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September 2026

## FEATURE ARTICLES

- 7 Longevity Research Tsunami
- 24 Full-Body Benefits of Fish Oil
- 36 Restore More Youthful Cognition
- 46 Best B12 for the Job
- 57 Quercetin and Atherosclerosis
- 68 Clinical Update: Regulatory T-Cells

# Stay Mentally Sharp

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Kidney Dialysis Patients**



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References: 1. *Nat Rev Mol Cell Biol.* 2021 Feb;22(2):119-41. 2. *NPJ Aging.* 2022 May 1;8(1):5. 3. *Geroscience.* 2024 Oct;46(5):4671-4688.

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## REPORTS

### Stay Mentally Sharp

Page  
36  
ON THE  
COVER



In separate **clinical trials**, three **plant** compounds were associated with improvements in measures of **memory**, **learning** performance, and **multi-tasking** ability.

### 24 SYSTEMIC EFFECTS OF FISH OIL

Researchers continue to discover new benefits for fish oils including *boosting brain function*, *improving both cognitive and metabolic health* and *reducing inflammation*.



### 46 BEST B12 FOR THE JOB

Combining two **bioactive** forms of **B12** promotes **brain** and **nerve function**, as well as overall health.



### 57 QUERCETIN REDUCES ATHEROSCLEROSIS

Preclinical research shows that the flavonoid **quercetin** may help *mitigate* development and progression of **atherosclerosis**.



### 68 IMMUNE REGULATORY T CELLS

Three scientists won a **Nobel Prize** for their work on **regulatory T cells**, which *defend* healthy tissues from **immune cell attack**. Their discovery is transforming into clinical practice to combat autoimmune diseases, cancer, and more.



## DEPARTMENTS

### 7 AS WE SEE IT: LONGEVITY RESEARCH TSUNAMI

A wave of converging technologies could *result* in **biological age reversal** in our lifetime.

### 17 IN THE NEWS

Multivitamin/mineral use linked to greater health benefits; CoQ10 reduces statin-associated muscle symptoms; gotu kola increases macular

pigment optical density; fish oil lowers risk of cardiovascular events in kidney dialysis patients.

### 67 SUPERFOODS: MUSHROOMS

Low in fat and calories, edible mushrooms are recognized as a functional food that has been shown to support cognition, mood, immune markers, and overall health and wellbeing.



Page 7



17



67

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**References:** 1. *Antioxidants (Basel)*. 2021 Jun 3;10(6):906. 2. *Int J Mol Sci*. 2024 Jun 20;25(12):6765. 3. *Int J Mol Sci*. 2023 Jan 30;24(3):2585. 4. Data on File. Manuscript in prep: 2025.  
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A randomized controlled trial in a small number of older adults suggests that relatively high doses of glycine plus N-acetylcysteine may help support several functional and structural factors associated with decline during aging.<sup>3</sup>

#### References

1. *Oxid Med Cell Longev.* 2017;2017:1716701.
2. *Ochsner J.* 2018 Spring;18(1):81-7.
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# Longevity Research Tsunami

BY WILLIAM FALOON



For nearly 50 years, I've professionally advocated that substantial resources be allocated to support **longevity research**.

My early talks/articles were met with skepticism by those who could not conceive of older people growing biologically *younger*.

In recent decades, scientific advances have enabled me to pursue and directly fund a concept that:

***Age reversal may become medically achievable within our lifetime.***

My recent lectures at biomedical conferences emphasize a convergence of technologies that are changing **aging research** into an exciting **bioengineering** endeavor.

Promising solutions include partial **cellular reprogramming**, senescent cell clearance, AI-driven drug discovery, organ regeneration, and therapies aimed at restoring **youthful** functionality.

While scientists remain cautious about timelines, I view laboratory developments occurring today as beyond *anything* previously seen in medicine.

This editorial describes a few topics from my recent live presentations on the science behind **biological age** reversal.

## Cellular Reprogramming

My research team, along with others, is funding research that adds copies of **genes** that have been shown to improve health and/or longevity in **old cells** and **old mice**.

In recent years, my presentations describe the discovery that **aged cells** may be pushed back toward a *younger biological* state<sup>1</sup> through the use of **reprogramming** factors first identified by Dr. Shinya Yamanaka.<sup>2,3</sup>

These “**Yamanaka factors**” — often abbreviated as **OSKM** or **OSK** — demonstrate that mature (old) cells can be reverted to a more *youthful* state.<sup>4</sup>

Note that **OSK** is the abbreviation for three of the four Yamanaka transcription factors.

Yamanaka factors are one of the most important discoveries in modern biology.

Research around these factors suggests **aging** may not simply be passive wear and tear, but a **reversible** process via **genetic optimization**.

In this editorial, I highlight findings from experiments in which **old mice** experienced restoration of tissue function, improved regeneration, and/or extension of remaining lifespan after **partial cell reprogramming**.<sup>1,5,6</sup>

If restoring the *youthful* identity of your **old cells** by resetting your **epigenome** seems speculative, understand that the **vitamin D** you take is known to directly affect at least **hundreds** of genes, and indirectly affects thousands more.

It both upregulates and downregulates target genes involved in diverse physiological processes.<sup>7-9</sup>

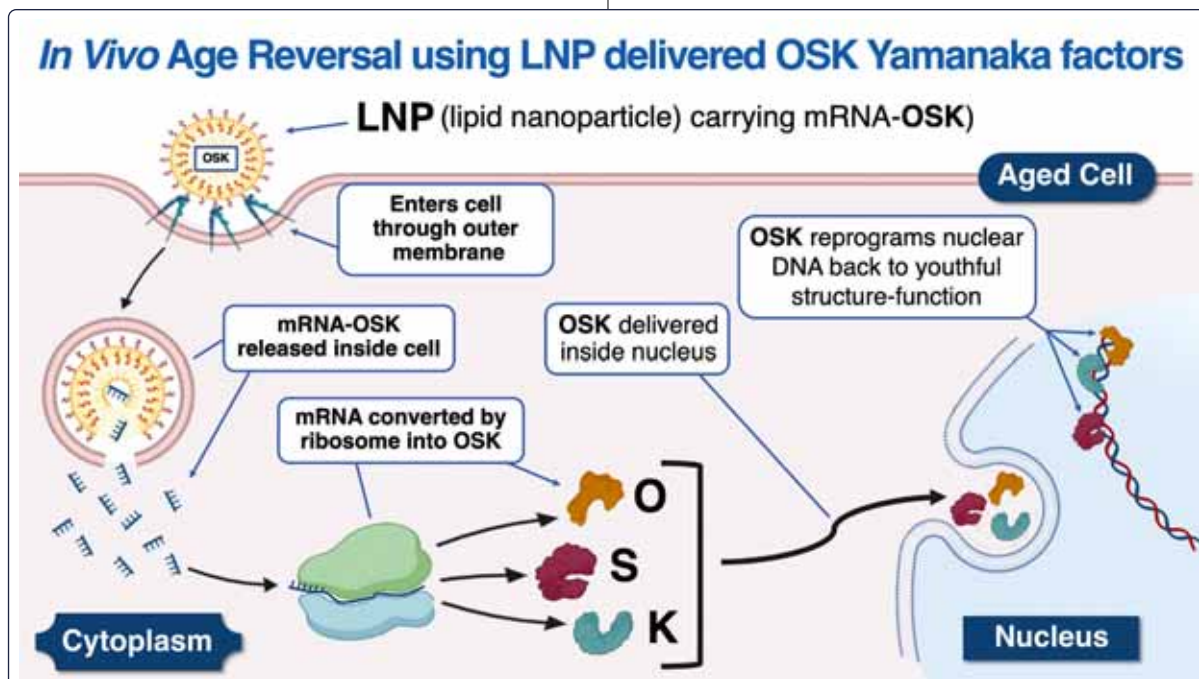
For those who are not familiar with the term **epigenome**, this is a set of mechanisms inside cells that regulate which **genes** are turned “on” and “off”.<sup>10</sup>

(Note: While **vitamin D** beneficially impacts gene expression, it does NOT perform **cellular reprogramming** in the same sense as epigenetic reprogramming observed with Yamanaka factors.)<sup>9</sup>

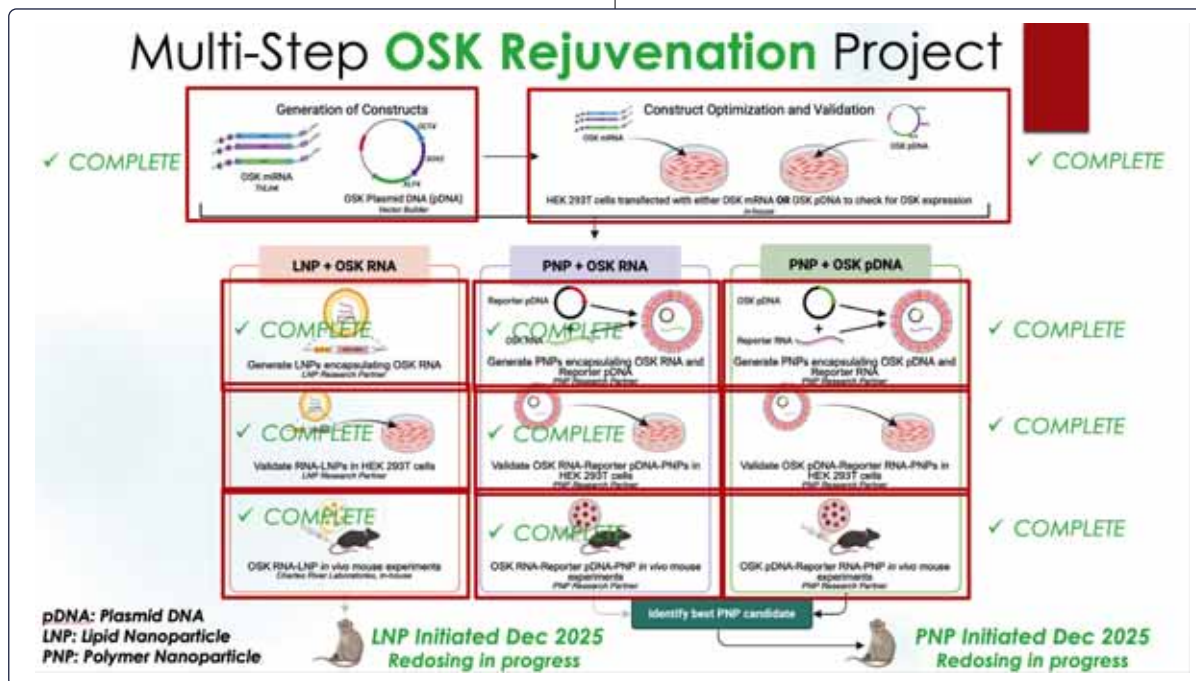
Rather than viewing **aging** as an irreversible accumulation of damage, I present evidence showing our body may be capable of restoring *younger* functions if properly activated via **cellular reprogramming** and other interventions.

The graphic on this page is what I present at scientific conferences to depict delivery of **OSK** into nuclear DNA, where it can **reprogram** old cells back to a more youthful state, as shown in preclinical studies.

Our research team is funding a study using OSK *in vivo* in an attempt to **reverse** aging in old primates.



See how we encase the **OSK** RNA blueprint into a lipid nanoparticle to enable it to easily cross the cell membrane. Once inside, the lipid nanoparticle releases the OSK blueprint that is converted to OSK proteins by ribosomes. These OSK proteins then pass through pores in the nucleus where they bind to nuclear DNA and induce a “**reprogramming**” effect that enables old cells to regain *youthful* structure-function.<sup>11</sup>



## Cellular Reprogramming: From Petri Dish to Preclinical Validation

Preclinical evaluation pipeline for OSK-based reprogramming constructs, including in vitro validation, in vivo testing in mouse models, and subsequent evaluation in non-human primates.

### Measuring Biological Age

Starting in the mid-**1990s**, our **Life Extension®** group attempted to develop tests to assess **biological age**.

We knew that, to rapidly determine whether a therapy might extend a healthy lifespan, we required a way to determine if experimental **interventions** reduce **biological age** markers.

The state of biomedical technology in that era prevented us from achieving consistent results.

