer programs to accelerate the phases of new drug development.^{6,7}

The company’s AI platform, known as **Pharma.AI**, uses millions of data sources and samples (including patents, medical journals, clinical trial reports, and test data such as RNA sequencing). There are three distinct arms comprising this AI platform:

- **PandaOmics**, which reduces the time required to identify and analyze drug targets,⁸
- **Chemistry42**, which utilizes data to design new drugs (by predicting active drug molecules),⁹ and
- **InClinico**, which designs and makes predictions about clinical trials.¹⁰



These arms of the Insilico AI platform lead directly to preclinical and clinical trials. As an example, Insilico’s candidate to treat the lung disease **idiopathic pulmonary fibrosis** was the *first* to be discovered and designed using AI. This drug is *already* in **phase 1** clinical trials.^{11,12}

In 2019, Insilico published research in *Nature Biotechnology* showing that its approach was able to find **six** promising treatments for idiopathic pulmonary fibrosis **in just 21 days**.¹³

Robotic Lab

Huge savings in drug development costs could be realized if the lab testing procedure were *automated*. So, the next step for Dr. Zhavoronkov is a fully automated **robotic lab**.

The lab will be powered by its own AI system and will employ robots to conduct experiments.⁹

“These robots are faster and more precise than humans,” notes Zhavoronkov. “As they perform experiments, they feed the AI system with data.”¹⁴

This robotic lab has been in the design phase for two years and is expected to be fully operational **within months**.

Geroprotectors and Autophagy Activators

A unique aspect of Insilico’s research into dietary ingredients is its focus on **geroprotectors**, interventions/compounds that mitigate the process of aging and aim to extend lifespan in animals and humans.¹⁵ It is hoped that this could eventually facilitate a *young*, healthy state in *older* human tissues.¹⁶

This research has enabled the company to identify nutrients that target drivers of aging such as **cellular senescence** and declining **stem cell health**. These nutrient-based geroprotectors could be used to create formulations that promote longevity.

Another cause of aging is *reduced autophagy*, or “cellular housekeeping.”^{17,18}

Autophagy declines with age and poor diet, causing cells to become overwhelmed by damage and metabolic waste. This leads to **accelerated aging** and risk for chronic disease.¹⁸

Working in collaboration with **Life Extension®**, scientists at **Insilico** identified two nutrients that work together to *activate* autophagy: **luteolin** and **piperlongumine**.

WHAT
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Using Technology to Fight Aging

- Insilico Medicine is using a form of artificial intelligence (AI) that helps to find compounds/drugs quickly and efficiently with the potential to treat disease and prolong life.
- Working with **Life Extension**[®], scientists at Insilico have found two nutrients that activate autophagy (“cellular house-keeping”), which keeps cells functioning youthfully: luteolin and piperlongumine.
- Insilico’s founder, Dr. Alex Zhavoronkov, has also used AI to identify five blood components that are predictive of biological age: albumin, glucose, alkaline phosphatase, urea, and erythrocytes.
- Using AI and robotics, Insilico aims to develop new, personalized drugs that can simultaneously target disease and aging itself.

Luteolin, a flavonoid found in many plants, works by *increasing* the activity of **AMPK**,^{19,20} an enzyme that activates autophagy.²¹ In preclinical and phase 1 clinical trials, activating AMPK has been shown to improve metabolic health^{22,23} and increase **lifespan**.²⁴

Luteolin also *inhibits* signaling of **mTOR**, a protein that *shuts off* autophagy.²⁵⁻²⁷

Piperlongumine is a compound isolated from the long pepper plant.²⁸ It has been shown in animal and cell studies to **activate autophagy** by inhibiting mTOR signaling, which is considered a beneficial longevity mechanism.^{29,30}

Together, these nutrients can help keep cells functioning *youthfully* for improved health.



Human Aging Clocks

Dr. Zhavoronkov was inspired in his efforts by the promise of predicting human age through the use of what are known as **DNA methylation clocks**.³¹

Predicting biological age can be valuable in human **longevity** studies. That’s because it offers a relatively *quick* way to measure whether a therapeutic intervention will successfully slow or reverse aging, rather than having to wait decades for a lifespan to play out.

