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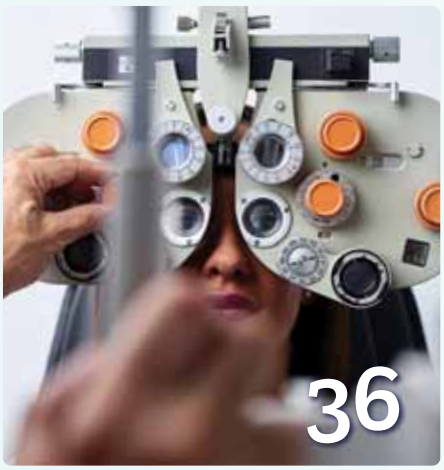

DEPARTMENTS

LIFE EXTENSION®

The Science of a Healthier Life®

LifeExtension.com September 2021

Volume 27 • Number Nine
Publisher • LE Publications, Inc.

LIFE EXTENSION (ISSN 1524-198X) Vol. 27, No. 9 ©2021 is published monthly except bi-monthly in April by LE Publications, Inc. at 3600 West Commercial Blvd., Fort Lauderdale, FL 33309-3338. Published 13 times a year. Subscription rate: $40 per year in the United States. US $47 in Canada. US $60 in other countries. Mail subscriptions or address changes to: LE Publications, Inc., P.O. Box 407198, Fort Lauderdale, FL 33340-7198, USA. Or phone us toll-free at: 1-800-841-5433. Canada Subscriptions: Publications mail agreement number 40028967. Return undeliverable Canadian addresses to PO Box 503, RPO West Beaver Creek, Richmond Hill, ON L4B4R6. You will be sent your first issue within six weeks after LE Publications, Inc. receives your subscription fee. Periodicals Postage paid at Fort Lauderdale, FL and at additional mailing offices. POSTMASTER: Send address changes to Life Extension, P.O. Box 407198, Ft. Lauderdale, Florida 33340-7198, USA. Printed in USA.

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

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

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

L. Ray Matthews, MD, FACS, is a professor of surgery and director of Surgical Critical Care at Morehouse School of Medicine in Atlanta, GA, and a trauma and critical care surgeon at Grady Memorial Hospital. He has published widely and is known as one of the top vitamin D experts. Dr. Matthews has spoken before the U.S. Food and Drug Administration several times, presenting a recent update about clinical research on vitamin D.

Ralph W. Moss, PhD, is the author of books such as Antioxidants Against Cancer, Cancer Therapy, Questioning Chemotherapy, and The Cancer Industry, as well as the award-winning PBS documentary The Cancer War. Dr. Moss has independently evaluated the claims of various cancer treatments and currently directs The Moss Reports, an updated library of detailed reports on more than 200 varieties of cancer diagnoses.

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

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Xiaoxi Wei, PhD, is a chemist, expert in supramolecular assembly and development of synthetic transmembrane nanopores with distinguished selectivity via biomimetic nanoscience. She has expertise in ion channel function and characterization. She founded X-Therma Inc., a company developing a radical new highway towards non-toxic, hyper-effective antifreeze agents to fight unwanted ice formation in regenerative medicine and reduce mechanical icing.

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LETHAL DELAYS

WILLIAM FALOON

When a new **lifesaving** therapy is announced, few people calculate how many **died** in the waiting room.

Delays in introducing better drugs extend beyond the **FDA's** bureaucratic quagmire.

Pharmaceutical companies spend years negotiating their financial "cut" of a medical discovery and patent ownership.

More years slip by as the owners seek funding for **clinical trials** and negotiate future marketing rights.

As these delays accumulate, a staggering number of Americans needlessly **suffer** and **die**.

Even worse are promising compounds that don't garner financial backing. These therapies fall off the radar screen and are sometimes lost **forever**.

A recent study on the mortality **risk-reducing** effects of **metformin** enabled our scientific team to conduct a startling calculation.[1]

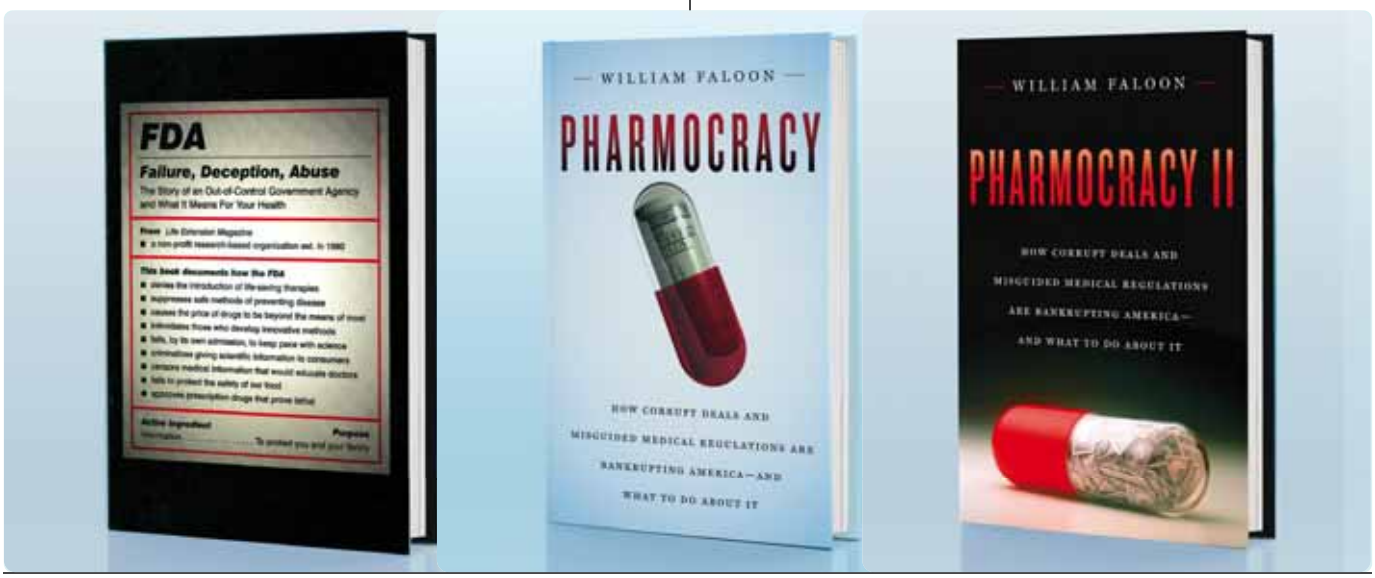
More than **eight million** Americans may have died because of the **37-year delay** in this one drug becoming available.