But fortunately, starting in 2011, other research groups succeeded in developing **DNA methylation**-based age measurement tools using saliva<sup>12</sup> and blood samples, as well as a composite **phenotypic age** score derived from existing blood tests such as **C-reactive protein (CRP)**, **glucose**, **immune cells**, etc.<sup>13</sup>

These transformative tools (and other tests) allow scientists to quantify aging in ways that were impossible decades ago.

Instead of waiting years to determine whether a therapy extends lifespan, researchers can now examine whether interventions appear to reduce biological **age** markers in months or even weeks.

### Counteracting Other Aging Mechanisms

We are funding an expensive primate project using nanoparticle-delivered **OSK gene addition** therapy.

We are simultaneously studying other interventions with significant regenerative potential.

I've enlightened audiences about **senescent cells** that secrete destructive compounds into surrounding tissue. Senescent cells contribute to frailty, fibrosis, vascular disease, osteoarthritis, and systemic **inflammation**.<sup>14</sup>

Even if **OSK** genes succeed in **reprogramming** old cells back to youth, we still may need to eliminate **senescent cells** using **senolytic** compounds such as fisetin, quercetin, and senolytic drugs that are being developed.<sup>15</sup>

Animal studies that use **senolytics** to clear senescent cells have shown improvements in physical function and an extended lifespan.<sup>16</sup> Senolytics may be analogous to periodically removing malfunctioning components from an aging machine. While human evidence remains limited, **senolytic** interventions could eventually become part of routine **preventive** medical practice.

Artificial intelligence-driven drug discovery offers tremendous potential.<sup>17</sup> I often discuss companies such as **Insilico Medicine**, which we helped **fund** in its early years.

Insilico has pioneered machine learning systems capable of identifying therapeutic compounds at unprecedented speeds.

**Insilico** has entered into “a significant deal of up to **\$2.75 billion**, including **\$115 million** up front with pharma giant **Eli Lilly**” to rapidly develop new drugs, some intended to counteract **biological aging**.<sup>18</sup>

**AI** is compressing timelines that once required decades of pharmaceutical development.

These computational systems can predict candidate drugs, optimize structures, and identify targets far faster than traditional approaches.<sup>17</sup>

The intersection of AI, genomics, and biologics is producing a beneficial compounding effect.

I view this as a “**biomedical renaissance**” where **aging research** is advancing exponentially.

To put this into historic perspective, prior to year **2014**, there was little in the way of **regenerative therapies** we could expect to become clinically available in the foreseeable future. Today multiple youth restoration **interventions** are being aggressively studied.

**March 30, 2026**

## Eli Lilly invests **\$2.75 billion** in deal with AI-longevity company **Insilico Medicine**

Eli Lilly is putting up nearly **\$3 billion** for an exclusive, world-wide license to pre-clinical oral drug candidates identified by **Insilico Medicine's** AI research models.

“This deal will involve a collaboration on identifying the next **generation of AI-predicted longevity drugs**”



**March 30<sup>th</sup>, 2026** <https://longevity.technology/news/lilly-races-to-become-first-longevity-big-pharma/>

**April 27<sup>th</sup>, 2026**

## “A new therapy has the potential to cure hundreds of diseases — and even reverse aging.”

“Many scientists now believe that mastering **cellular rejuvenation** may be the key to transforming how long and how well we live.”

Some hope that they might eventually be able to harness the process to cure hundreds of diseases, **extend life** by decades and even **fend off aging** entirely.”

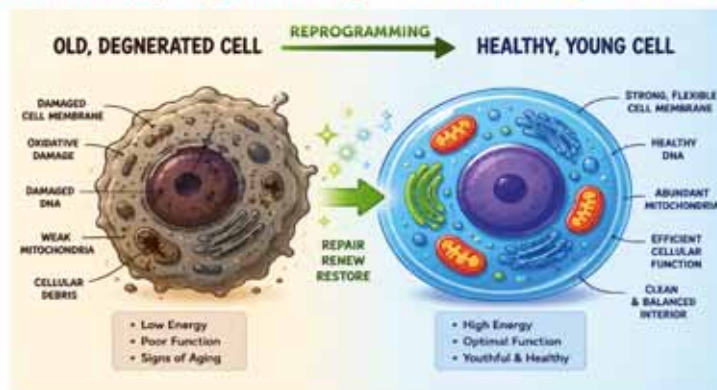


<https://www.nytimes.com/2026/04/24/magazine/eternal-life-longevity-world-leaders.html>

News media sometimes describes:

April 27, 2026

## Cellular Reprogramming as Cellular Rejuvenation



OSK reprograms old cells into young healthy adult cells

### Rapid Fire Progress

**Fibrosis** is the excessive accumulation of dysfunctional connective tissue and other extracellular matrix components. This pathological process contributes to countless **deaths** worldwide.<sup>19,20</sup>

Think pulmonary **fibrosis**, cardiac **fibrosis**, liver **fibrosis**, kidney **fibrosis** et al.

**Fibrosis** and its inflammation-associated damage are implicated in **degenerative** aging.<sup>21</sup>

A recently identified mediator of **fibrosis** is a cytokine called **interleukin-11** (IL-11).<sup>22</sup>

A study published in 2024 showed that neutralizing IL-11 in mice improved healthspan and median lifespan (**23–25%**) when given to 75-week-old mice (roughly equivalent to 55 years old in **human** years).<sup>23,24</sup>

These findings are significant because they beneficially circumvent multiple **age-related** mechanisms. This includes measures of frailty, metabolism, fibrosis, and cancer incidence.

Research involving **IL-11 inhibitors** has drawn attention from biotechnology firms and longevity-focused investors.<sup>23,25,26</sup> **Calico** (Google's research arm) struck a deal to develop an IL-11–targeting drug, paying \$25 million up front with up to \$571 million in milestone payments (\$600 million total).<sup>27</sup>

What's exciting is a potent **IL-11 inhibitor** drug advanced into clinical trials in **2025**<sup>28</sup> only **18 months** after the **mouse** study was published!<sup>23</sup> It usually takes many years for research to move from **mouse** to **human** study...if ever.

## Rapid Fire Progress!

- In 2024, **IL-11 inhibition** was a fascinating life extending mouse study.
- Today, it's in human trials backed by more than **\$600 million** in funding.
- A timeline that would have been unthinkable a decade ago.
- Advances in **AI-driven** drug discovery, **computational** biology, and streamlined **clinical trial** design are compressing what used to take **15-20 years** into **a fraction of that**.

Jan. 7<sup>th</sup>, 2026
<https://foreveryoungfilm.substack.com/p/googles-calico-labs-has-an-anti-aging>

If this **anti-IL-11 antibody drug** proves effective in humans, we may add it to our list of repurposed drugs (like **metformin**) that help neutralize pathologic aging processes.

Most of our readers supplement with nutrients with anti-fibrotic activity including **curcumin**,<sup>29,30</sup> **resveratrol**,<sup>29</sup> and **quercetin**.<sup>29-31</sup> If the anti-IL-11 antibody **drug** becomes available, I anticipate it will be more effective in suppressing the pathologic (IL-11) cytokine.

The fact that we are living in this era of rapid **innovation** is *beyond* fascinating. We may **live long** enough to personally benefit.

## Huge Amounts of Research Funding

The media has extensively reported on the growing role of wealthy investors and major biotechnology firms entering the **longevity research** field.

An enormous influx of capital is pouring into charities and companies pursuing **rejuvenation science**. Recent advances have moved anti-aging research from fringe science into mainstream biotechnology.

Most groups involved in funding distinguish between extending lifespan and improving healthspan. They argue that the central goal is not merely increasing years lived, but preserving *youthful* function, cognition, mobility, and independence.

## IL-11 as a Longevity Target

- **It worked in both sexes.** Many longevity interventions only work in male mice, or work far better in one sex. IL-11 inhibition extended lifespan **22.5%** in males and **25%** in females.
- **It improved healthspan, not just lifespan.** The mice weren't just surviving longer in a decrepit state. They showed comprehensive **improvements in health** across virtually every metric.
- **It worked even when started late in life.** Treatment began at 75 weeks—roughly equivalent to **55 years old in humans**—yet still produced huge benefits. Transitioned from preclinical to **human** trials in **18 months**.

Jan. 7<sup>th</sup>, 2026

<https://foreveryoungfilm.substack.com/p/googles-calico-labs-has-an-anti-aging>

- April 27<sup>th</sup>, 2026

**“Rejuvenation is one of the newest and most promising developments in longevity research...”**

“Major figures in Silicon Valley, including **Peter Thiel**, **Larry Ellison** and **Sam Altman**, have collectively **invested billions** in biotech companies and research centers devoted to slowing the **aging** process.”



<https://www.nytimes.com/2026/04/24/magazine/eternal-life-longevity-world-leaders.html>

# A Tidal Wave of Longevity Research

## Coinbase Founder's Startup Triples in Value

"NewLimit, a longevity startup co-founded by Coinbase CEO Brian Armstrong, completed a fundraising that brings its valuation to **\$3.1 billion**, the company said, more than triple what it was a year ago, on growing enthusiasm for **drugs that promise to slow or reverse aging**."

"Investors poured **\$435 million** into NewLimit, which is focused on **reversing cellular aging** but doesn't have any products on the market yet."

June 2<sup>nd</sup>, 2026

<https://www.wsj.com/business/newlimit-startup-brian-armstrong-value-82ab9830>

Aging is the dominant risk factor underlying most chronic diseases.<sup>32</sup> Rather than treating cancer, dementia, heart disease, and frailty as separate phenomena, increasing numbers of influential individuals recognize that most degenerative diseases are downstream consequences of **aging** biology.

And while improved healthspan is an often-stated objective, the benefit of increased **lifespan** is being recognized as a bridge to future advances in **medicine**.

In other words, individuals today may benefit by engaging in interventions to remain **alive** long enough to benefit from revolutionary rejuvenation therapies.

This is one of several motivating factors that is causing **billions** of dollars of mostly private money to go toward **longevity research**...enabling a virtual **tsunami** of discoveries/innovation.



## Systemic Interventions

Successful **age reversal** will require **interventions** that have **system-wide** regenerative effects. This differs from single-pill studies that often do not yield meaningful results.

Laboratory and clinical advances today are improving gene regulation, inflammatory signaling, stem cell functionality, and regenerative capacities.

What was once viewed as speculative anti-aging enthusiasm now involves major universities, pharmaceutical companies, AI laboratories, and billions of dollars of investment capital.

The implications are profound. If biological aging can be slowed, halted, or partially reversed, then medicine can shift from treating individual diseases toward preserving **youthful** function itself.

The emergence of **rejuvenation biotechnology** may ultimately represent the largest transformation in human history — not simply adding years to life, but potentially redefining what aging means altogether.

My recurring messaging is urgency. We are all degenerating.

I use proceeds from Life Extension® **blood tests** and **supplement sales** to support several promising longevity projects.

Your ongoing patronage is enabling precedent setting advances in the biomedical research arena.

For longer life,

William Faloon, Co-Founder  
Life Extension



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# In the News



## New Data on Health Benefits of Multivitamin/Mineral Supplement Use

A review of 19 meta-analyses that included 214 studies with a total of about 5.5 million people, consolidated the evidence for the health benefits of multivitamin/mineral use.\*

Analysis of randomized, controlled trials found that multivitamin/mineral use was associated with better global cognition, episodic memory, and immediate recall in cognitively intact or older adults.

The scientists also found decreased psychological symptoms in healthy individuals, and lower systolic blood pressure among people with high blood pressure or chronic diseases.

In observational studies, multivitamin/mineral use was associated with lower risks of cataracts, coronary heart disease, colorectal cancer, and hip fracture in adults.

**Editor's Note:** Meta-analyses of studies that evaluated the use of multivitamin/mineral formulas among pregnant women found reductions in the risks of giving birth to infants who were small for their gestational age, had neural tube defects, or developed cancer.

\* *Ageing Res Rev.* 2026 Jan;114:102965.