Dr. Zhavoronkov trained deep neural networks on **60,000** human blood samples, which identified **five** blood components that are predictive of age:³²

- **Albumin**, a protein that carries hormones, vitamins, and enzymes,
- **Glucose**,
- **Alkaline phosphatase** or **ALP**, an enzyme involved in processes throughout the body,
- The waste product **urea**, and
- **Erythrocytes**, red blood cells packed with hemoglobin.

When these five components are inputted to proprietary software and analyzed, they can be helpful in predicting a patient’s biological age.

Looking Ahead

Dr. Zhavoronkov's goals in **longevity biotechnology** are wide-ranging:

- Discover **drugs** and **nutrient** formulas to target **aging** and **disease** *simultaneously*,
- Develop better **aging clocks** to track human biological aging,
- **Personalize drugs**, employing robotics and AI to *individualize* drug discovery,
- Open **research hospitals** that use AI and robotics to bring longevity innovations closer to people in need, and
- Develop **cryobiology** innovations, including rapidly freezing, reheating, and reviving organs, animals, and humans.

Insilico licenses its AI platform to other pharmaceutical companies to help them accelerate *their* drug development programs. Dr. Zhavoronkov has also founded **Longevity Medicine**, which offers a **degree** course in longevity for medical professionals.³³

Still, Dr. Zhavoronkov can't help but feel frustrated. "Many very talented human beings choose to focus on inventing, making, and selling stuff and content that people can easily live without," he notes, "instead of contributing to fighting [aging], the one silent enemy."[•]

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

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45 TIMES GREATER BIOAVAILABILITY *Curcumin*



Patented **turmeric** and **fenugreek blend** (500 mg) results in **45 times** greater bioavailability of free **curcuminoids**.

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500 mg, 60 vegetarian capsules

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Same 500 mg potency of patented **turmeric** and **fenugreek blend** with added benefits of **ginger** and other **turmeric** actives.

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Super Omega-3 provides higher EPA/DHA potencies PLUS components found in Mediterranean-style diets.

This advanced formula provides:

- 1. EPA/DHA Fish Oil**
(ultra pure/highly concentrated)
- 2. Olive polyphenols**
(to inhibit LDL oxidation)
- 3. Sesame lignans**
(to extend stability of DHA in the blood)
- 4. Astaxanthin**
(protects against lipid peroxidation)
- 5. Krill oil**
(a source of EPA/DHA)



Item #01988 • 120 softgels

1 bottle **\$38.25**

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ACTIVE LIFESTYLE & FITNESS

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- 02020 Super Carnosine
- 02023 Tart Cherry with CherryPURE®
- 02186 Wellness Bar - Chocolate Brownie
- 02246 Wellness Code® Advanced Whey Protein Isolate Vanilla
- 02221 Wellness Code® Muscle Strength & Restore Formula
- 02127 Wellness Code® Plant Protein Complete & Amino Acid Complex
- 02261 Wellness Code® Whey Protein Concentrate Chocolate
- 02260 Wellness Code® Whey Protein Concentrate Vanilla
- 02243 Wellness Code® Whey Protein Isolate Chocolate
- 02242 Wellness Code® Whey Protein Isolate Vanilla

AMINO ACIDS

- 00038 Arginine Ornithine Powder
- 01253 Branched Chain Amino Acids
- 01829 Carnosine
- 01671 D,L-Phenylalanine Capsules
- 01624 L-Arginine Caps
- 01532 L-Carnitine
- 00345 L-Glutamine
- 00141 L-Glutamine Powder
- 01678 L-Lysine
- 01827 Taurine
- 00133 Taurine Powder