Although there is significant uncertainty with this estimate, it's more than all Americans killed in all wars since the inception of this country!

I've written books exposing **flaws** in today's drug-development process that was long ago rendered **obsolete**.

This article summarizes the loss of life that theoretically may have occurred because **type II diabetics** were denied access to **metformin** and how these tragedies can be prevented.

I also discuss **cancer treatments** using "off-label" drugs that are demonstrating remarkable **survival improvements**.



In **1995** I was given an ultimatum by the **FDA**.

Either I stop educating ***Life Extension***® readers about lower cost drugs from other countries or I would face criminal charges and years in prison.

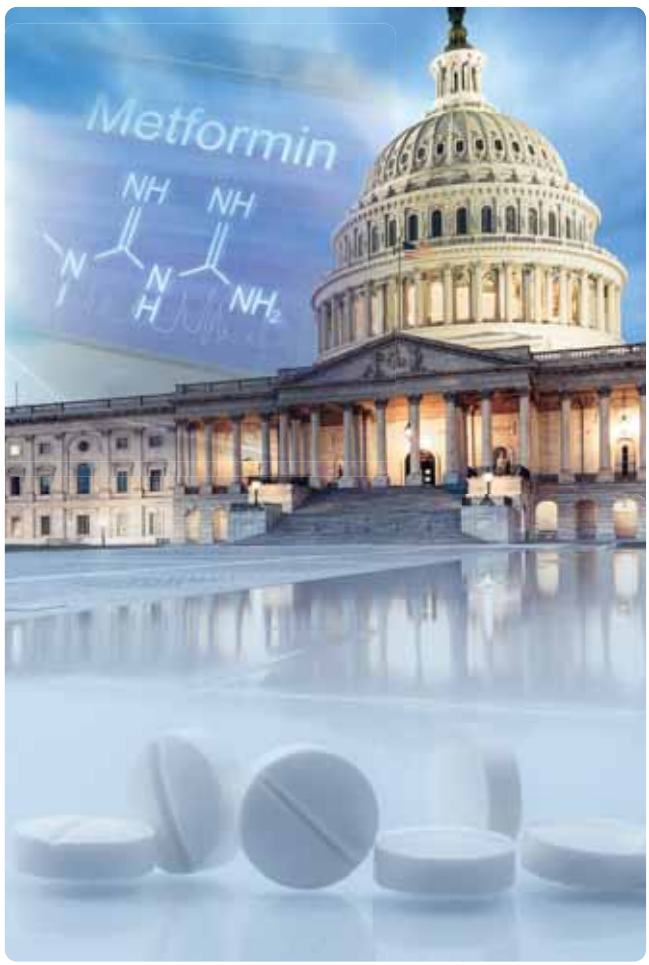
I respectfully declined to accept the FDA's **censorship** dictate that would deny ***Life Extension***® readers access to lifesaving medications.

Having just defeated the **FDA** in a **nine-year** legal battle, I was confident the public would continue to support our efforts to accelerate the availability of more advanced medications.

To put the situation into context, the **Internet** was in its infancy in the mid-1990s. Americans could not readily find pharmacies in other countries to send them medications.

By censoring ***Life Extension***® magazine, as the **FDA** attempted, few Americans would know about better ways to treat their disease.

This included drugs like **metformin** for **type II diabetics** and **ribavirin** as an adjunctive **hepatitis C** medication.



Censored Drugs Now Widely Prescribed

Back in the 1980s-1990s, **Life Extension®** fought a multi-decade battle with the FDA to force the approval of an **antiviral** drug called **ribavirin**.

When **ribavirin** was combined with interferon-alpha, treatment outcomes in **hepatitis C** patients markedly improved. Today's hepatitis C drugs (like Sovaldi®) are curing over **95%** of patients.

Yet, when drugs like Sovaldi® were approved in **2013-2014**, most still relied on co-administration of **ribavirin**.

More recent hepatitis C protocols are combining Sovaldi® with newer drugs (in lieu of ribavirin) to better eradicate hepatitis C.

We have no financial interest in **ribavirin**. We identified its efficacy in the early **1980s** and relayed this information to our supporters.

Metformin is often the first drug prescribed to **type II diabetics**, assuming reasonable cardiac and renal function. Many non-diabetics now take **metformin** for its potential anti-aging properties. With today's Internet, ordering lower-cost medications from Canada and other countries has become routine and may soon be formally legalized.

Before the **Internet**, the **FDA** bowed to pharmaceutical **lobbyists** and attacked those seeking to educate Americans about better drugs at lower prices.

The magnitude of this tragedy cannot be overstated. Our efforts to accelerate approval of **ribavirin** alone may have saved thousands of American lives.

Why Metformin Was Delayed So Long

Metformin was first discovered in **1922** but fell by the wayside as doctors saw more immediate results prescribing **insulin** or **insulin-boosting drugs** (in the sulfonylurea class).

Sulfonylurea drugs stimulate insulin release from the pancreas. This results in a temporary drop in blood sugar (glucose).

Insulin injections immediately reduce glucose, which is needed in advanced stages of type II diabetes, and by type I diabetics who make little or no **insulin** themselves.

The problem with this approach is it inadequately addresses the underlying causes of **type II diabetes** which include **beta-cell dysfunction** and **insulin resistance**.