## CoQ10 Effects Against Statin-Induced Muscle Symptoms

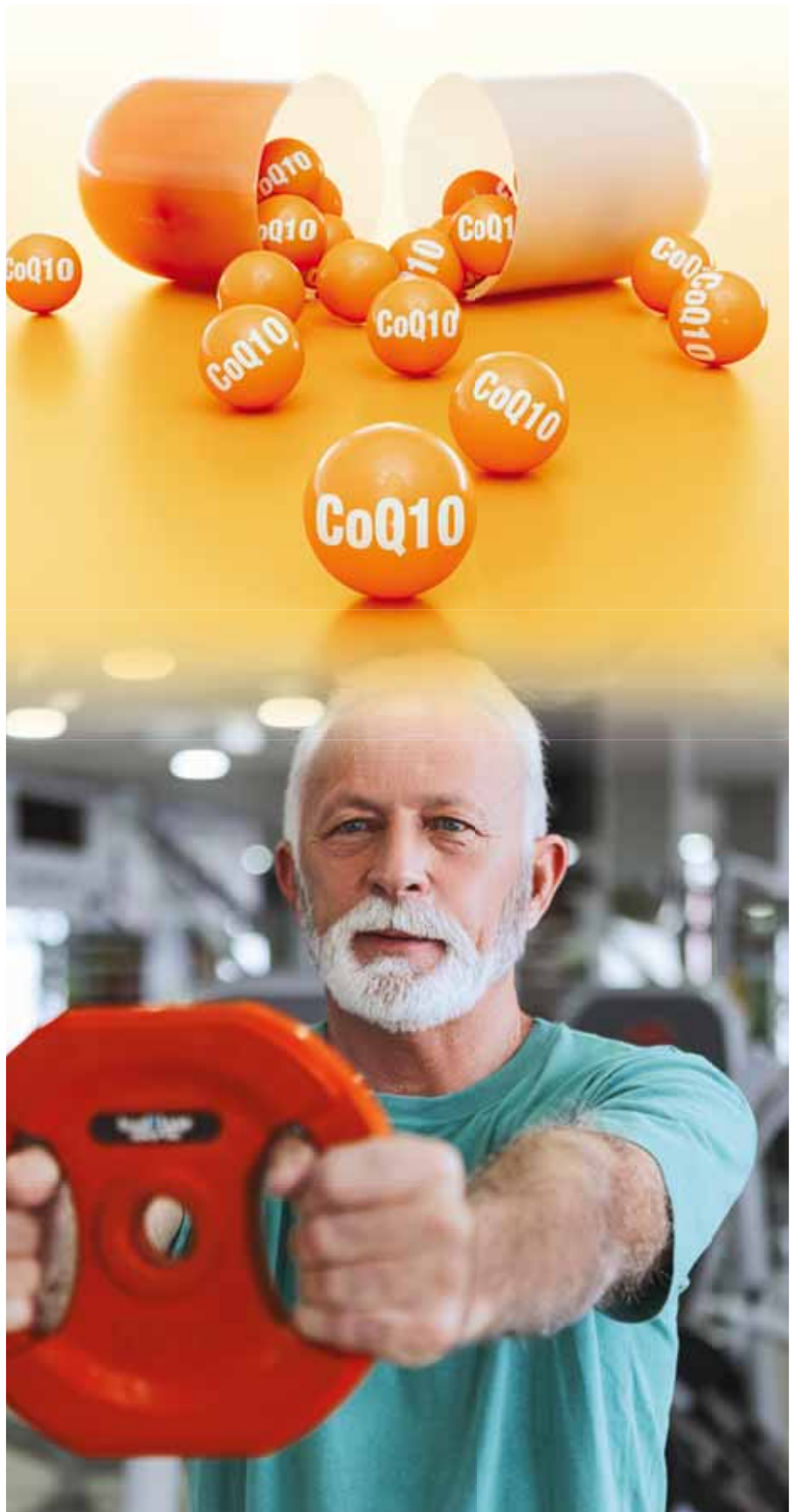
CoQ10 has been studied as a possible treatment for statin-associated muscle symptoms since the late 1980s, with mixed results in clinical trials. A new systematic review and meta-analysis of clinical trials concluded that CoQ10 may be more likely to have a benefit.\*

Statin-associated muscle symptoms include muscle pain, cramps, weakness, stiffness, and, less often, a condition characterized by muscle tissue breakdown. Because CoQ10 is depleted by statin drugs, the addition of CoQ10 to a nutritional regimen has been suggested for statin users to protect against statin-associated muscle symptoms and other side effects.

The meta-analysis included seven randomized, controlled trials that enrolled a total of 389 patients. Trial duration ranged from 30 to 90 days and daily CoQ10 doses ranged from **100 mg** to **600 mg**. Statin dosages ranged from **10 mg** to **80 mg** per day. The meta-analysis showed that the pooled results found a significant reduction in statin-associated muscle side effects in CoQ10-treated individuals.

**Editor's Note:** CoQ10 is a molecule that is made by the body and occurs in some foods. It is essential for producing energy by the cells' "power plants" known as mitochondria, but declines with aging.

\* *J Nutr Sci.* 2025 Oct 10;14:e72.





## Gotu Kola Increases Macular Pigment Optical Density

A randomized, controlled trial found that *Centella asiatica* (known as gotu kola) significantly improved **macular pigment optical density**, a biomarker of macular antioxidant status, among middle-aged adults.\*

The researchers hypothesized that gotu kola would enhance macular pigment optical density by improving the retinal antioxidant environment.

The clinical trial included men and women between the ages of 45 to 65 years. A total of 80 people were split to receive **300 mg** per day of a standardized gotu kola extract or a placebo for 180 days. Macular pigment optical density was measured before the treatment period, on the 60th and 120th days, and at the end of the trial.

Significant improvements were shown beginning at 120 days in the participants who received gotu kola for macular pigment optical density in the left eye, right eye, and the average of both eyes compared with the placebo. An even greater improvement was shown at the 180-day mark.

**Editor's Note:** The participant selection included middle-aged adults with relatively low baseline MPOD.

\* *Nutrients*. 2026 Mar 12;18(6):905.

## Fish Oil Shown to Help Protect Kidney Dialysis Patients from Cardiovascular Events

A randomized, controlled trial revealed a significantly lower risk of serious cardiovascular events among individuals undergoing hemodialysis who received fish oil supplements, compared with those who received a placebo.\*

The trial included **1,228** dialysis patients who received **4 grams** of omega-3 polyunsaturated fatty acids or a placebo daily with a median follow-up of 3.5 years.

During a median 3.5 years of follow-up, the rate of serious cardiovascular events was **43% lower** among participants who received fish oil compared with those who received a placebo.

Participants who received fish oil had a **44%** lower risk of fatal and nonfatal heart attack, a **43%** lower risk of peripheral vascular disease that led to amputation, a **63%** lower risk of fatal and nonfatal stroke, and a **27%** lower risk of a first cardiovascular event or death from any cause, compared with the placebo recipients.

**Editor's Note:** Noncardiac deaths were **33%** lower and cardiac deaths were **45%** lower among those who received fish oil.

\* *N Engl J Med.* 2026 Jan 8;394(2):128-137.





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\* Studied against powder fisetin (98% purity).



# Systemic Effects of **FISH OIL**



BY JACK FILMORE

As far back as the **1970s**, studies have shown cardiovascular benefits of **fish oil** rich in **omega-3** fatty acids.<sup>1-3</sup>

Omega-3s, however, have shown wide-ranging effects throughout the body.<sup>4-6</sup>

In **human** studies, taking fish oil or omega-3s has:

- Been associated with improvements in aspects of metabolic health, including triglycerides and inflammatory markers, in diabetics,<sup>7,8</sup> and non-diabetics<sup>9</sup>
- Shown potential cognitive benefits, particularly in mild cognitive impairment,<sup>10-12</sup>
- Lowered risk for heart disease and cardiac-related death.<sup>13,14</sup> and
- Reduced headaches,<sup>15,16</sup>

A major observational study found that people with the *highest* blood levels of **omega-3s** lived almost **two years longer** than those with the lowest levels.<sup>17</sup>

Modern diets are often low in omega-3s.<sup>18</sup> Oral intake of **fish oil** is a method to fill this dietary gap.



## Why Are Omega-3s So Important?

Fish oil-derived omega-3 fatty acids, **DHA** (docosahexaenoic acid) and **EPA** (eicosapentaenoic acid),<sup>19,20</sup> are required for numerous biological functions.

Fatty acids are building blocks of all human **cell membranes**.<sup>20</sup> These structures are critical to cellular function.

In the **brain**, for example, cell membranes make cellular communication possible.<sup>21,22</sup>

Omega-3 fatty acids are also precursors to **signaling** compounds throughout the body that help fine-tune immune function and regulate inflammation. Some of these, called **specialized pro-resolving mediators**, help *resolve inflammation* that could otherwise continue and become chronic, contributing to rapid aging and disease.<sup>23</sup>

Omega-3s can also regulate **gene expression** in ways that reduce inflammation<sup>24</sup> and lower inflammatory markers.<sup>25,26</sup> Fish oil consumption is associated with reduced triglyceride levels<sup>27,28</sup> and modest reductions in blood pressure.<sup>27,29</sup>

As a result, omega-3 fatty acids may help ward off various ailments, both acute and chronic, from headaches to heart disease.

## Headache Relief

Noting that omega-3s help control inflammation and regulate pain pathways, researchers investigated whether increasing their dietary intake could relieve **headaches**.<sup>15,30-32</sup>

In clinical trials in patients with **migraine**, dietary interventions increasing omega-3 fatty acid intake significantly reduced headache frequency and severity,<sup>15,30,32</sup> while also improving sleep quality.<sup>33</sup>

One meta-analysis even found that fish oil was associated with greater preventative benefits than **pharmaceutical competitors** included in the analysis.<sup>34</sup> The study authors suggested that EPA and DHA could be considered a promising option for **migraine** prevention.

Data also suggest that fish oils benefit other headache types. In one trial of frequent headache sufferers, a diet high in omega-3 fatty acids led to significant reductions in the **number** and **duration** of headaches.<sup>30</sup>

## Improved Metabolic Health

**Metabolic disorders** are associated with accelerated aging<sup>35,36</sup> and increased risk for age-related disease.<sup>37</sup>

Numerous human studies have found that fish oil intake can improve metabolic health.<sup>38-40</sup>

A meta-analysis of 30 human studies suggested that omega-3 supplementation may help improve fasting blood **glucose** levels and markers of **insulin resistance** in subjects receiving omega-3 for diabetes treatment or prevention.<sup>41</sup>

In another randomized, double-blind, placebo-controlled trial, 8 weeks of DHA-rich fish oil supplementation significantly decreased **waist circumference** and body fat mass in patients with type 2 diabetes.<sup>42</sup>



## Protection from Pollution

From wildfires to traffic jams, sources of **air pollution** seem to be everywhere.

In China, where particulate air pollution is a major issue, scientists gave healthy young adults **2.5 grams of fish oil** or a **placebo** daily for four months.<sup>43</sup>

Compared to those who did not receive fish oil, the fish oil group showed protection from some of the negative impacts of air pollution. Markers of inflammation, blood vessel health, oxidative stress, and stress responses were generally better in those receiving fish oil.