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- 02004 Arterial Protect
- 02497 Endothelial Defense™ Pomegranate Plus
- 56885 Natto Activ Cardiovascular & Respiratory Support
- 02320 NitroVasc™ Boost
- 01953 Pomegranate Complete
- 00956 Pomegranate Fruit Extract
- 02024 Triple Action Blood Pressure AM/PM
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- 02123 Bone Restore Chewable Tablet
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- 01727 Bone Restore with Vitamin K2
- 01725 Bone Strength Collagen Formula
- 01963 Calcium Citrate with Vitamin D
- 01506 Dr. Strum's Intensive Bone Formula
- 02417 Mega Vitamin K2
- 01476 Strontium Caps

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- 01974 Acetyl-L-Carnitine Arginate
- 02419 B12 Elite
- 02510 Brain Fog Relief
- 01659 CDP Choline
- 02321 Cognitex® Basics
- 02396 Cognitex® Elite
- 02397 Cognitex® Elite Pregnenolone

- 01540 DMAE Bitartrate
- 02006 Dopa-Mind™
- 02413 Dopamine Advantage
- 01658 Ginkgo Biloba Certified Extract™
- 01527 Huperzine A
- 00020 Lecithin
- 02101 Memory Protect
- 00709 Migra-Eeze™
- 01603 Neuro-Mag® Magnesium L-Threonate Caps
- 02032 Neuro-Mag® Magnesium L-Threonate Powder
- 00888 Optimized Ashwagandha
- 01676 PS (Phosphatidylserine) Caps
- 02406 Quick Brain Nootropic
- 01327 Vinpocetine

CHOLESTEROL MANAGEMENT

- 01828 Advanced Lipid Control
- 01910 CHOL-Support™
- 01304 Theaflavins Standardized Extract
- 00372 Vitamin B3 Niacin Capsules

DIGESTION SUPPORT

- 02412 Bloat Relief
- 02514 Easy Fiber
- 01736 Effervescent Vitamin C - Magnesium Crystals
- 02021 Enhanced Super Digestive Enzymes
- 02022 Enhanced Super Digestive Enzymes and Probiotics
- 02033 EsophaCool™
- 01737 Esophageal Guardian
- 01706 Extraordinary Enzymes
- 02100 Gastro-Ease™

ENERGY MANAGEMENT

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- 01630C Adrenal Energy Formula • 120 veg capsules
- 00972 D-Ribose Powder
- 01473 D-Ribose Tablets
- 01900 Energy Renew
- 01544 Forskolin
- 01805 Ginseng Energy Boost
- 01869 Mitochondrial Basics with PQQ
- 01868 Mitochondrial Energy Optimizer with PQQ
- 01904 NAD+ Cell Regenerator™ • 100 mg, 30 veg capsules
- 02344 NAD+ Cell Regenerator™ 300 mg, 30 veg capsules
- 02348 NAD+ Cell Regenerator™ and Resveratrol Elite™
- 01500 PQQ Caps • 10 mg, 30 vegetarian capsules
- 01647 PQQ Caps • 20 mg, 30 vegetarian capsules
- 00889 Rhodiola Extract
- 02003 Triple Action Thyroid

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- 01923 Astaxanthin with Phospholipids
- 00893 Brite Eyes III
- 02323 Digital Eye Support
- 01514 Eye Pressure Support with Mirtogenol®
- 01992 MacuGuard® Ocular Support with Saffron
- 01993 MacuGuard® Ocular Support with Saffron & Astaxanthin
- 01873 Standardized European Bilberry Extract
- 01918 Tear Support with MaquiBright®

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- 02218 Mega GLA Sesame Lignans
- 01983 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 60 softgels
- 01988 Super Omega-3 Plus EPA/DHA Fish Oil, Sesame Lignans, Olive Extract, Krill & Astaxanthin
- 01982 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 softgels
- 01985 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 60 enteric coated softgels
- 01984 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 120 enteric coated softgels
- 01986 Super Omega-3 EPA/DHA Fish Oil, Sesame Lignans & Olive Extract • 240 softgels
- 01812 Provinal® Purified Omega-7
- 01640 Vegetarian DHA