These two PowerPoint slides are from live presentations where I advocate for faster access to lifesaving medications:

Catastrophic Loss of Life

A **2019** study tabulated reductions in **cardiovascular mortality** in type II diabetics using **metformin.**[1]

Life Extension® calculated how many **cardiovascular deaths** may have occurred in response to metformin's **37-year delay.**

Almost **4 million** American diabetics may have died because of the **delay** in this one drug (metformin) becoming available.

This exceeds the death toll of all wars America has ever fought.

1. Association of Treatment With Metformin vs Sulfonylurea With Major Adverse Cardiovascular Events Among Patients With Diabetes and Reduced Kidney Function. ***JAMA.*** **2019 September 19:1-11.**

Even More Lives Lost!

Reductions in **cardiovascular deaths** from *JAMA* (2019) study[1] were added to **overall mortality** data from CDC, National Institutes of Health, American Diabetes Association and NHANES III.

The following **total excess deaths** were estimated:

As many as **8.6 million** American diabetics may have prematurely died from metformin's 37-year delay.[2]

1) Lethal Delays. ***Life Extension®*** Magazine. September 2021
2) Association of Treatment With Metformin vs Sulfonylurea With Major Adverse Cardiovascular Events Among Patients With Diabetes and Reduced Kidney Function. ***JAMA.*** **2019 September 19:1-11.**

Metformin functions via several mechanisms to combat high **blood sugar** including activating the **AMPK** enzyme, favorably altering the gut **microbiota**, and improving **insulin sensitivity** in the liver and peripheral muscle cells.[2,3]

A chemical cousin of metformin called **phenformin** inflicted a lethal condition called **lactic acidosis** in some people. This caused doctors to fear drugs in this class, especially with the quick-fix effects of sulfonylurea drugs or insulin injections.

What puzzled us back in the **1990s**, however, was that **metformin** had been approved in **England** in **1958**, **Canada** in **1972**, and much of the world shortly thereafter.

Lactic acidosis was not occurring unless people had significant preexisting kidney, liver, heart, and/or lung failure.

Catastrophic Loss of Life

Metformin became widely available to Americans in late **1995** at relatively high prices (sold under the tradename **Glucophage®**).

In **2019**, a study was published that tabulated the reductions in **cardiovascular mortality** in type II diabetics who use **metformin.**[4]

We at **Life Extension®** took these data along with data on diabetes prevalence from the **CDC** and **NHANES III**, death rates from the **National Institutes of Health** and the **American Diabetes Association**, as well as studies assessing the impact of metformin on mortality.

We performed a series of calculations to estimate how many premature deaths may have occurred from **cardiovascular** causes as a result of metformin's **37-year delay**.

The calculations include a range of possible values, based on the estimate that between 1958 and 1995, there may have been between 1.35 to 28.8 million people with diabetes who died in the United States, of whom 880,000 to 18.7 million died due to diabetes-related **cardiovascular disease**.

Obviously, there is a large degree of uncertainty with such a series of calculations and estimates from the published literature, but assuming that **100%** of people with diabetes had taken **metformin** beginning in **1958**, we can crudely estimate that 405,200 to 8.6 million people might have been spared **premature death** had **metformin** been approved in **1958** instead of **1995**.

More specifically, we estimate that 175,600 to 3.7 million people might have been spared death from diabetes-related **cardiovascular disease**.

This is only one example of a **broken system** that continues to deny Americans rapid access to lifesaving therapies.

One can debate the absolute numbers of **total deaths** that occurred because of metformin's delay. But even at the lower end of our calculations, a staggering number of American **type II diabetics** perished prematurely.

Metformin also Reduces Cancer Risk

When attacking the **delays** in approval of lifesaving medications as I've done for the past **41 years**, I use published, peer-reviewed references that provide objective information for accuracy.

As it relates to the delay in approving metformin, however, the **death toll** (up to **8.6 million** Americans) extends beyond classic diabetic complications.

That's because metformin also reduces **cancer risk** in type II diabetics.

A study conducted at **MD Anderson** found that type II diabetics prescribed metformin had a **62%** reduced risk of **pancreatic cancer**.[5] This malignancy is more prevalent in diabetics and kills over **48,000** Americans each year.[6]

Based upon published data, and if all the cancer deaths that metformin could have prevented are assumed, the **total mortality** resulting over this **37-year delay** period means up to **8.6 million** American lives might have been spared if metformin was approved sooner.

These needless deaths are intolerable. The solution is introducing aggressive **free market** reforms to the obsolete drug development process that plagues us today.