## Boosting Brain Function

Multiple human studies suggest that fish oil intake may help preserve cognitive function, especially in individuals with mild cognitive impairment.<sup>12,44,45</sup> In one small clinical study of adults with mild cognitive impairment, for example, fish oil improved multiple aspects of **memory** and **recall**.<sup>44</sup>

These benefits may be due, in part, to the ability of omega-3s to boost **brain-derived neurotrophic factor**, as confirmed by a meta-analysis of 12 randomized controlled trials.<sup>46</sup>

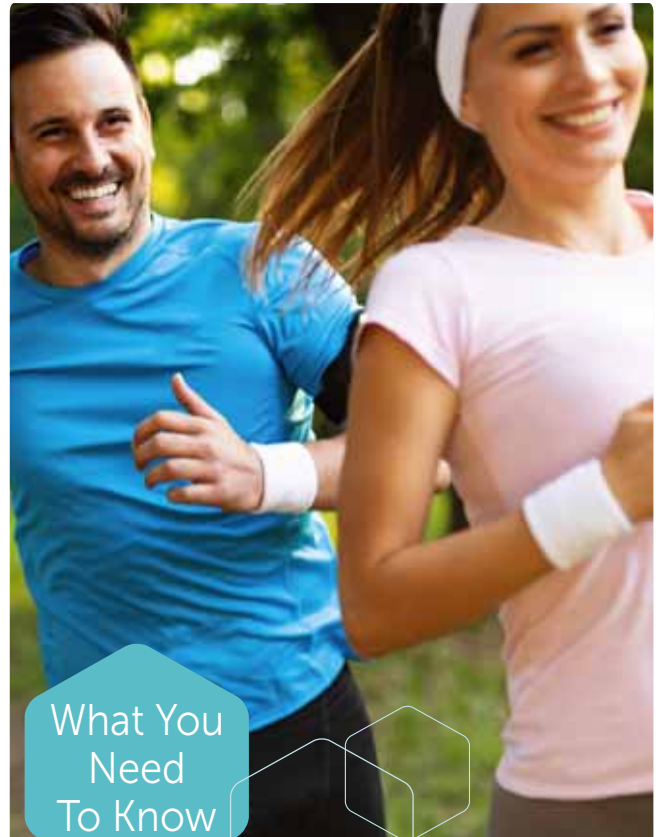
Fish oil may also help protect **mental health**. In a meta-analysis of 31 observational studies involving over 255,000 individuals, higher fish consumption and omega-3 fatty acid intake were associated with a significantly **reduced** risk of **depression**.<sup>47</sup>

In a meta-analysis of 67 randomized controlled trials, omega-3 supplementation at approximately **1.5 grams/day** significantly **improved** depressive symptoms in adults with existing **depression**.<sup>48</sup>

## Cardiovascular Benefits

Fish oil intake benefits **heart** and **blood vessel health** in many ways, including by:

- Maintaining healthy heart structures after myocardial infarction,<sup>49</sup>
- Preventing abnormal blood clot formation,<sup>50</sup> and
- Protecting blood vessel function.<sup>51</sup>



What You  
Need  
To Know

## Body-Wide Benefits of Omega-3s

- Fish oil-derived omega-3 fatty acids are valuable nutrients with numerous biological functions throughout the body. Life Extension suggests a daily intake of at least 2,000 mg of EPA and DHA from fish oil may help ensure adequate levels.
- Fish oil intake has been associated with reduced risk for cardiovascular disease, stroke, heart attack, and cardiovascular-related death.
- Studies have demonstrated a wide range of additional benefits, including metabolic health, cognitive function, headache, and more.

Fish oil also contributes to cardiovascular health by lowering **triglyceride** levels and may modestly reduce blood pressure when consumed at higher doses.<sup>27,52,53</sup>

Among its cardiovascular benefits, fish oil has shown particular promise in the management of elevated **triglycerides**.<sup>54-56</sup> Omega-3 fatty acids help lower triglycerides and raise **HDL (“good”) cholesterol levels**.<sup>56</sup>

Clinical studies have demonstrated that fish oil supplementation at doses of **≥4 grams/day** can effectively lower elevated triglyceride levels, with reductions of up to **45%** in individuals with severe **hypertriglyceridemia**.<sup>57,58</sup>

Evidence further suggests that higher circulating levels of omega-3 fatty acids are associated with a lower risk of **cardiovascular disease**,<sup>59</sup> **coronary heart disease**,<sup>59</sup> **stroke**,<sup>60</sup> and **mortality**.<sup>59,61</sup>

Consistent with these findings, meta-analyses of randomized controlled trials have reported that omega-3 supplementation is associated with reduced risks of myocardial infarction and coronary heart disease events, with benefits appearing to increase with dose.<sup>13,14</sup>

Notably, one meta-analysis of randomized controlled trials with 135,267 participants found that **EPA** and **DHA** intake was associated with a **35% lower risk of fatal myocardial infarction**.<sup>13</sup>

The **Framingham Heart Study**, a prospective cohort study of 2,692 older U.S. adults followed for up to 16 years, found that individuals in the *highest* quintile of plasma omega-3 fatty acid levels lived an average of about 2 more years after age 65 than those in the low-est quintile.<sup>62</sup>

**Life Extension®** suggests daily intake of at least **2,000 mg** of EPA and DHA from highly purified fish oil.

## Summary

The **omega-3 fatty acids** DHA and EPA, found in **fish oil**, serve as building blocks for critical biological structures and compounds in the body.

Studies have found significant benefits to fish oil intake, including supporting **brain health**, controlling **inflammation**, improving **metabolism**, and reducing risk for **cardiovascular disease**. ■

If you have any questions on the scientific content of this article, please call a **Life Extension** Wellness Specialist at 1-866-864-302

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120 vegetarian capsules

**1 bottle \$33**

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**Benfotiamine** helps support cellular health by impeding formation of **advanced glycation end products (AGES)**.<sup>1,2,3</sup>

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**Item #00925**  
120 vegetarian capsules  
1 bottle **\$23.25**  
4 bottles \$20 each



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This supplement should be taken in conjunction with a healthy diet and regular exercise program. Individual results are not guaranteed, and results may vary.



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**Arterial Protect** supports the body's natural processes for managing arterial debris to help maintain endothelial and circulatory health.\*

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



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Stan

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GMO  
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## Olive Polyphenols + Fish Oil + Sesame



**2,400 mg  
EPA/DHA  
in four softgels**  
Plus Standardized  
Olive Extract and  
Sesame Lignans

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120 softgels

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4 bottles \$27.50 each

Contains sesame.



**2,520 mg  
EPA/DHA  
in four softgels**  
with Standardized  
Olive Extract,  
Sesame Lignans, Krill  
and Astaxanthin

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shellfish (krill), sesame.

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**Super Omega-3** provides healthy components of the Mediterranean diet including highly purified **fish oil**, **sesame lignans**, and standardized **olive extract**.

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# Stay MENTALLY Sharp

BY MARSHA MCCULLOCH, MS, RD

Cognitive decline during aging is well documented, with age being the strongest risk factor for **dementia**.<sup>1</sup>

In the U.S., an estimated **10%** of adults aged 65 and older have dementia and **22%** have mild cognitive impairment.<sup>1,2</sup>

Specific **plant** compounds have demonstrated neuroprotective effects.<sup>3</sup>

In preclinical studies, **green oat extract** promoted faster **learning performance** and reduced markers of brain **inflammation**.<sup>4,5</sup>

In a clinical trial, a combination of **Boswellia** tree resin and **haritaki** fruit extract significantly improved measures of **short-term and long-term** memory.<sup>6</sup>

In another clinical trial, standardized **green oat extract** showed significantly better performance than a placebo.<sup>4</sup>

Combining these ingredients is a science-based strategy to optimize cognitive function and promote long-term **brain health**.



## Understanding the Aging Brain

Inside the brain, billions of **neurons** (nerve cells) communicate with each other at junctions called **synapses**.<sup>7</sup>

Neurons use **neurotransmitters** to send messages across synapses.<sup>7</sup>

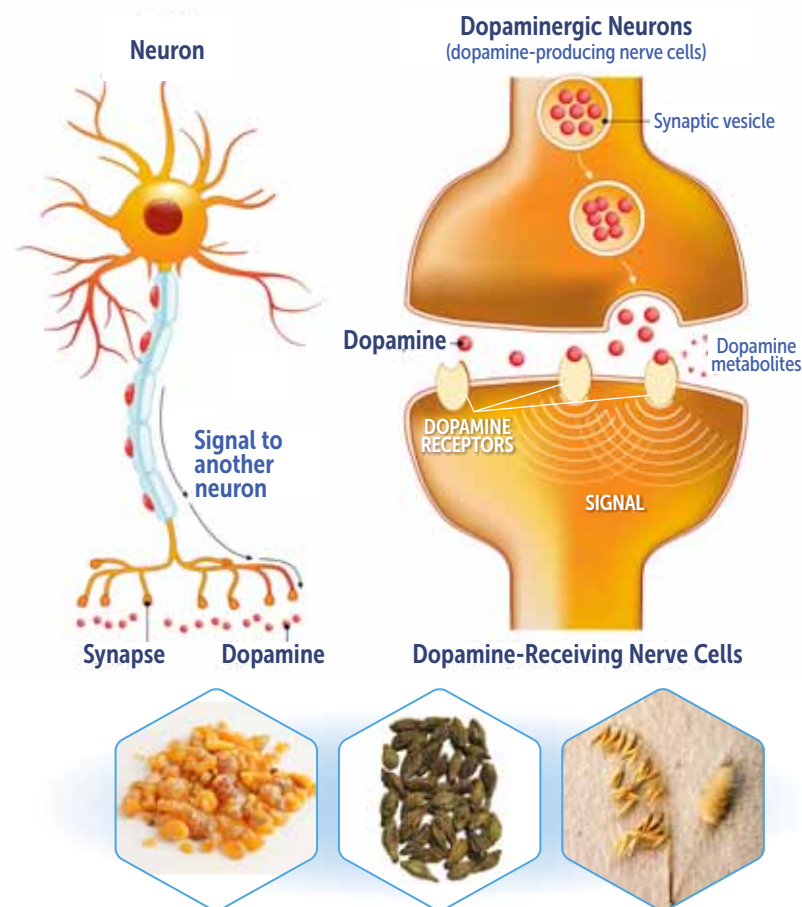
As we age, cognitive function gradually declines. One reason is decreased production and release of neurotransmitters, including **acetylcholine** and **dopamine**.<sup>8</sup>

**Acetylcholine** is essential for learning and memory, including **episodic memory**, the recall of life events.<sup>8,9</sup>

**Dopamine** helps regulate **synaptic plasticity** (the ability to form new synaptic connections) and **neurogenesis** (the ability to generate new neurons), both of which are also critical for learning and memory.<sup>8,10</sup>

With aging, levels of **brain-derived neurotrophic factor (BDNF)** also fall. This protein promotes the growth of neurons and synapses and supports acetylcholine-associated memory processes.<sup>11</sup> Therefore, BDNF plays a crucial role in **learning** and **memory**.<sup>11,12</sup>

Scientists have identified botanicals that target these and other mechanisms of cognitive aging and help keep the brain sharp.



## Brain Botanicals

Ayurveda, an ancient holistic medical system, has traditionally used ***Boswellia serrata*** (Indian frankincense) resin<sup>13,14</sup> and **haritaki** (*Terminalia chebula*), a fruit from Southeast Asia,<sup>15-17</sup> for various medicinal purposes.

Modern preclinical research has since explored the neuroprotective potential of ***Boswellia***<sup>18-20</sup> and **haritaki** plants,<sup>21,22</sup> including their effects on **cognitive function**.

Preclinical research shows that ***Boswellia***<sup>20,23,24</sup> and **haritaki**<sup>25</sup> may help inhibit the activity of the *enzyme* responsible for breaking down the neurotransmitter acetylcholine.

In a randomized, double-blind, placebo-controlled study, 100 adults aged 40–65 with subjective memory complaints received either **300 mg** of a standardized ***Boswellia serrata*** and **haritaki extract** or placebo daily for 120 days.<sup>6</sup>

Cognitive function was assessed using the **Rey Auditory Verbal Learning Test**, where participants listen to and recall word lists several times, then remember them again after short and longer delays, and finally recognize the words from a larger list.

Compared to **placebo**, the treatment group showed statistically significant improvements in:<sup>6</sup>

- **Immediate** (short-term), and **delayed recall**,
- **Overall learning** and **learning rate**,
- **Total learning capacity**, and
- **Recognition memory**.

Some improvements were observed as early as **15 days** after treatment initiation.

An additional battery of **computerized tests** was used to assess non-verbal cognition. Compared to placebo, the treatment group demonstrated significant improvements in **visual learning**, **processing speed** and **task accuracy**.

The intervention also significantly improved **sleep** quality and increased **serum brain-derived neurotrophic factor (BDNF)** levels, a biomarker associated with neuronal health and synaptic plasticity.<sup>6</sup>

## Green Oat Supports Cognition

**Green oat (*Avena sativa*)** has been traditionally used as an antispasmodic, diuretic, and neurotonic agent. Its extract is rich in avenanthramides, flavonoids, triterpenoid saponins, and sterols.<sup>26</sup>

Preclinical research suggests that a standardized **green oat extract** may help reduce markers of brain inflammation and improve measures of cognitive function.<sup>5</sup>

It exerts these effects through multiple mechanisms, including:<sup>5</sup>

- Activating the **Nrf2/HO-1 antioxidant defense** pathway, which mitigates oxidative stress-related neuronal damage,
- Inhibiting the **NF-κB/MAPK neuroinflammatory signaling** pathway in microglial cells, reducing inflammatory responses, and
- Upregulating the **CREB/BDNF** pathway, which supports neuroprotection and memory formation.