FOOD

- 02008 California Estate Extra Virgin Olive Oil
- 02170 Rainforest Blend Decaf Ground Coffee
- 02169 Rainforest Blend Ground Coffee
- 02171 Rainforest Blend Whole Bean Coffee

GLUCOSE MANAGEMENT

- 01503 CinSulin® with InSea²® and Crominex® 3+
- 01620 CoffeeGenic® Green Coffee Extract
- 02122 Glycemic Guard™
- 00925 Mega Benfotiamine
- 01803 Tri Sugar Shield®

HEART HEALTH

- 01066 Aspirin (Enteric Coated)
- 01842 BioActive Folate & Vitamin B12 Caps
- 01700 Cardio Peak™
- 02121 Homocysteine Resist
- 02508 Omega-3 Fish Oil Gummy Bites
- 02018 Optimized Carnitine
- 01949 Super-Absorbable CoQ10 Ubiquinone with *d*-Limonene • 50 mg, 60 softgels
- 01951 Super-Absorbable CoQ10 Ubiquinone with *d*-Limonene • 100 mg, 60 softgels
- 01929 Super Ubiquinol CoQ10
- 01427 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 50 mg, 30 softgels
- 01425 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 50 mg, 100 softgels
- 01437 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 100 mg, 30 softgels
- 01426 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 100 mg, 60 softgels
- 01431 Super Ubiquinol CoQ10 with Enh Mitochondrial Support™ • 200 mg, 30 softgels
- 01733 Super Ubiquinol CoQ10 with PQQ
- 01859 TMG Liquid Capsules
- 00349 TMG Powder

HORMONE BALANCE

- 00454 DHEA • 15 mg, 100 capsules
- 00335 DHEA • 25 mg, 100 capsules
- 00882 DHEA • 50 mg, 60 capsules

- 00607 DHEA • 25 mg, 100 vegetarian dissolve in mouth tablets
- 01689 DHEA • 100 mg, 60 veg capsules
- 02368 Optimized Broccoli and Cruciferous Blend
- 00302 Pregnenolone • 50 mg, 100 capsules
- 00700 Pregnenolone • 100 mg, 100 capsules
- 01468 Triple Action Cruciferous Vegetable Extract
- 01469 Triple Action Cruciferous Vegetable Extract and Resveratrol

IMMUNE SUPPORT

- 02411 Day Elderberry Immune
- 02302 Bio-Quercetin
- 02410 Black Elderberry + Vitamin C
- 02433 Echinacea Elite
- 01961 Enhanced Zinc Lozenges
- 01704 Immune Modulator with Tinofend®
- 02425 Immune Packs with Vitamin C & D, Zinc and Probiotic
- 02005 Immune Senescence Protection Formula™
- 01681 Lactoferrin (Apolactoferrin) Caps
- 02426 Mushroom Immune with Beta Glucans
- 01903 NK Cell Activator™
- 01394 Optimized Garlic
- 01309 Optimized Quercetin
- 01811 Peony Immune
- 01708 Reishi Extract Mushroom Complex
- 01906 Standardized Cistanche
- 01097 Ultra Soy Extract
- 01561 Zinc Lozenges

INFLAMMATION MANAGEMENT

- 01639 5-LOX Inhibitor with AprèsFlex®
- 02324 Advanced Curcumin Elite™ Turmeric Extract, Ginger & Turmerones
- 01709 Black Cumin Seed Oil
- 02310 Black Cumin Seed Oil and Curcumin Elite™
- 02467 Curcumin Elite™ Turmeric Extract 30 veg capsules
- 02407 Curcumin Elite™ Turmeric Extract 60 veg capsules
- 01804 Cytokine Suppress® with EGCG
- 02223 Pro-Resolving Mediators
- 56886 Restore Activ Joint Muscle & Tissue
- 01203 Specially-Coated Bromelain
- 00407 Super Bio-Curcumin® Turmeric Extract