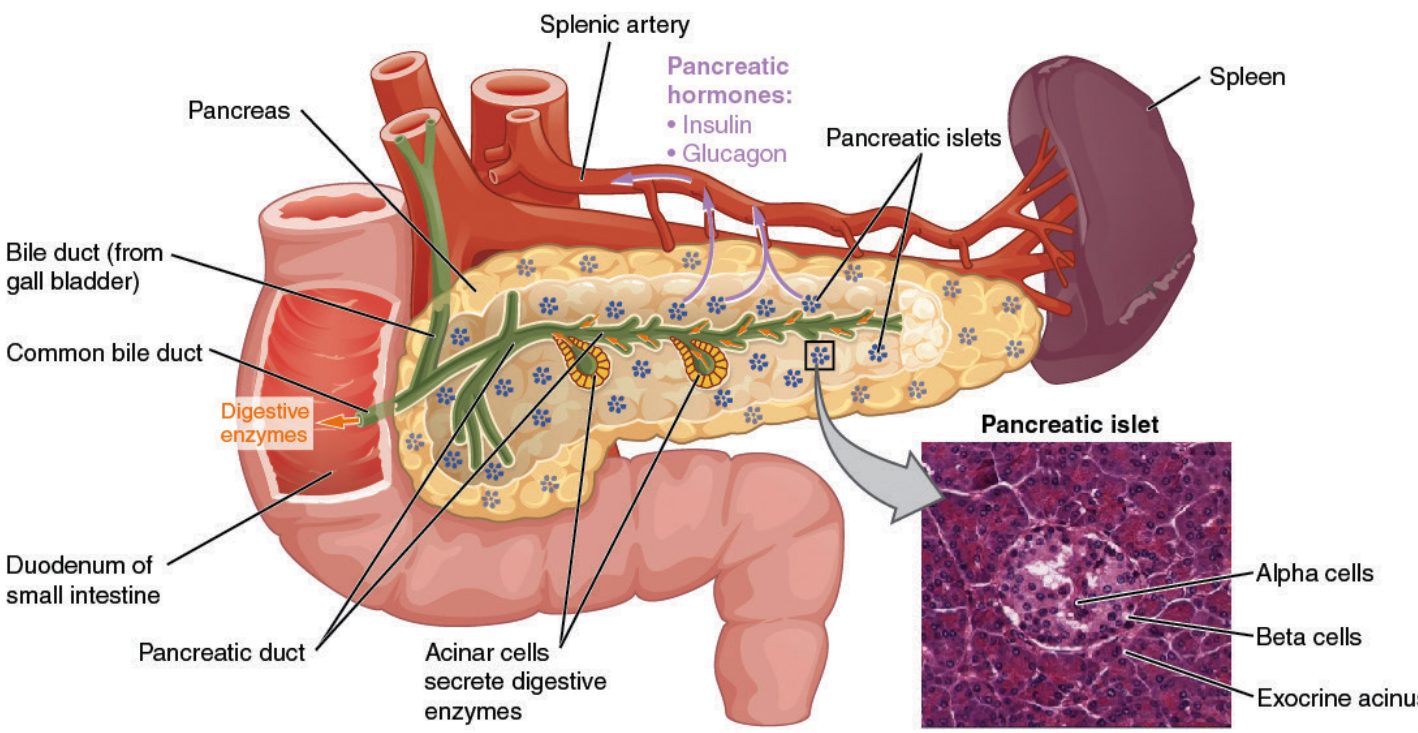
Consequences of Denial

Politicians are debating a lot of topics right now, but the most important problem facing Americans is not being discussed.

Once you or a loved one is diagnosed with a serious disease, all other issues become irrelevant. Your overriding concern is whether there is a **cure** available.

That's why it's imperative that **free market** reforms are enacted that place the **FDA** in an **advisory** role that allows **rapid** medical progress unimpeded by central government bureaucrats.

Back in **2012**, the former **FDA Commissioner** wrote a scathing editorial *against* the agency (FDA) from which he had resigned.[7]



Several doctors responded with complimentary letters and emphasized even more **deregulation** of **FDA** control is needed to bring about cures for today's killer diseases.[22]

Some of these letters exposed how dysfunction and unpredictability at the FDA are precluding vital *early-stage* scientific research.

Despite these exposés from **FDA insiders**, most Americans remain in a state of **denial** about the lethal consequences of today's antiquated **regulatory structure**.

This denial turns into **harsh reality** when one is diagnosed with an illness for which there is no current **cure**.

Pleas of Former FDA Commissioner Ignored

An increasing number of respected individuals concur that **delaying** lifesaving therapies can no longer be tolerated. This includes former FDA Commissioner Andrew von Eschenbach.

Dr. von Eschenbach was a director of the National Cancer Institute and later served as FDA Commissioner from 2005 to 2009.

Back in **2012**, he authored an editorial published in *The Wall Street Journal* that was critical of the FDA's ability to evaluate and approve new lifesaving therapies.[7]

December 2012

The editorial began with Dr. von Eschenbach stating:

"We stand on the cusp of a revolution in health care. Advances in molecular medicine will allow us to develop powerful new treatments that can cure or even prevent diseases like Alzheimer's and cancer."[7]

"What's missing," according to Dr. von Eschenbach, "*is a modernized Food and Drug Administration that can rapidly and efficiently bring new discoveries to patients*."[7]

Dr. von Eschenbach cited then-current FDA Commissioner Margaret Hamburg's concession before Congress that, "*The FDA is relying on 20th century regulatory science to evaluate 21st century medical products.*"[7]

The most compelling arguments Dr. von Eschenbach made for meaningful reform were:[7]

"The FDA should approve drugs based on safety and leave efficacy testing for post-market studies. Congress can ensure that the FDA serves as a bridge—not a barrier—to cutting-edge technologies."

Said differently, once a potentially **effective therapy** has been cleared for **safety**, it should be made immediately available to people who may otherwise suffer and die.

While the **FDA** has expedited some procedures like "fast-tracking" certain drugs to terminal patients, the bureaucratic barriers continue to result in horrific delays.

Pancreatic cancer patients, for example, shouldn't have to wait for years for FDA-required efficacy studies. They need **rapid access** to new therapies that offer some hope of saving their lives.

What's scary about **Dr. von Eschenbach's** criticisms are that they were made back in **2012**. Yet relatively little has been done to rectify the most lethal threat to the lives of aging Americans, i.e. long delays in introducing lifesaving therapies.

Our 41-Year Battle to Reform Drug Approval

We at **Life Extension** continue our relentless campaign to alert policy makers and the public about the urgent need to accelerate the introduction of new therapies.

This goes beyond relegating the **FDA** to an advisory role, away from its current arbitrary power.

The entire drug development process, from start to finish, requires radical change.

Medical innovations need rapid testing on patients who are fully apprised of risks and potential benefits, without costly bureaucratic interference.

Unlike other issues, failure to effect meaningful **reforms** will continue the needless carnage of human suffering and death.

This is a ***priority*** matter that politicians should be debating today!

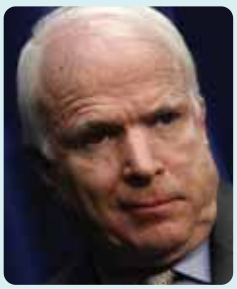
The box on page 15 reveals marked survival **improvements** in **brain tumor** patients treated with combinations of "off-label" drugs that include **metformin**.