In an animal model of **mild cognitive impairment (similar to Alzheimer's symptoms)**, mice were given a standardized green oat extract for 14 days, while a control group received no treatment.<sup>5</sup>

The extract attenuated **spatial memory learning impairments**, as assessed by maze tests.

### Improve Memory and Multitasking

The benefits of green oat extract have been seen in human studies as well.

In a clinical trial of 132 healthy adults (ages 35 to 65), those who took **430 mg** of standardized **green oat extract** daily for 29 days showed significantly better performance than a placebo group on a computerized test of visuospatial working **memory**.<sup>4</sup>

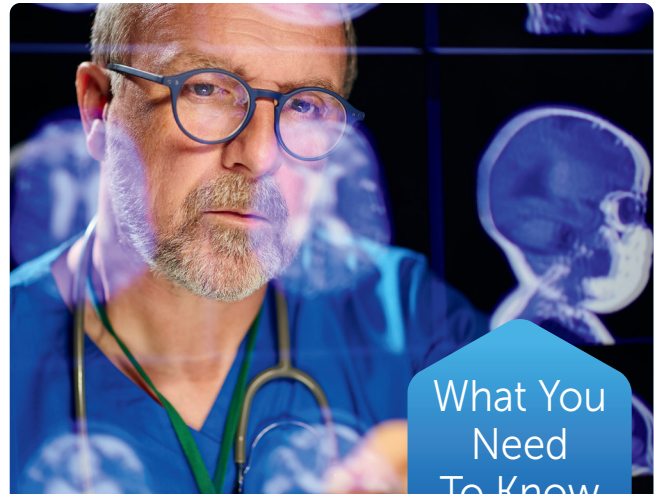
This test requires a participant to reproduce a sequence of blocks in the same order as they were presented, with difficulty increasing over time.

In everyday life, visuospatial working memory is important for tracking locations of moving objects and navigating dynamic environments, such as when driving.

Participants also completed a **multitasking** test that involved performing serial subtraction while simultaneously tracking an asterisk moving across a screen.<sup>4</sup>

Participants taking **430 mg** of standardized green oat extract demonstrated improved tracking performance without compromising subtraction accuracy, suggesting improved divided attention.

This may translate to better performance in real-world situations that require managing multiple tasks at once, such as driving while holding a conversation.



What You  
Need  
To Know

## Supporting Healthy Cognitive Aging

- **Age-related memory loss and cognitive dysfunction** are *not* inevitable.
- Preclinical studies suggest that extracts from ***Boswellia serrata*** resin, **haritaki** fruit, and **green oat** may help preserve **acetylcholine activity**, a neurotransmitter involved in learning and memory.
- ***Boswellia*** and **haritaki** extracts increased serum **brain-derived neurotrophic factor (BDNF)** levels in one clinical trial, which supports the brain's ability to adapt and form new connections.
- In a clinical trial of adults with subjective memory complaints, intake of ***Boswellia*** resin and **haritaki** fruit extracts increased **BDNF** levels while improving measures of short- and long-term memory.
- Another clinical trial of healthy adults found that intake of **green oat extract** improved performance on tests of visuospatial working memory and multitasking.

Taking a **combination** of *Boswellia*, haritaki, and green oat extracts daily may help support cognitive performance and long-term brain health.

## Summary

Specialized botanical extracts may help support cognitive performance and promote healthy brain aging.

***Boswellia*** tree resin, **haritaki** fruit, and **green oat** extracts have been studied for their effects on acetylcholine activity and BDNF levels, which are involved in cognitive function.

In clinical trials, daily intake of these extracts was associated with improvements in several measures of **memory**, **learning** performance, and improvements in **multitasking** ability. ■

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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1 bottle \$18 • 4 bottles \$17 each



MacuGuard® Ocular Support  
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Each bottle lasts for two months.

MacuGuard® Ocular Support is available with or without astaxanthin.

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<sup>Δ</sup> 3-O-acetyl-11-keto- $\beta$ -boswellic acid.

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**FLORASSIST® GI with Phage Technology** supports digestive health by:

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# You lived it. Don't lose it.

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**Ultra Memory & Recall™** is an advanced **memory support formula**, containing standardized botanical extracts of **Boswellia**, **chebulic myrobalan**, and **green oat**.

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- A proprietary **green oat extract** supported visual-spatial working memory, as well as encouraging multitasking speed.<sup>2</sup>

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References: 1. *Front Nutr.* 2025 Dec 8;12:1695341. 2. *Nutrients.* 2020 May 29;12(6):1598.



# The Best **B12** for the Job



Low energy. Tingling or numbness in the feet. Brain fog. Poor balance.

These are just a few possible symptoms of low **vitamin B12**. Some signs are subtle and may be overlooked, potentially resulting in serious damage.<sup>1</sup>

Taking **oral B12** may help provide a safety net by ensuring adequate B12 status.<sup>2</sup> However, *not* all forms are the same.

Only two types of B12 are active in cells:

**Adenosylcobalamin** and **Methylcobalamin**.<sup>3</sup>

These bioactive forms may help address common age-related conditions, including neurological dysfunction:

- In preclinical models of **Parkinson's** disease, **adenosylcobalamin** helped protect dopamine-producing neurons.<sup>4</sup>
- In a human study, oral **methylcobalamin** was associated with improvements in **nerve pain** in adults with diabetic peripheral neuropathy, which is commonly experienced by people with diabetes.<sup>5</sup>

Together, oral **methylcobalamin** and **adenosylcobalamin** can help optimize the body's vitamin B12 status.

## The Importance of B12

**Vitamin B12** is critical for the development and maintenance of the central nervous system. A *deficiency* can lead to neurological concerns, including nerve damage, balance issues, cognitive impairment, and dementia.<sup>6</sup>

Vitamin B12 is found primarily in foods of animal origin, including meat, poultry, some eggs, and dairy products.<sup>7</sup>

The need for supplementation is rising as more people move to **plant-based** diets,<sup>8,9</sup> and due to the decreased absorption of food-based B12, which many people face as they **age**.<sup>8-10</sup>

Two bioactive forms of **vitamin B12** are:

- **Adenosylcobalamin**, which is active in the mitochondria, the energy powerhouse within each cell,<sup>11</sup> and
- **Methylcobalamin**, which is active in the cytosol (gel-like fluid) inside the body's cells.<sup>11,12</sup>

B12 is needed to form healthy red blood cells, DNA, and the myelin covering of nerves.<sup>12,13</sup>

Some individuals have **genetic variants** that can impair the body's ability to convert vitamin B12 into its active forms. That may make the bioactive B12 forms preferable.<sup>14</sup>

People generally don't know their B12-related genetics. Oral intake of both **adenosylcobalamin** and **methylcobalamin** may help support B12 levels.<sup>14</sup>

## Adenosylcobalamin Against Parkinson's Disease

Low levels of vitamin B12 have been associated with progression of **Parkinson's** disease.<sup>15</sup>

Parkinson's involves the progressive loss of **neurons** that produce the neurotransmitter **dopamine** in the brain.<sup>16</sup> This gradually impairs muscle control, balance, mobility, and cognitive function.<sup>17</sup>

A mutation resulting in overactivity of the **LRRK2 enzyme** and destruction of **dopamine-producing neurons** is a top genetic cause of Parkinson's disease.<sup>18</sup>

In preclinical research, scientists discovered that **adenosylcobalamin** inhibited LRRK2 activity and reduced markers of neurotoxicity in experimental models involving dopamine neurons.<sup>4</sup>

In these studies, scientists tested adenosylcobalamin in roundworms genetically modified to express the LRRK2 gene mutation. These worms exhibited symptoms (age-dependent dopaminergic neurodegeneration and behavioral deficits) similar to human Parkinson's disease.<sup>4</sup>

When the young worms were given **adenosylcobalamin**, it prevented the destruction of **dopamine neurons** and related symptoms when they became adults. Similar neuroprotection was found in fruit flies.

In mice, adenosylcobalamin alleviated deficits in dopamine release sustainability caused by LRRK2 disease variants.<sup>4</sup>

## Methylcobalamin and Neurological Health

Older adults with elevated levels of **homocysteine** are at increased risk of **stroke**<sup>19</sup> and **dementia**.<sup>20,21</sup>

Vitamin B12 serves as a cofactor to help lower homocysteine levels.<sup>22,23</sup>

**Clinical** (human) research has shown benefits of methylcobalamin for **diabetic peripheral neuropathy**, a condition marked by painful tingling, burning, or hot/cold sensations in the arms, legs, hands, and feet.<sup>5</sup>

Peripheral neuropathy commonly affects people with **diabetes** and can occur in **prediabetes**.<sup>24</sup> The nerve pain and other symptoms can also be triggered by physical injuries<sup>25</sup> and insufficient **vitamin B12** levels.<sup>25,26</sup>





## What You Need To Know

### Bioactive Forms of B12 for Neurological Health

- With aging and low intake of animal-based foods, risk of **vitamin B12** deficiency rises. Food sources of B12 can also be challenging to absorb.
- Not all oral B12 is the same. **Adenosylcobalamin** and **methylcobalamin** are the only two readily active forms of B12. Each has unique functions that support neurological and overall health.
- Preclinical research suggests that adenosylcobalamin may help support **dopamine-related pathways**. Low dopamine levels are tied to Parkinson's disease.
- In a human trial, methylcobalamin significantly improved **peripheral neuropathy pain scores** in adults with **diabetic peripheral neuropathy** and **low vitamin B12 levels**. Nerve pain is common in diabetes.
- A combination of adenosylcobalamin and methylcobalamin may help support optimal vitamin B12 levels for neurological and overall health.

In a one-year clinical trial, researchers gave **1,000 mcg** of **oral methylcobalamin** or a placebo daily to 90 adults with **type 2 diabetes** who had diabetic **neuropathy** and vitamin B12 blood levels below **400 picomoles (pmol)/L**.<sup>5</sup>

All subjects had been taking **metformin**—a diabetes drug that can impair B12 absorption—for at least four years. In the **methylcobalamin** group, neuropathy pain scores significantly **improved**, while the **placebo** group's pain scores significantly **worsened**.

In addition, the B12 treatment group raised their serum B12 levels from **232.0 pmol/L** at baseline to **776.7 pmol/L**. B12 levels did not significantly change in the **placebo** group.<sup>5</sup>

Though vitamin B12 levels below **148 pmol/L** are typically used as the threshold for diagnosing deficiency,<sup>27</sup> neurological dysfunction can occur even in individuals with levels higher than this.<sup>27,28</sup>

A randomized, double-blind, placebo-controlled trial enrolled patients with type 2 diabetes on metformin who had B12 levels below **400 pmol/L** and demonstrated that **B12 supplementation** improved neuropathy outcomes, suggesting that even levels considered “sufficient” by conventional standards may be suboptimal in this population.<sup>5</sup>

Additional research published in **2025** found that even vitamin B12 levels within the normal range were linked to markers of neurological injury and reduced function in healthy older adults, suggesting that current definitions of optimal **B12** levels may need to be re-evaluated.<sup>28</sup>

Oral intake of **1,000 mcg** of a combination of **adenosylcobalamin** and **methylcobalamin** may help support vitamin B12 status and neurological health.

## Summary

**Vitamin B12** is critical for maintaining **neurological health** and other essential functions.

Several forms of oral vitamin B12 are available. **Methylcobalamin** and **adenosylcobalamin** are the two forms used directly by enzymes in the body.

Preclinical data show that **adenosylcobalamin** may help preserve **dopamine** levels. Loss of dopamine is tied to the development of **Parkinson's disease**.

In a clinical study, oral **methylcobalamin** improved peripheral neuropathy pain in adults with diabetic **peripheral neuropathy**.

Combining these two bioactive forms of B12 may help support optimal levels for brain and nerve function, as well as overall 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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\* regular luteolin defined as **98%** pure powder luteolin

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2. Bio-Luteolin Bioavailability Study. Data on file. 2025.