JOINT SUPPORT

- 02404 Arthro-Immune Joint Support
- 02238 ArthroMax® Advanced NT2 Collagen™ & AprèsFlex®
- 01617 ArthroMax® with Theaflavins & AprèsFlex®
- 02138 ArthroMax® Elite
- 00965 Fast-Acting Joint Formula
- 02430 Fast Acting Relief
- 00522 Glucosamine/Chondroitin Capsules
- 02420 Glucosamine Sulfate
- 02424 Joint Mobility
- 01600 Krill Healthy Joint Formula
- 00451 MSM (Methylsulfonylmethane)
- 02231 NT2 Collagen™

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- 00862 Cran-Max® Cranberry Whole Fruit Concentrate
- 01424 Optimized Cran-Max®
- 01921 Uric Acid Control
- 01209 Water-Soluble Pumpkin Seed Extract

LIVER HEALTH & DETOXIFICATION

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- 01925 Advanced Milk Thistle • 120 softgels
- 02240 Anti-Alcohol Complex
- 01651 Calcium D-Glucarate
- 01571 Chlorophyllin
- 02402 FLORASSIST® Liver Restore™
- 01541 Glutathione, Cysteine & C
- 01393 HepatoPro
- 01608 Liver Efficiency Formula
- 01522 Milk Thistle • 60 veg capsules
- 01534 N-Acetyl-L-Cysteine
- 01884 Silymarin
- 02361 SOD Booster

LONGEVITY & WELLNESS

- 00457 Alpha-Lipoic Acid
- 01625 AppleWise
- 02414 Bio-Fisetin
- 01214 Blueberry Extract
- 01438 Blueberry Extract and Pomegranate
- 02270 DNA Protection Formula
- 02431 Essential Youth - L-Ergothioneine
- 02119 GEROPROTECT® Ageless Cell™
- 02415 GEROPROTECT® Autophagy Renew
- 02401 GEROPROTECT® Stem Cell
- 02211 Grapeseed Extract
- 00954 Mega Green Tea Extract (decaffeinated)
- 00953 Mega Green Tea Extract (lightly caffeinated)
- 01513 Optimized Fucoidan with Maritech® 926
- 02230 Optimized Resveratrol Elite™
- 01637 Pycnogenol® French Maritime Pine Bark Extract
- 02210 Resveratrol Elite™
- 02301 Senolytic Activator®
- 01208 Super R-Lipoic Acid
- 01919 X-R Shield

LUNG HEALTH

- 02512 Healthy Lungs

MEN'S HEALTH

- 02209 Male Vascular Sexual Support
- 00455 Mega Lycopene Extract
- 02306 Men's Bladder Control
- 02515 Men's Vitality Packs
- 01789 PalmettoGuard® Saw Palmetto and Beta-Sitosterol
- 01790 PalmettoGuard® Saw Palmetto/Nettle Root Formula and Beta-Sitosterol
- 01373 Prelox® Enhanced Sex for Men
- 01940 Super MiraForte with Standardized Lignans
- 02500 Testosterone Elite
- 01909 Triple Strength ProstaPollen™
- 02029 Ultra Prostate Formula

MINERALS

- 01661 Boron
- 02107 Extend-Release Magnesium
- 01677 Iron Protein Plus
- 02403 Lithium
- 01459 Magnesium Caps
- 01682 Magnesium (Citrate)
- 01328 Only Trace Minerals
- 01504 Optimized Chromium with Crominex® 3+
- 02309 Potassium with Extend-Release Magnesium
- 01740 Sea-Iodine™
- 01879 Se-Methyl L-Selenocysteine
- 01778 Super Selenium Complex
- 00213 Vanadyl Sulfate
- 01813 Zinc Caps

MISCELLANEOUS

- 00577 Potassium Iodide
- 00657 Solarshield® Sunglasses

MOOD & STRESS MANAGEMENT

- 02519 Ashwagandha Plus
- 02434 Calm-Mag
- 02312 Cortisol-Stress Balance
- 00987 Enhanced Stress Relief
- 01683 L-Theanine
- 02175 SAME (S-Adenosyl-Methionine) 200 mg, 30 enteric coated vegetarian tablets
- 02176 SAME (S-Adenosyl-Methionine) 400 mg, 30 enteric coated vegetarian tablets
- 02174 SAME (S-Adenosyl-Methionine) 400 mg, 60 enteric coated vegetarian tablets
- 02429 Theanine XR™ Stress Relief