For 41 consecutive years, we at **Life Extension®** advocated for multipronged treatments for lethal diseases. The scientific literature continues to validate this approach across a spectrum of degenerative disorders.

For longer life,

William Faloon, Co-Founder
Life Extension Buyers Club

Why Didn't John McCain Act Up?



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John McCain died from a **glioblastoma** brain tumor in **August 2018**.

Nine years prior, **Ted Kennedy** also died from **glioblastoma**.

Both senators cordially worked together for decades on Capitol Hill.

John McCain attended Ted Kennedy's funeral and gave a eulogy.

My question is how could **John McCain** witness **Ted Kennedy** in a "box" without **Senator McCain** using his enormous legislative power to ensure the same did not happen to him?

I know my thinking process differs from most others', but when anyone I know develops a serious medical disorder, I instinctively spend hours searching the medical literature seeking a better way to treat it.

In some cases, I help launch and fund clinical trials to see if a potential treatment yields real-world results.

Effective Brain Cancer Treatments

After John McCain's death, ***Scientific American*** published an insightful essay as to why glioblastoma is such a difficult malignancy to treat.[8]

Omitted from the ***Scientific American*** report, however, were a plethora of potentially effective therapies that have encountered outlandish delays.

These include a roughly **10-year delay** in advancing **genetically modified poliovirus** that has demonstrated impressive responses in some glioblastoma patients.[9] We described this therapy in the **September 2015** issue of ***Life Extension®*** magazine.[10]

Even more omissions relate to adjuvant therapies about which ***Life Extension®*** previously published. Some of these include:

Valganciclovir: Treatment of **glioblastoma** patients with **valganciclovir** produced an unheard-of median overall survival of **56.4** months (4.7 years).[11]

Note: Ted Kennedy lived only **15** months and **John McCain** about **14** months after their

glioblastoma diagnosis. I don't know if they tried **valganciclovir**, but there were good data to support it. The clinical trial showed glioblastoma patients treated with **valganciclovir** lived almost **four times *longer*** than Senators Kennedy and McCain.

Not only has ***valganciclovir*** been shown to extend survival in ***glioblastoma*** patients, but it may be considered along with other complementary therapies that could improve outcomes even more!

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Metformin: In glioblastoma patients, survival time without evidence of disease worsening was longer in diabetics receiving **metformin** (10 months) than in other diabetics (less than five months) and nondiabetics (less than seven months).[12]

Note: As of mid-2021, there were five clinical trials (two phase II and three phase I) registered with ClinicalTrials.gov that address the potential benefits of metformin in people with glioblastoma (ClinicalTrials.gov 2021). Results of these trials will help establish the value of metformin as an adjuvant therapy for glioblastoma. If I had glioblastoma, however, I would not wait for these clinical trials to complete—I'd initiate metformin immediately. (I've been using metformin as a preventative since around year 2000).

Cimetidine: A 2017 study on seven glioblastoma patients found that, when combined with the chemo drug temozolomide, a cocktail of drugs that included **cimetidine**, **lithium**, **olanzapine**, and **valproate** led to longer-than-expected survival.[13]

Note: Multi-drug therapy is the most rational approach to inducing complete responses, yet a study like this, using four different off-label medications is uncommon. More of these kinds of multi-drug studies are needed.

Dichloroacetate: An open-label phase I trial on 15 adults with grade III or IV gliomas or brain metastases from other cancers found that dichloroacetate treatment was feasible and well tolerated.[14]

Antidepressants: Fluoxetine (Prozac), a common antidepressant drug, has been shown to selectively kill **glioblastoma cells** in laboratory experiments.[15]

Additionally, **fluoxetine** may make glioblastoma cells more sensitive to temozolomide.[16] Other antidepressant drugs, such as imipramine (Tofranil) and amitriptyline (Elavil), have been shown to stop glioblastoma stem cells from producing more stem cells.[17]

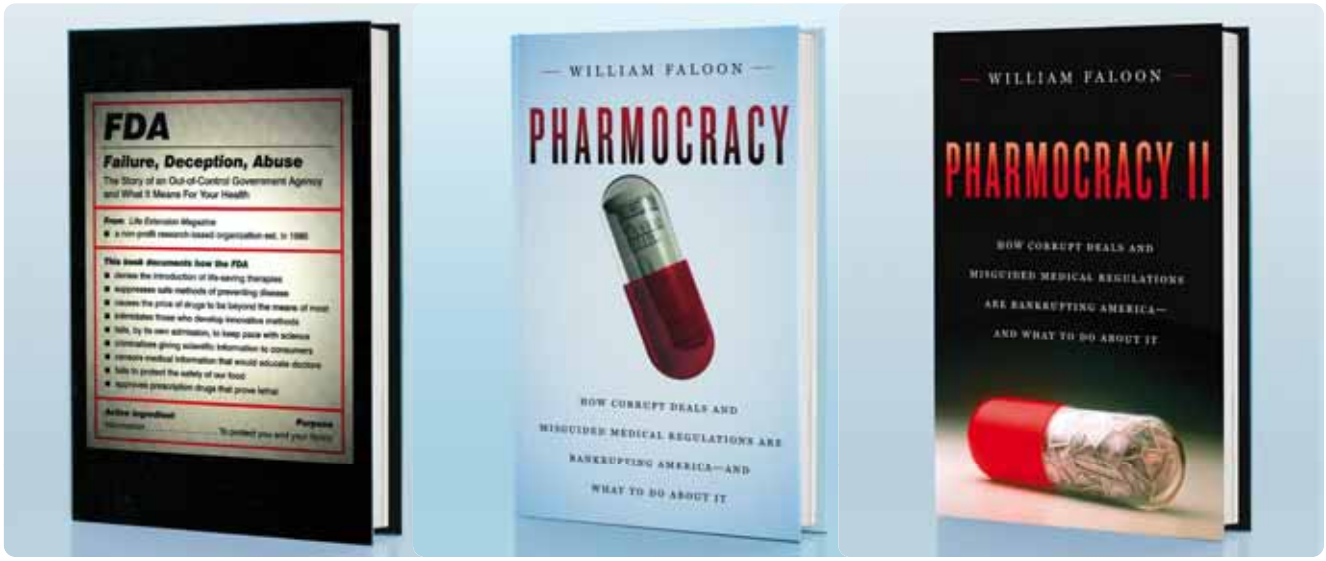
Natural interventions, such as vitamin D, quercetin, selenium, and melatonin are being explored, with intriguing preliminary results.[18-21]

Encouraging findings about a new multi-drug (off-label) cocktail treatment for **glioblastoma** appear at the end of this editorial.