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**References:** 1. *Nutrients*;14:5235.10.3390/nu14245235. 2. *J Alzheimers Dis.* 2016;49(4):971-90.  
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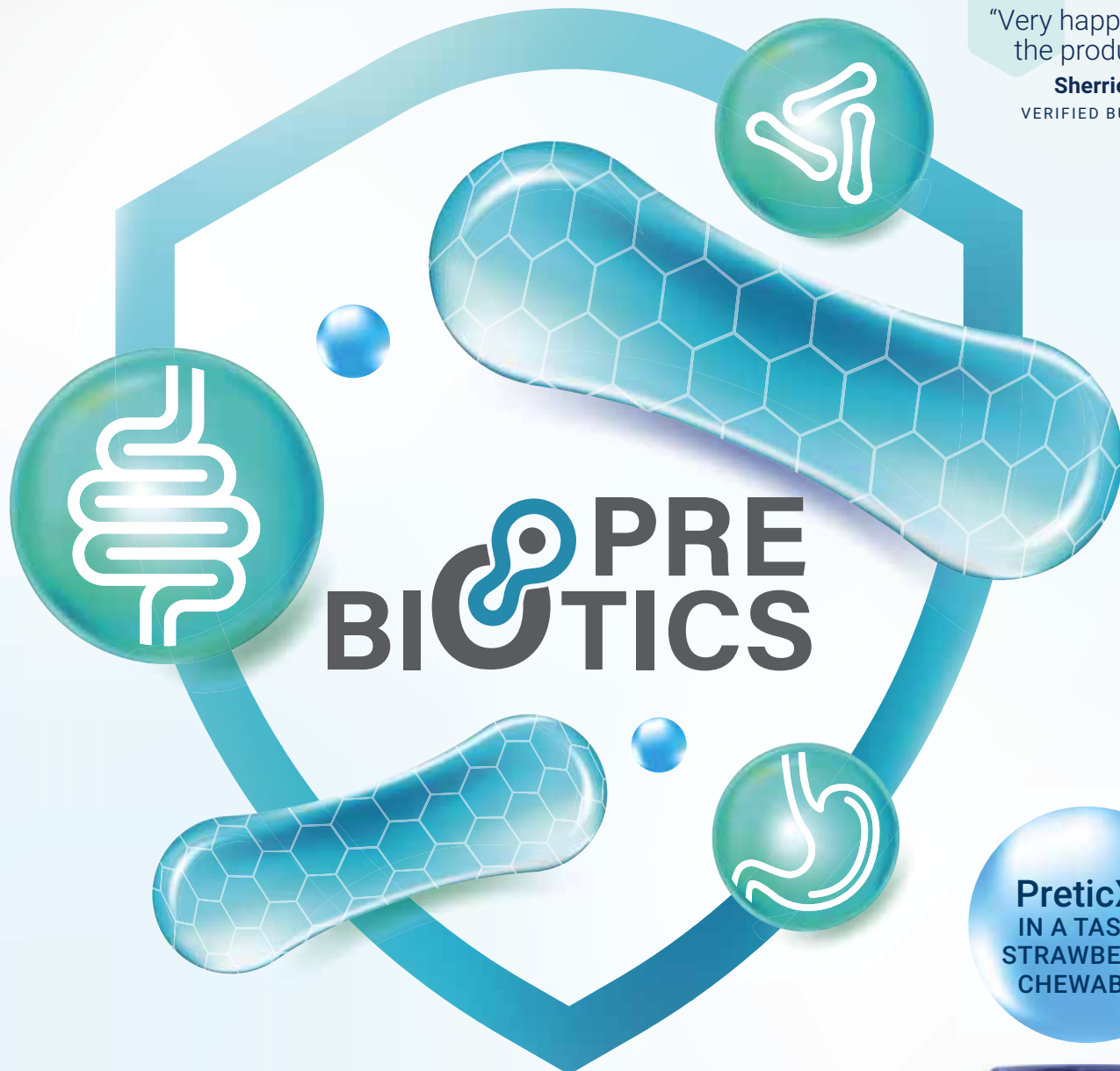


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Item #02203 | 60 vegetarian chewable tablets  
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#### References

1. *Front Microbiol.* 2016;7:1204.
2. *Food Func.* 2014;Jan(5):436-445.



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# Quercetin Reduces Atherosclerosis

BY RICHARD TEMPLETON



It's difficult to overstate just how dangerous and common **atherosclerosis** is.

Atherosclerosis is the progressive buildup of plaque in the arteries and is a leading cause of cardiovascular disease, including coronary artery disease (CAD), peripheral artery disease (PAD), and cerebrovascular disease.<sup>1</sup>

Preclinical research over the last few years has shown that **quercetin** can play a role in mitigating the development and progression of atherosclerosis, helping to protect the heart and potentially reduce risk for these dangerous conditions.

## How Atherosclerosis Drives Cardiovascular Disease

**Atherosclerosis-driven coronary artery disease** develops over time as lipids, inflammatory cells, smooth muscle cells, and dead cell debris accumulate beneath the vessel's inner endothelial lining.

Its major complications, including myocardial infarction and stroke, substantially contribute to morbidity, loss of independence, and reduced quality of life.<sup>2</sup>

Nearly half of U.S. adults have at least one major risk factor for coronary heart disease, such as high blood pressure, high lipids, or smoking. Meanwhile, **12%** have diabetes, a serious risk factor; and 115 million adults have prediabetes, yet another potential contributor.<sup>4</sup>

As plaque accumulates, several pathological changes can occur:<sup>2</sup>

- **Endothelial dysfunction**, in which the endothelium loses its protective role, leading to reduced vasodilation, increased inflammation, and endothelial cell senescence.<sup>5</sup> Endothelial dysfunction is also the first step in the process that initiates atherosclerosis.<sup>6</sup>
- **Narrowing of blood vessels** (often **> 50%**), which reduces blood flow and causes angina, particularly during physical exertion or stress,<sup>2</sup> and
- **Blood clot formation** can be triggered by rupture-prone fat and inflammation-rich plaques, blocking blood flow to the heart, causing a heart attack, or traveling to the brain resulting in stroke.<sup>2</sup>

Emerging preclinical research suggests that quercetin may influence several biological processes involved in atherosclerosis progression.



## What Is Quercetin?

Quercetin is a naturally occurring compound found in a variety of plant foods, including onions, leafy green vegetables such as kale, cruciferous vegetables like broccoli and cabbage, as well as tea, berries, and certain herbs.<sup>7</sup>

Quercetin has been studied for its role in mitigating age-related deterioration and disease, largely because of its **antioxidant** and **anti-inflammatory** effects.<sup>7</sup> Preclinical studies also suggest quercetin may have **senolytic activity**, meaning it may help target **senescent cells**, though this has primarily been demonstrated in experimental models.<sup>8,9</sup>

Recent research suggests that quercetin may influence key biological processes involved in atherosclerosis. Evidence from animal and human cell studies indicates that quercetin reduces plaque formation and improves vascular health.

## Activating Cellular Defenses

Preclinical studies suggest that quercetin's antioxidant<sup>10</sup> and anti-inflammatory effects<sup>11,12</sup> target key processes involved in atherosclerotic plaque formation.

Quercetin also activates specific cell pathways critical to cellular defense and rejuvenation in blood vessels.

One way quercetin may support cellular defenses is by increasing activity of a protein called **Nrf2**. When activated, *Nrf2 switches on protective genes* that defend cells against threats like oxidative damage.<sup>13,14</sup>

**Nrf2** activity can be suppressed when it binds to another protein, **KEAP1**. A study found that quercetin binds to KEAP1 and causes it to separate from Nrf2, allowing Nrf2 to activate cellular defenses. As a result, Nrf2 activation helps reduce inflammatory cell death in macrophages.<sup>13</sup>

Quercetin also increases the production and activity of another cellular defender, **SIRT1**.<sup>15-17</sup> SIRT1 and other sirtuins are proteins vital to cellular defense and rejuvenation.

Activating SIRT1 has been associated with prolonged cellular lifespan in experimental models.<sup>15,18</sup> Quercetin boosts SIRT1 expression and activity, which may contribute to its observed effects in atherosclerosis.<sup>17</sup>

In preclinical studies, quercetin has also been shown to increase the activity of **AMPK**, an enzyme that plays a key role in metabolic regulation (including blood sugar, lipids, and insulin resistance).<sup>15,19,20</sup> *Reduced* AMPK activity is tied to insulin resistance and metabolic syndrome, major risk factors for cardiovascular disease including atherosclerosis.<sup>21</sup>

Through all these actions, quercetin can further block the oxidative damage and inflammation that contribute to atherosclerosis.

For example, it impedes the **oxidation of LDL cholesterol**, which contributes to fat deposits in arterial plaques.<sup>14,15</sup>

These effects of quercetin have been associated with protection against atherosclerosis in animal models.

## Blocking Dangerous Abnormalities

Several types of cells are damaged or altered in **atherosclerosis**, worsening the condition.

**Quercetin** has been shown in preclinical studies to protect against damage to:

- **Macrophages.** A type of immune system cell, damaged macrophages can invade arterial plaques and transform into **foam cells**, which rapidly accelerate plaque buildup. Quercetin has been shown to *reduce* transformation of macrophages into forms that promote atherosclerosis.<sup>13,15,22</sup>
- **Endothelial cells.** These cells line the inside of arteries and are critical to healthy blood flow. When these cells become damaged, they drive atherosclerosis. Quercetin has been shown to *block* endothelial cell damage and death.<sup>12,14,15</sup>
- **Vascular smooth muscle cells.** Smooth muscle cells in arterial walls allow the vessel to constrict or dilate to regulate blood flow. In atherosclerosis, these cells spread and migrate to abnormal locations within the vessel. This is associated with inflammation, calcification, and thickening of the plaque.<sup>23</sup> Quercetin has been shown to *inhibit* the harmful proliferation and migration of these cells.<sup>24,25</sup>

## Improving Gut Health

A healthy mix of gut microbes benefits the heart and overall health.<sup>26</sup>

In preclinical models, quercetin intake has been associated with improvements in gut microbial

composition.<sup>27-29</sup> In turn, healthy gut microbes metabolize quercetin into bioactive compounds that circulate throughout the body.

**Higher** levels of these metabolites have been linked to reduced atherosclerosis in experimental animals.<sup>26</sup> In one animal study quercetin intake not only altered the gut microbiota but also reduced harmful lipid metabolites.<sup>30</sup>

A review of 30 preclinical studies suggests that quercetin supplementation, across a range of doses, may exert cardioprotective effects in experimental high-fat diet models.<sup>31</sup> Clinical trials are needed to determine whether these findings translate to human atherosclerosis.

## Summary

**Cardiovascular disease** is the leading killer in the world. Atherosclerotic **plaque** in blood vessels is its most common driver.