MULTIVITAMINS

- 02199 Children's Formula Life Extension Mix™
- 02354 Life Extension Mix™ Capsules
- 02364 Life Extension Mix™ Capsules without Copper
- 02356 Life Extension Mix™ Powder
- 02355 Life Extension Mix™ Tablets
- 02357 Life Extension Mix™ Tablets with Extra Niacin
- 02365 Life Extension Mix™ Tablets without Copper
- 02292 Once-Daily Health Booster • 30 softgels
- 02291 Once-Daily Health Booster • 60 softgels
- 02313 One-Per-Day Tablets
- 02428 Plant-Based Multivitamin
- 02317 Two-Per-Day Capsules • 60 capsules
- 02314 Two-Per-Day Capsules • 120 capsules
- 02316 Two-Per-Day Tablets • 60 tablets
- 02315 Two-Per-Day Tablets • 120 tablets

NERVE & COMFORT SUPPORT

- 02202 ComfortMAX™
- 02303 Discomfort Relief

PERSONAL CARE

- 02322 Hair, Skin & Nails Collagen Plus Formula
- 01278 Life Extension Toothpaste
- 00408 Venotone
- 02304C Youthful Collagen
- 02252 Youthful Legs

PET CARE

- 01932 Cat Mix
- 01931 Dog Mix

PROBIOTICS

- 01622 Bifido GI Balance
- 01825 FLORASSIST® Balance
- 02421 FLORASSIST® Daily Bowel Regularity
- 02125 FLORASSIST® GI with Phage Technology
- 01821 FLORASSIST® Heart Health
- 02250 FLORASSIST® Mood Improve
- 02208 FLORASSIST® Immune & Nasal Defense
- 02120 FLORASSIST® Oral Hygiene
- 02203 FLORASSIST® Prebiotic
- 02505 FLORASSIST® Probiotic Women's Health

SKIN CARE

- 02423 Daily Skin Defense
- 01938 Shade Factor™
- 02129 Skin Care Collection Anti-Aging Serum
- 02130 Skin Care Collection Day Cream
- 02131 Skin Care Collection Night Cream
- 02096 Skin Restoring Ceramides

SLEEP

- 01512 Bioactive Milk Peptides
- 02300 Circadian Sleep
- 01551 Enhanced Sleep with Melatonin
- 01511 Enhanced Sleep without Melatonin
- 02234 Fast-Acting Liquid Melatonin
- 01669 Glycine
- 02308 Herbal Sleep PM
- 01722 L-Tryptophan
- 01668 Melatonin • 300 mcg, 100 veg capsules
- 01083 Melatonin • 500 mcg, 200 veg capsules
- 00329 Melatonin • 1 mg, 60 capsules
- 02503 Melatonin • 3 mg, 60 gummies
- 00330 Melatonin • 3 mg, 60 veg capsules
- 00331 Melatonin • 10 mg, 60 veg capsules
- 00332 Melatonin • 3 mg, 60 veg lozenges
- 02201 Melatonin IR/XR
- 01787 Melatonin 6 Hour Timed Release
300 mcg, 100 veg tablets
- 01788 Melatonin 6 Hour Timed Release
750 mcg, 60 veg tablets
- 01721 Optimized Tryptophan Plus
- 01445 Quiet Sleep Melatonin • 5 mg, 60 veg capsules
- 02502 Rest & Renew

VITAMINS

- 01533 Ascorbyl Palmitate
- 00920 Benfotiamine with Thiamine
- 01945 BioActive Complete B-Complex
- 00102 Biotin
- 00084 Buffered Vitamin C Powder
- 02229 Fast-C® and Bio-Quercetin Phytosome
- 02075 Gamma E Mixed Tocopherol Enhanced with
Sesame Lignans
- 02070 Gamma E Mixed Tocopherol & Tocotrienols