To review Life Extension's glioblastoma protocol, log on to: https://www.lifeextension.com/glioblastoma.

How I Am Fighting Back

I've written hundreds of articles that meticulously describe how misguided FDA policies are the leading causes of disability and death. Many of these articles are compiled into the following three books:



The first exposé book is titled: *FDA: Fraud, Deception, Abuse* (2009) • Item # 33816
Retail price $20
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My second rendering is titled: *Pharmocracy* (2011) • Item # 33835
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My latest-published book is titled: *Pharmocracy II* (2017)
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In response to today's healthcare price conundrum, *Pharmocracy II* documents why conventional medicine costs so much, and provides practical solutions that Congress (not influenced by pharmaceutical lobbyists) can implement to help resolve this nation's worsening healthcare cost crisis.

Pharmocracy II advocates for a **free-market** approach that can spare Medicare and other government entitlement programs from insolvency, while improving the health of all Americans.

This book provides a rational basis for removing the compulsory aspect of healthcare regulation and allowing free-market forces to compete against government-sanctioned medicine.

More importantly, *Pharmocracy II* empowers the citizenry to inundate Congress with a unified demand to tear down corrupt regulations that are bankrupting the United States and suppressing cures for killer diseases.

The cover price for *Pharmocracy II* is $20. Your price is $15. Please consider buying four or more copies at only $9 each, to send to your representatives and two senators to educate them about misguided and corrupt government policies that are causing needless loss of human life.

Any of these books can be ordered by calling **1-800-544-4440** (24 hours/7 days).

New Hope for Glioblastoma Patients

Life Extension® has long advocated for combination use of "**off-label**" drugs that have specific **anti-cancer** mechanisms. We have suggested these off-label drugs be considered alongside certain conventional treatments. (The **FDA** did not concur!)

A group called **Care Oncology Clinic** was established in London, England in 2013. They study the clinical delivery of repurposed (off-label) drugs to target cancer metabolism.

Using a combination-drug approach that included metformin, doxycycline, mebendazole, and atorvastatin, they were able to dramatically improve survival as summarized below:[23]

Retrospective analysis was done of 95 patients with advanced (stage IV) **glioblastoma** who were prescribed an adjuvant off-label drug protocol alongside standard care.

Median survival for patients receiving off-label protocol alongside maximal standard care was **27.1 months**, compared to **14.8 months** for historic controls not receiving the off-label drug combination.

Two-year overall survival for patients receiving the off-label drug protocol alongside maximal care was **55.8%**. This is more than double the two-year survival rate **(26.3%)** for standard care **glioblastoma** patients.

The protocol of off-label drugs was well-tolerated by most patients.

Recall that Senators **John McCain** and **Ted Kennedy** lived only **14-15 months** after diagnosis, whereas patients treated with these **off-label drugs** survived about **one year *longer*** on average.

It is important to note that these positive results are preliminary and require further higher quality evidence.

To learn more about the **Care Oncology Clinic** of London, please visit https://careoncology.com/

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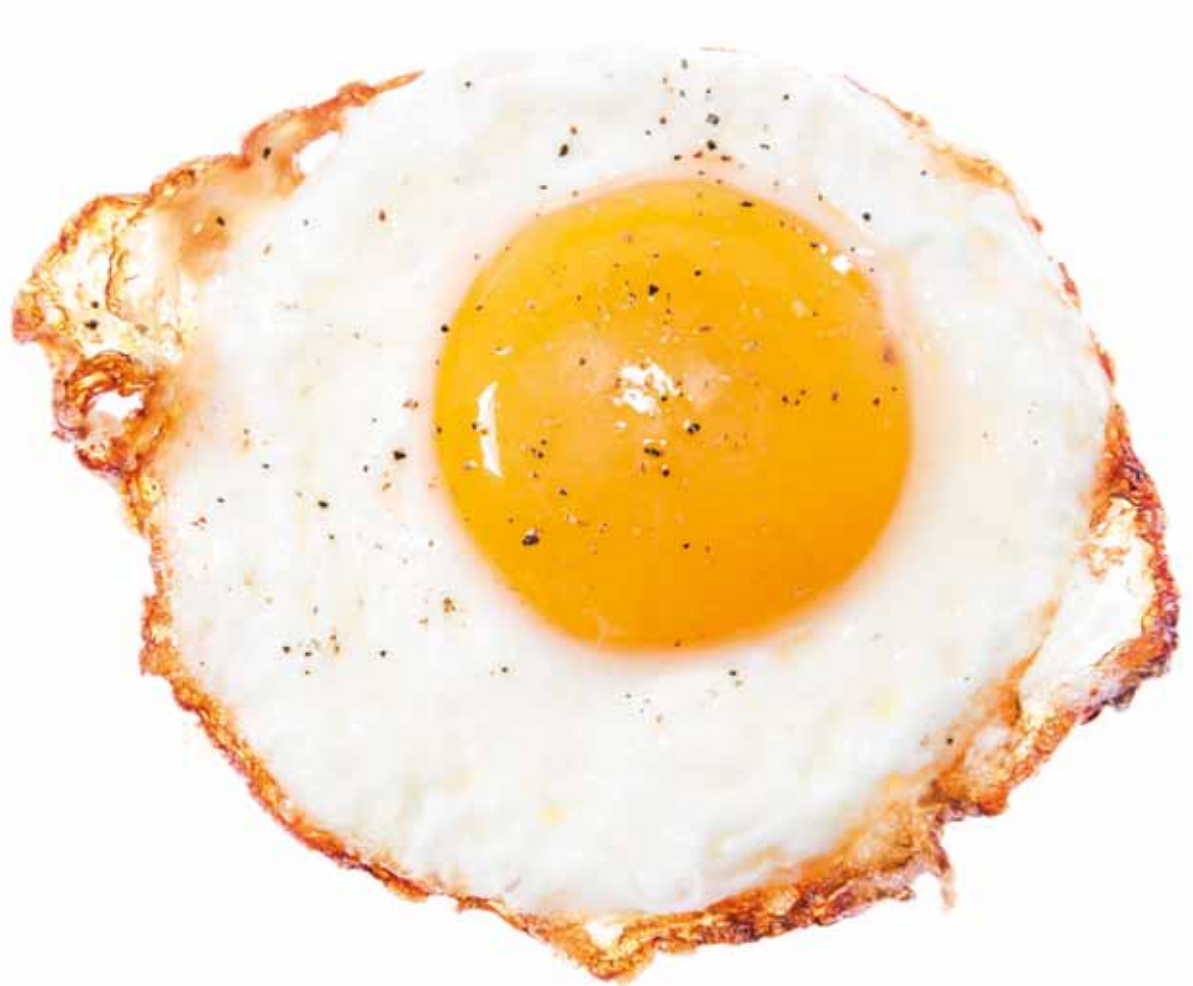