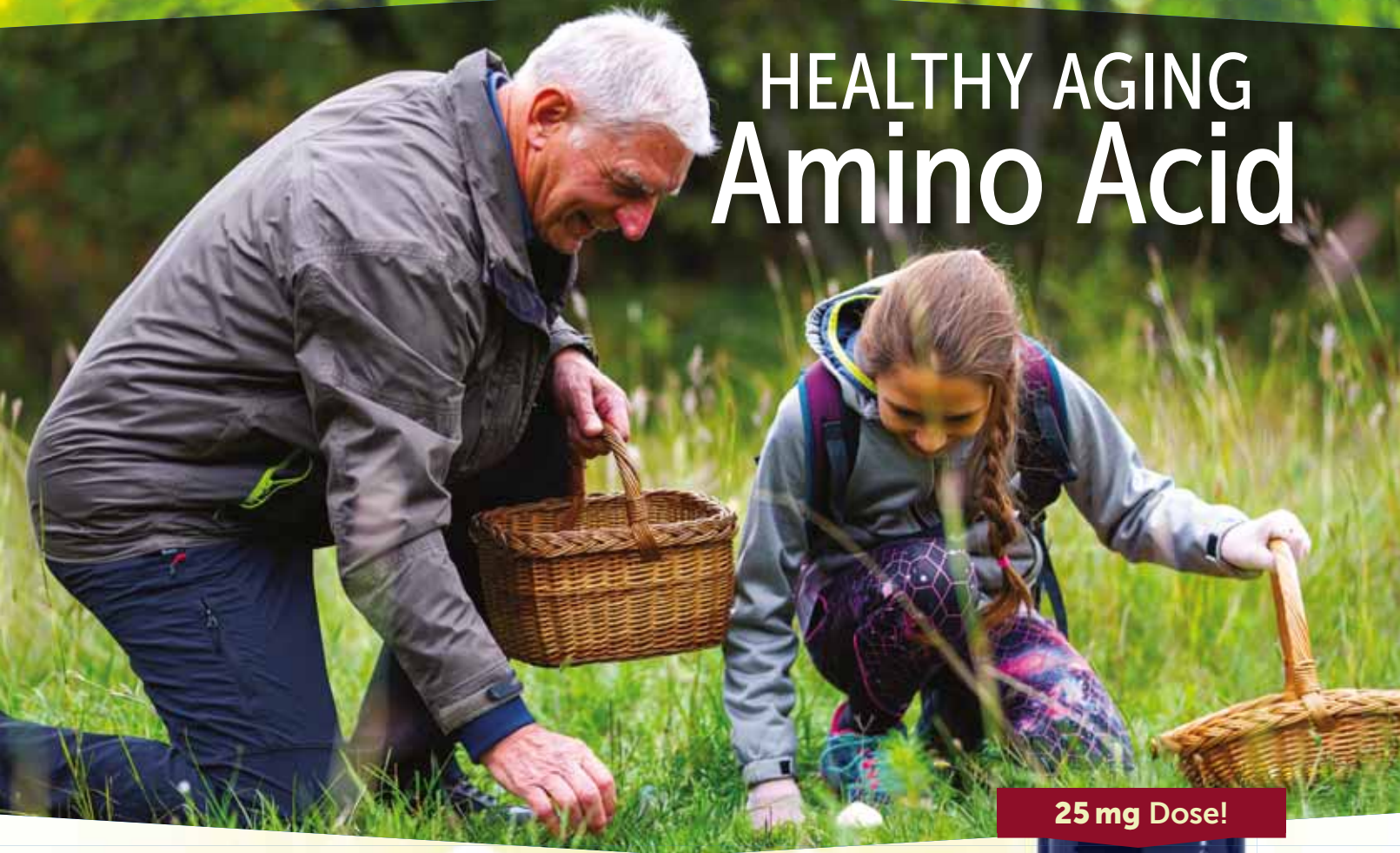
**Quercetin** has been studied for its potential effects on atherosclerosis formation and progression. By boosting cellular defenses and blocking damaging processes that contribute to atherosclerosis in cell and animal models, it shows promise for lowering the burden of atherosclerosis in humans. ●

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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\* European Journal of Nutrition. 2011;50(5):387-389.

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| Vitamin K2 (MK7) | 100 mcg            |
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**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.

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# Mushrooms

BY LAURIE MATHENA

Edible mushrooms have been utilized in Traditional Chinese Medicine for thousands of years. Today, species such as lion's mane, shiitake, and reishi are recognized as *functional foods* for their ability to support overall health and wellbeing.<sup>1</sup>

Reishi (*Ganoderma lucidum*), long referred to as the “immortality mushroom,”<sup>2</sup> is just one of approximately 700 medicinal mushroom species that have been studied to date. Collectively, these fungi have been associated with 126 medicinal functions, including antitumor, immunomodulating, antioxidant, antiviral, antibacterial, antiparasitic, antifungal, hepatoprotective, and antidiabetic effects.<sup>1,3</sup>

Mushrooms are low in fat and calories, yet provide meaningful amounts of protein, fiber, and micronutrients.<sup>4</sup>

The widely cultivated species *Agaricus bisporus* (which includes white button, cremini, and portobello mushrooms) contains approximately **3 grams** of protein per **100 grams**.<sup>6</sup>

Cognitive health may also be influenced by mushroom intake. A systematic review evaluated 34 human studies and found that epidemiological evidence generally supported a significant benefit of dietary patterns including mushrooms on cognition and mood.<sup>6</sup>

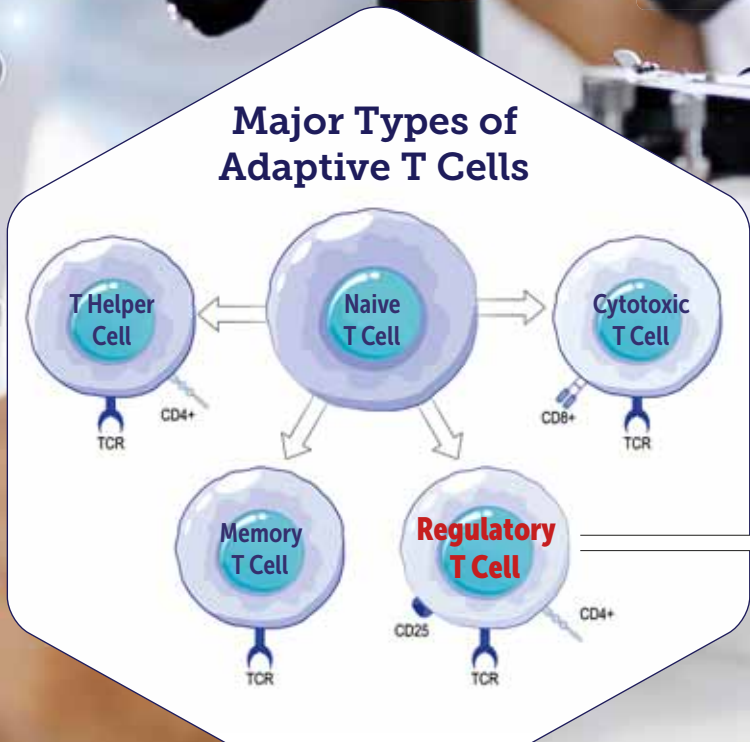
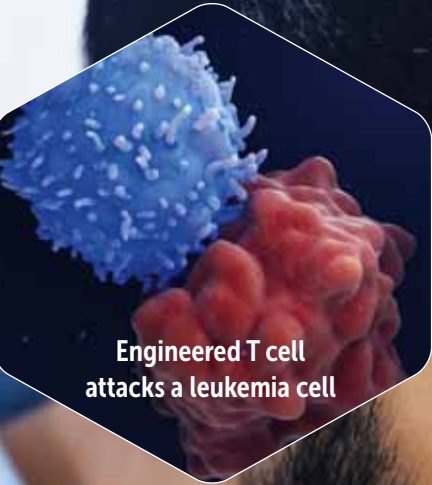
Mushrooms may also support immune function. In a randomized dietary intervention, 52 healthy young adults who consumed either **5 or 10 grams** per day of dried shiitake mushrooms for four weeks demonstrated improved immune markers.<sup>7</sup>

Mushrooms can be incorporated into a variety of meals—from eggs to stir-fries—and work well as a meat substitute in dishes such as chili or meatballs. Even simple preparation methods, such as sautéing with olive oil, garlic, and a pinch of salt, can add rich flavor and nutritional value to any meal.

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# IMMUNE Regulatory T Cells: A Nobel-Winning Revolution in Medicine



BY RAYNA CARRUTHERS

Last October, the Nobel Assembly at the Karolinska Institute awarded the 2025 **Nobel Prize in Physiology or Medicine** to Mary E. Brunkow, Fred Ramsdell, and Shimon Sakaguchi.

Their collective work has deciphered a fundamental aspect of our **immune system**:

The critical function of  
**regulatory T cells** (Tregs)

This discovery is reshaping our approach to **autoimmune** diseases, cancer, and beyond.

→ formed following  
activation of helper  
or cytotoxic T cells

## Premise

Our immune system relies on **T cells** to act as soldiers, identifying and eliminating threats like viruses.<sup>1</sup>

But every powerful army needs a strict command structure to prevent friendly fire. This control center largely resides in the **thymus**, a gland in the chest where T cells are rigorously programmed into functional cells after being produced by bone marrow stem cells.<sup>2</sup>

One challenge is that our **thymus gland** shrivels as we age, with functional thymic epithelial tissue being progressively replaced by adipose tissue, so that by age 55 very little **structural thymic** tissue remains.<sup>3</sup>

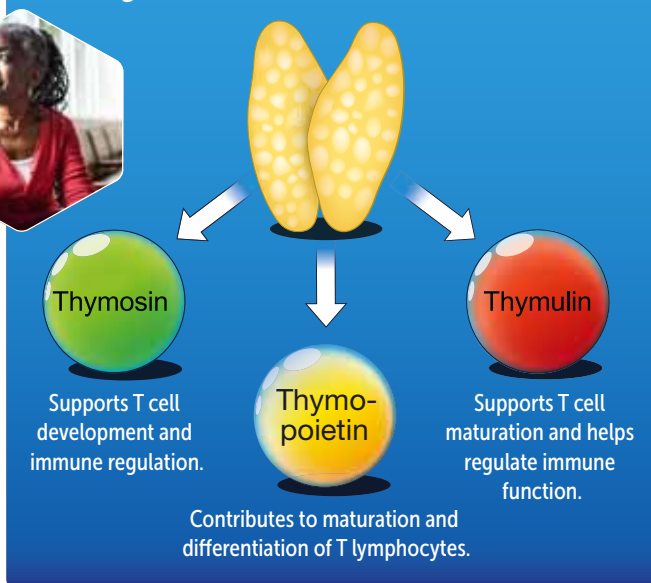
Nevertheless, even in individuals over 55 years of age, some **functional thymic tissue** remains capable of producing a limited number of new T cells. This residual activity is important for maintaining immune diversity and resilience, but it is far less robust than in youth.<sup>3</sup>

## Function of Regulatory T cells

Nobel Prize winners Shimon Sakaguchi, Mary E. Brunkow, and Fred Ramsdell discovered that a special class of T cells graduates from thymic training with a unique mission.<sup>4,5</sup>

Known as **Regulatory T cells** (Tregs), they are the immune system's dedicated "peacekeepers" helping protect against immune cell attack on healthy tissues.<sup>6,7</sup>

### Thymus and its Hormones



In a landmark experiment, Sakaguchi showed that mice deprived of their Tregs developed severe autoimmune disease, while reconstituting these **cells** prevented the autoimmune disease from developing. The conclusion was clear:<sup>7</sup>

**Tregs calm other T cells that mistakenly attack healthy tissue, preventing a destructive civil war within the body.**

The story deepened with the work of Mary E. Brunkow and Fred Ramsdell, who identified the gene responsible for the *scurfy* mutation in mice.<sup>8</sup> This genetic defect cripples the development of Tregs, causing the immune system to spiral into a fatal "mutiny."<sup>9</sup> Their work provided the genetic blueprint for how this peacekeeping force is built, transforming Tregs from an observation into a defined biological pathway.

## Clinical Case Histories

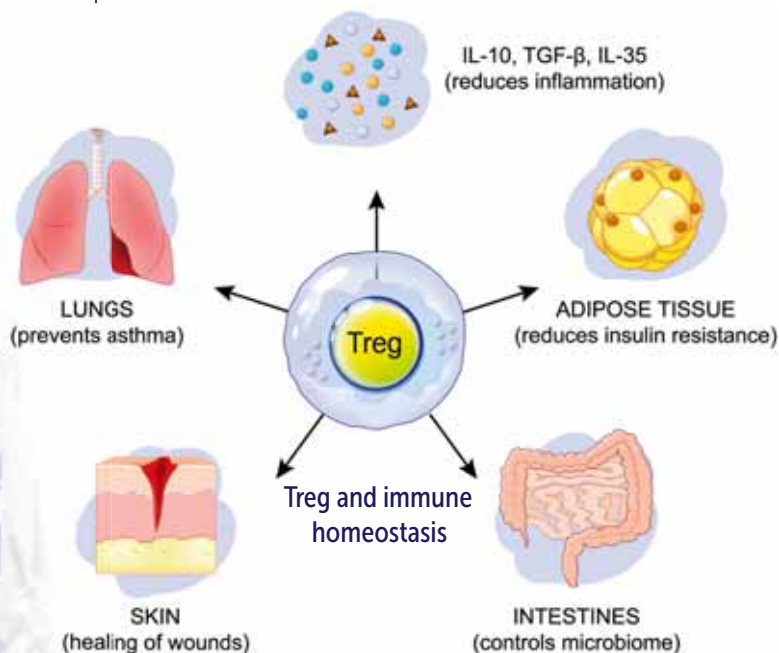
For the millions living with conditions like multiple sclerosis, rheumatoid arthritis, or type 1 diabetes, this Nobel-winning science is not abstract; it is the foundation of a new therapeutic paradigm.

The goal is no longer just to broadly suppress immunity, but to precisely enhance its natural peacekeeping force. This approach is called personalized precision immunotherapy.