- 01913 High Potency Optimized Folate
- 01674 Inositol Caps
- 02244 Liquid Vitamin D3 • 50 mcg (2000 IU)
- 02232 Liquid Vitamin D3 (Mint) • 50 mcg (2000 IU)
- 01936 Low-Dose Vitamin K2
- 00373 No Flush Niacin
- 01939 Optimized Folate (L-Methylfolate)
- 01217 Pyridoxal 5'-Phosphate Caps
- 01400 Super Absorbable Tocotrienols
- 02334 Super K
- 01863 Super Vitamin E
- 02422 Vegan Vitamin D3
- 02028 Vitamin B5 (Pantothenic Acid)
- 01535 Vitamin B6
- 00361 Vitamin B12 Methylcobalamin
- 01536 Vitamin B12 Methylcobalamin
1 mg, 60 veg lozenges
- 01537 Vitamin B12 Methylcobalamin
5 mg, 60 veg lozenges
- 02228 Vitamin C and Bio-Quercetin Phytosome
60 veg tablets
- 02227 Vitamin C and Bio-Quercetin Phytosome
250 veg tablets
- 01753 Vitamin D3 • 25 mcg (1000 IU), 90 softgels
- 01751 Vitamin D3 • 25 mcg (1000 IU), 250 softgels
- 01713 Vitamin D3 • 125 mcg (5000 IU), 60 softgels
- 01718 Vitamin D3 • 175 mcg (7000 IU), 60 softgels
- 01758 Vitamin D3 with Sea-Iodine™
- 02040 Vitamins D and K with Sea-Iodine™

WEIGHT MANAGEMENT & BODY COMPOSITION

- 02479 7-Keto® DHEA Metabolite
100 mg, 60 veg capsules
- 02207 AMPK Metabolic Activator
- 02504 Body Trim and Appetite Control
- 02478 DHEA Complete
- 01738 Garcinia HCA
- 02506 Mediterranean Weight Management
- 01432 Optimized Saffron
- 00818 Super CLA Blend with Sesame Lignans
- 02511 Thermo Weight Control
- 02509 Waistline Control™

WOMEN'S HEALTH

- 01942 Breast Health Formula
- 01626 Enhanced Sex for Women 50+
- 01894 Estrogen for Women
- 02204 Menopause 731™
- 02319 Prenatal Advantage
- 01649 Soy Isoflavones
- 02513 Women's Bladder Support

Munch,

Crunch, Digest
Your Lunch
(Or breakfast, or dinner...)



Uncomfortable after eating?

Digestive enzymes are specialized proteins that help you break down the foods you eat.*

Enhanced Super Digestive Enzymes combines 10 vegetarian-friendly enzymes to help you break down hard-to-digest foods and encourage a healthy gastrointestinal balance...so you can feel good after you eat!

* Curr Drug Metab. 2016;17(2):187-93.