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In the News

Higher Selenium Levels Could Improve Breast Cancer Survival

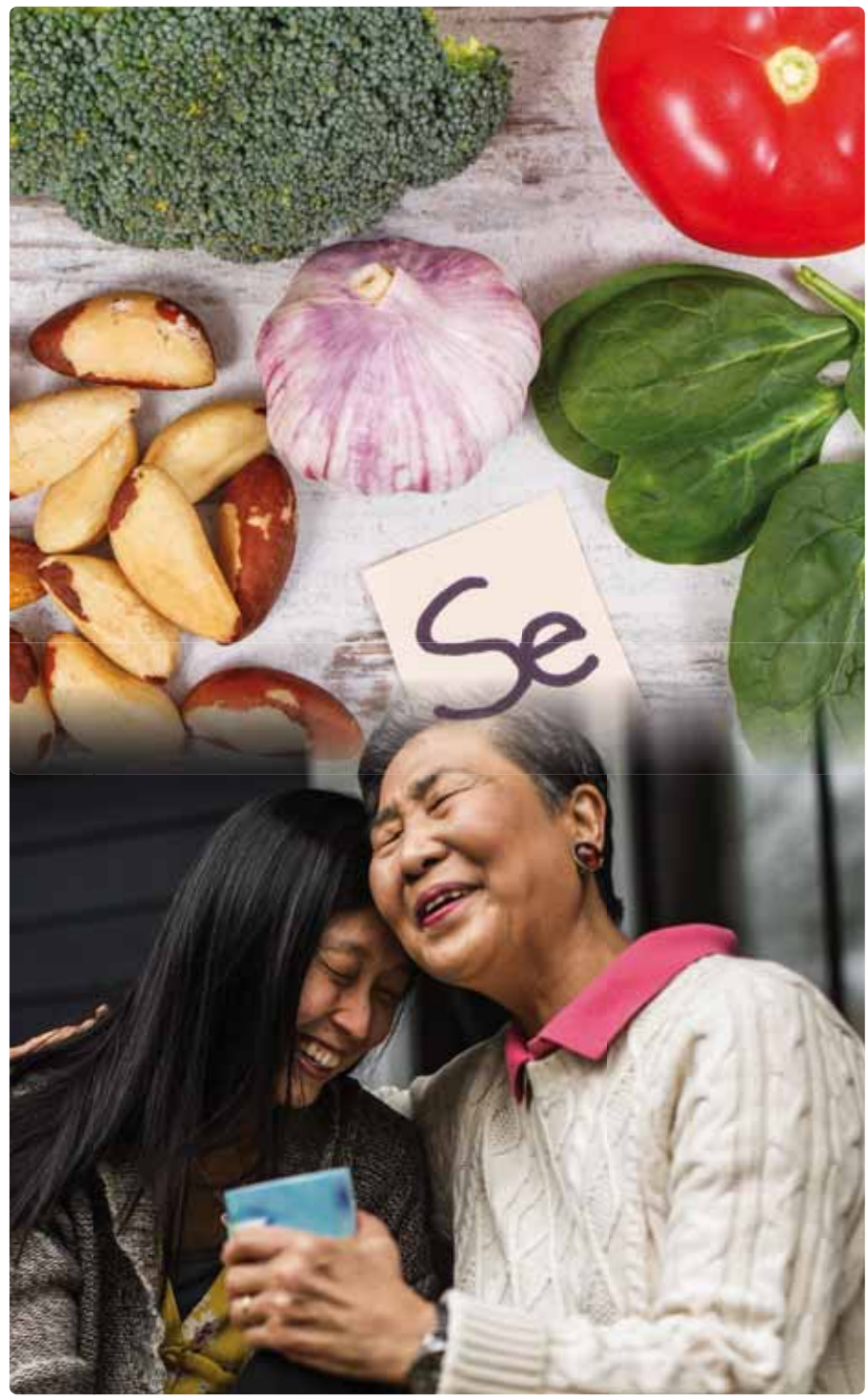
Higher **selenium** blood levels are associated with improved breast cancer **survival rates**.*

The 10-year survival rate was **65.1%** in women with the lowest **selenium** blood level.

The 10-year survival rate in women with the **highest selenium** blood levels was **86.7%**.

Editor's Note: A previous study found that higher selenium levels were linked to improved **five-year** survival rates in women with breast cancer. The current study included **10-year** survival rates in 538 women from the prior study.

* *Nutrients.* 2021 Mar; 13(3):953.