Personalized precision immunotherapy is a pioneering treatment developed by Dr. Dipnarine Maharaj at The Maharaj Institute in Boynton Beach, Florida.

Dr. Maharaj, a stem cell transplant immunologist, first used this Treg modulating treatment in a patient named Gale, a former law enforcement officer battling **scleroderma**, **Raynaud's**, and **Madelung's disease**. After years of decline, she began treatment with Dr. Maharaj. She was told that she would need a feeding tube because of the severe contraction of her esophagus caused by the scar tissue formed by this **autoimmune** disease. Her other option was a side-effect-prone bone marrow transplant, risking often deadly *graft versus host* disease.

By measuring her T cells, including her Tregs, which were severely reduced, and correcting these with non-toxic cytokines which the body normally produces, Gale achieved a complete remission which persists today. "It's been something that my husband and I could not even have imagined," Gale says. "I can sleep lying down



again, and I can enjoy my favorite foods. It gave me my life back.”

Other developmental approaches to utilizing Tregs include cellular therapies, where a patient’s own stored Tregs or a donor’s, are isolated, multiplied into billions in the lab, and reinfused as a living, targeted treatment to restore immune balance.

Utilizing personalized precision immunotherapy since 2008, many patients with autoimmune diseases have been helped at the Maharaj Institute.

One of those patients, Linda B., recalls being told that nothing could stop her Parkinson’s-like illness from progressing. “Instead, I chose to try adult stem cell treatment in Florida. IT WORKED,” she says. “Exactly two weeks into treatment I woke up feeling great. I felt like myself.”

She describes her recovery in simple, powerful terms: “I could do little things that we all take for granted—like rummaging in my purse with my left hand, drying my back with both hands, walking normally again. I don’t want anyone out there to think there is not a treatment. There is.”

Another patient, Linda S., was diagnosed with Corticobasal Degeneration (CBD) — a rare and fatal neurodegenerative disease. Her husband, Jerry, remembers the devastating moment of diagnosis: “We were basically told that there was no hope.”

After traveling from Las Vegas to meet Dr. Maharaj, Linda S. began a novel immune-focused treatment that slowed her disease progression and restored significant

cognitive and motor function. “You can look at photos from a few years back and see how the life had been drained out of her,” Jerry says. “The treatment Dr. Maharaj administered brought her back to life. I see her motor skills and her ability to think and communicate clearly improving every day.”

That transformation is echoed by Tony, a retired United States Coast Guard officer, who accompanied his wife for treatment at the Maharaj Institute.

“The entire medical staff was the utmost professional, and their ongoing care was nothing short of outstanding,” he says. His wife, who was near the point of needing a permanent feeding tube, showed “significant positive changes” within three months. “*Using your own immune system to assist in dealing with illness and disease certainly is the way to go,*” he adds. “I predict that stem cell mobilization is the treatment of the future.”

Others, like Aniko and Paul, highlight how the same principles can address chronic inflammatory and autoimmune conditions. Aniko, suffering from psoriasis, and Paul, living with Crohn’s disease, both sought treatment at the Maharaj Institute after conventional therapies had failed to bring lasting relief.

Through the Institute’s personalized precision immune therapy, the goal was to restore immune balance and re-induce self-tolerance, targeting the root of their autoimmune activity rather than merely masking symptoms. Their cases illustrate the broader potential of immune restoration to improve quality of life across a wide spectrum of chronic immune-related diseases.

## Advancing the Science of Immunology

This **2025 Nobel Prize** helps validate a path that the Maharaj Institute of Immune Regenerative Medicine has been pioneering for over a decade. Since 2008, Dr. Dipnarine Maharaj has been at the forefront of personalized precision immunotherapy, leveraging advanced analysis of patients' peripheral blood immune systems, including their Tregs, to guide treatment for autoimmune diseases.

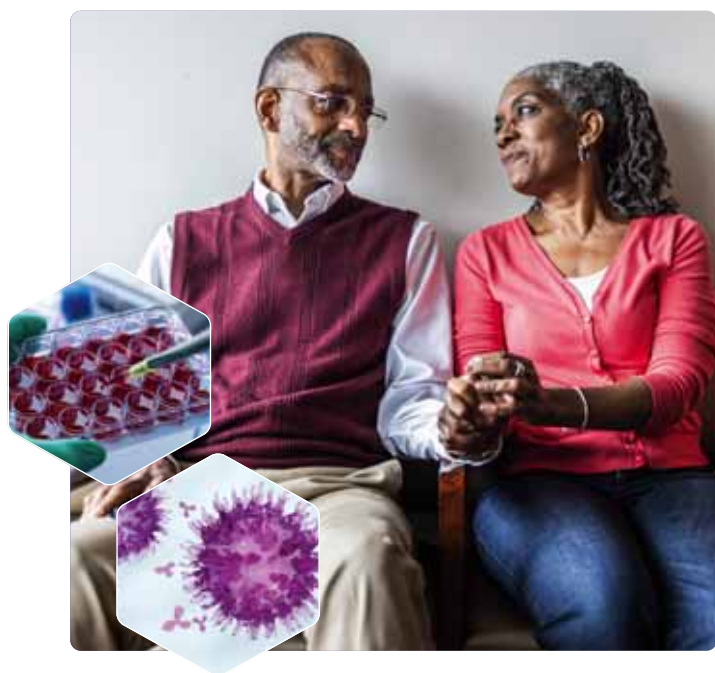
The laureates' work provides the fundamental blueprint, and the Maharaj Institute is building upon it. This prestigious recognition emboldens Dr. Maharaj's commitment to advancing the understanding of **immune regulation** and developing the innovative, life-changing treatments of tomorrow.

The Nobel Prize does not just honor past discovery—it accelerates the future of medicine, and the Maharaj Institute is proud to be part of that journey. ■

### Important notes:

In preparing this update, **Life Extension** staff interviewed all the patients quoted in this article to corroborate their favorable and durable responses to treatments.

Because Dr. Maharaj's treatments are not yet recognized by the medical mainstream, private insurance and Medicare do not cover them. This results in high out-of-pocket expenses for those who choose to participate.



To engage in these treatments at the Maharaj Institute, travel to South Florida is required several times for advanced blood testing, personalized treatments, and follow-up.

**Dr. Maharaj** is a member of the *Life Extension Magazine*® Scientific Advisory Board.

He is the founder and chief medical officer of South Florida Bone Marrow / Stem Cell Transplant Institute and its affiliate Stem Cell Cryobank—where individuals can store their stem cells for future use. He also maintains the Advanced Stem Cell Education Program for individuals wishing to learn more about the health benefits of stem cells.

If you or a loved one would like to measure your immune system from a comprehensive blood test and see how your Tregs are affecting your immune system, please contact Dr. Maharaj at 561-752-5522 or the Maharaj Institute in Boynton Beach at <https://maharajinstitute.com/meet-dr-maharaj/>

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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#### NERVE & COMFORT SUPPORT

- 02202 ComfortMAX™
- 02303 Discomfort Relief
- 02544 Migra-Health™

#### PERSONAL CARE

- 02322 Hair, Skin & Nails Collagen Plus Formula
- 01278 Life Extension® Toothpaste
- 00408 Venotone

#### PET CARE

- 01932 Cat Mix
- 01931 Dog Mix

#### PROBIOTICS

- 01622 Bifido GI 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
- 01825 FLORASSIST® Probiotic Balance
- 02505 FLORASSIST® Probiotic Women's Health
- 02539 FLORASSIST® Probiotic Youthful Gut

#### 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

- 02234 Fast-Acting Liquid Melatonin
- 01669 Glycine
- 01722 L-Tryptophan
- 01668 Melatonin • 300 mcg, 100 vegetarian capsules
- 01083 Melatonin • 500 mcg, 200 vegetarian capsules
- 00329 Melatonin • 1 mg, 60 capsules
- 00330 Melatonin • 3 mg, 60 vegetarian capsules
- 00331 Melatonin • 10 mg, 60 vegetarian capsules
- 00332 Melatonin • 3 mg, 60 vegetarian lozenges
- 02201 Melatonin IR/XR
- 01787 Melatonin 6 Hour Timed Release  
300 mcg, 100 vegetarian tablets
- 01788 Melatonin 6 Hour Timed Release  
750 mcg, 60 vegetarian tablets
- 01786 Melatonin 6 Hour Timed Release • 3 mg,  
60 vegetarian tabs
- 01445 Quiet Sleep Melatonin • 5 mg, 60 veg capsules
- 02502 Rest & Renew
- 02526 Serene Sleep

#### 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®
- 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 vegetarian lozenges
- 01537 Vitamin B12 Methylcobalamin  
5 mg, 60 vegetarian lozenges
- 02228 Vitamin C and Bio-Quercetin®  
60 vegetarian tablets
- 02227 Vitamin C and Bio-Quercetin®  
250 vegetarian 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 vegetarian capsules
- 02207 AMPK Metabolic Activator
- 02478 DHEA Complete
- 02506C Mediterranean Weight Management
- 01432 Optimized Saffron
- 02511 Thermo Weight Control
- 02509 Waistline Control™

#### WOMEN'S HEALTH

- 01942 Breast Health Formula
- 02537 Daily PMS Relief
- 02534 Estrogen Balance Elite
- 01894 Estrogen for Women
- 02541 Hair Growth for Women
- 02204 Menopause Relief
- 02319 Prenatal Advantage
- 02536 Sexual Health for Her
- 01649 Soy Isoflavones
- 02513 Women's Bladder Support

Liposomal-Hydrogel™

# C VITAMIN



"I feel better about my immune system with it."

**Mary**  
VERIFIED BUYER

GLUTEN  
FREE

NON  
GMO  
LE CERTIFIED



Item #02501 | 60 vegetarian tablets  
1 bottle \$25.50 | 4 bottles \$23 each

For full product description and to order  
**Vitamin C 24-Hour Liposomal Hydrogel™ Formula**,  
call 1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)

Buffered **ascorbate** encased in two plant extracts (liposomes plus hydrogel fenugreek) increases blood (plasma) exposure up to **seven times** more compared to an equivalent dose of vitamin C as calcium ascorbate.<sup>1</sup>

It also maintains vitamin C levels throughout the day.<sup>2</sup>

Just one vegetarian tablet daily provides **around-the-clock** vitamin C support.

**References** 1. Akay Internal Study. Liposomal vitamin C (calcium ascorbate) pharmacokinetics. Data on file. 2021.

2. Akay Internal Study. Liposomal hydrogel vitamin C pharmacokinetics. Data on file. 2021.

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.

# B

Brainy, Bubbly, Bold, Brave,  
Brilliant, Boundless.



**Item #01945**

60 vegetarian capsules

1 bottle \$9

4 bottles \$8 each



## B your best...with our very best vitamin B.

Supercharge your mental and physical superpowers with BioActive Complete B-Complex, a full-spectrum and highly absorbable vitamin B formula.

For full product description and to order  
**BioActive Complete B-Complex**, call  
1-800-544-4440 or visit [www.LifeExtension.com](http://www.LifeExtension.com)

**Caution:** Temporary flushing, itching, rash, or gastric disturbances may occur.

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## IN THIS EDITION OF *LIFE EXTENSION MAGAZINE*®



### 7 **LONGEVITY RESEARCH TSUNAMI**

A wave of **converging technologies** could *result* in biological **age reversal** in our lifetime.



### 24 **SYSTEMIC EFFECTS OF FISH OIL**

Research shows that **fish oils** *boost* **brain function**, *improve* both **cognitive** and **metabolic health** and *reduce* **inflammation**.



### 36 **STAY MENTALLY SHARP**

In separate **clinical trials**, three **plant** compounds improved measures of **memory**, **learning performance**, and **multi-tasking** ability.



### 46 **BEST B12 FOR THE JOB**

Two **bioactive** forms of **B12** *promote* different aspects of **brain** and **nerve** functions.



### 57 **QUERCETIN AND ATHEROSCLEROSIS**

Preclinical research shows that the flavonoid **quercetin** may help *mitigate* development and progression of **atherosclerosis**.



### 68 **IMMUNE REGULATORY T CELLS**

The **Nobel Prize** for work on **regulatory T cells**, which *defend* healthy tissues from **immune cell attack**, is transforming into clinical practice to combat various diseases.

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