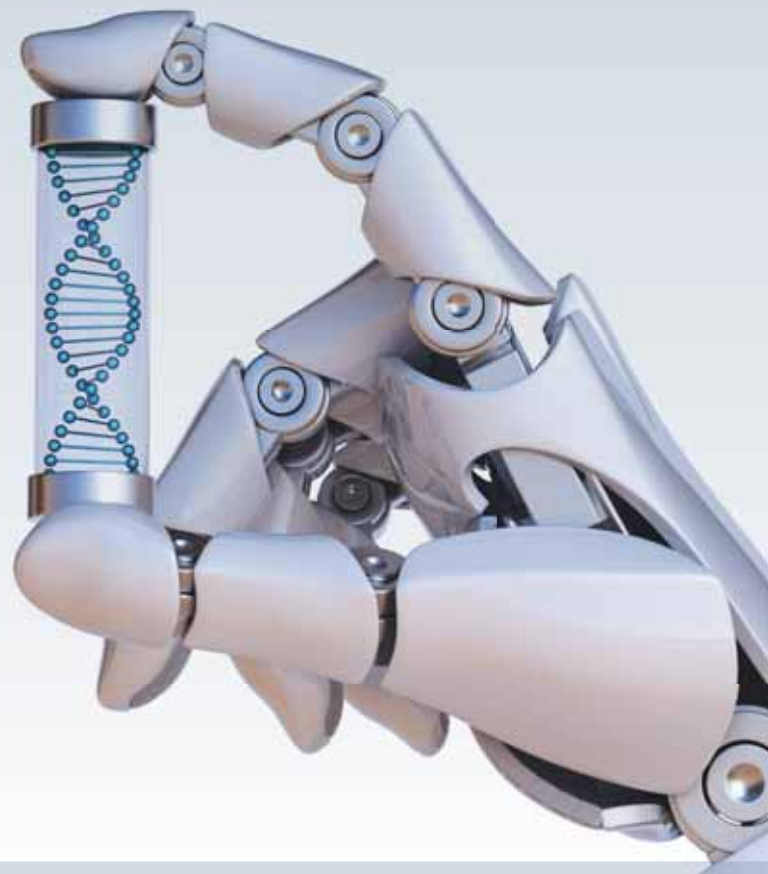
Item #02021 • 60 vegetarian capsules
1 bottle \$16.50 • 2 bottles \$15.75 each



For full product description and to order **Enhanced Super Digestive Enzymes**, call 1-800-544-4440 or visit www.LifeExtension.com

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ADVANCED CELL RENEWAL THROUGH AI



Life Extension® scientists in collaboration with Insilico Medicine have developed two cellular rejuvenation formulas, with ingredients tested in human cell lines, using Deep-Learning AI Technology.



GEROPROTECT® Autophagy Renew†

Two plant extracts,
piperlongumine^{1,2}
and **luteolin**^{3,4}:

- Promote ongoing cellular housekeeping¹⁻⁵
- Encourage healthy cell debris removal^{1,2,4}
- Inhibit mTOR signaling⁴

Item #02415 • 30 vegetarian capsules
1 bottle \$19.50 • 4 bottles \$17.50



GEROPROTECT® Stem Cell†

Three plant-based nutrients, **garcinol**,⁶⁻⁸
piceatannol,^{9,11} and
resveratrol¹²⁻¹³ activate
signaling pathways
that support **stem
cell** health.

Item #02401 • 60 vegetarian capsules
1 bottle \$36 • 4 bottles \$33 each

For full product description and to order GEROPROTECT® Autophagy Renew and GEROPROTECT® Stem Cell call 1-800-544-4440 or visit www.LifeExtension.com

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† Developed in collaboration with the Deep-Learning AI Technology at Insilico Medicine, Inc.



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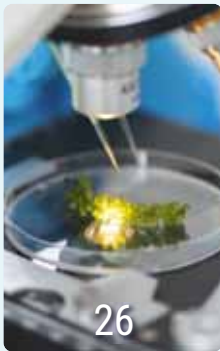


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7 THE LDL CHOLESTEROL DEBATE

A recent review argues that **LDL** levels should be *lower* than commonly advocated to prevent **atherosclerosis**.



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In clinical studies, **astaxanthin** *reduced* and *reversed* aspects of **skin aging**.



36 FRUIT EXTRACT CUTS CARDIOVASCULAR RISK

A **fruit extract** was clinically shown to *lower* artery-clogging **lipids** and **C-reactive protein**, while improving **endothelial function**.



48 GREEN TEA BOOSTS BRAIN HEALTH

Catechins in **green tea** *enhance* brain **signaling** while reducing **neurodegenerative** risks.



58 AN ANTIDOTE FOR INFLAMMATION

Various interventions *reduce* **inflammation**, but a critical missing step is to *resolve* ongoing damage to previously inflamed tissues.



68 INSILICO MEDICINE WAGES WAR ON AGING

Dr. Alex Zhavoronkov uses *deep neural network* artificial intelligence to analyze, understand, and mitigate **human aging**.