Calcium and Vitamin D Lower Fracture Risk in Vegan Women

A study published in the *American Journal of Clinical Nutrition* found that supplementation with **calcium** and **vitamin D** reduces fracture risk in vegan women, who have a *higher* risk of fracture than non-vegetarian women.*

Female vegans had a **53%** *higher* risk of experiencing a **hip fracture** than non-vegetarians.

Vegan women who supplemented with calcium and vitamin D *reduced* their hip fracture risk to that of non-vegetarians.

Editor's Note: Following a vegan diet may fail to provide adequate nutrients associated with greater bone mineral density, such as **calcium**, **vitamin D**, **zinc**, and **omega-3** fatty acids, thereby increasing fracture risk.

* *Am J Clin Nutr.* 2021 May 8.

Mediterranean Diet Protects Against Memory Loss and Dementia

A Mediterranean-style diet could protect against memory loss and dementia, a study published in the journal *Neurology* reported.*

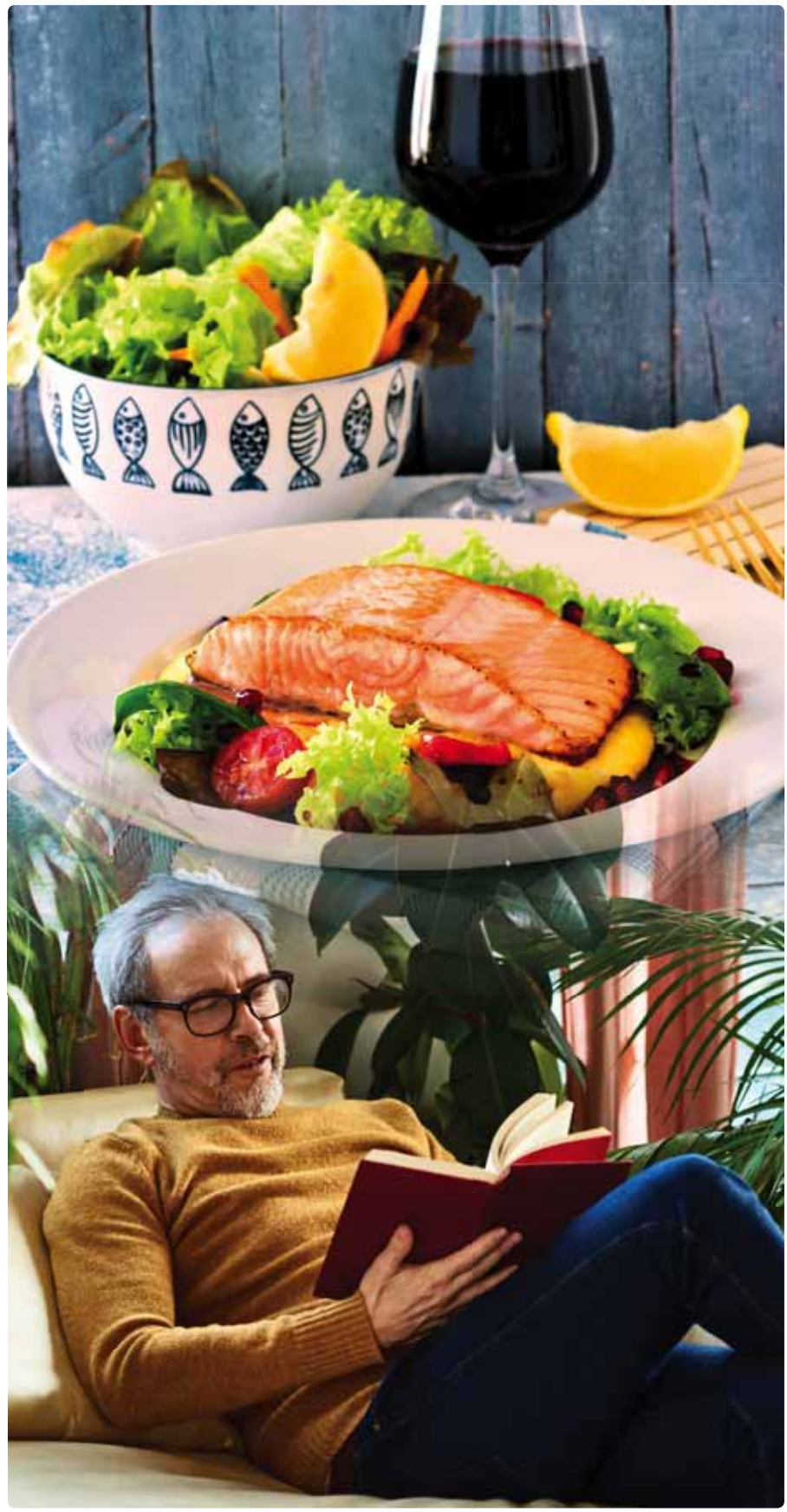
The 512 participants, with an average age of 70, completed food frequency questionnaires. They were then given MRI brain scans to determine brain volume, and neurological tests to examine their cognitive abilities and biomarkers for beta amyloid and tau proteins that characterize Alzheimer's disease.

People who ate an unhealthy diet had *higher* markers of amyloid beta and tau proteins in their cerebrospinal fluid, compared to those who followed a Mediterranean-style diet.

The unhealthy-diet eaters also performed *worse* on memory tests than those who ate healthy food.

Editor's Note: Participants who did *not* eat a healthy, Mediterranean-style diet were also found to have a smaller hippocampus volume (the area of the brain responsible for thinking and memory) than those who did. The hippocampus is known to atrophy (shrink) in those with Alzheimer's disease.

* *Neurology.* 2021;96(24):e2920-e32.



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PHAGES REGAIN MAINSTREAM RECOGNITION

BY MICHAEL DOWNEY

Bacteriophages were once recognized as powerful, life-saving weapons against **infection**.[1]

Called **phages** for short, they are tiny **DNA** or **RNA packages** wrapped in protein that attack ***specific bacteria***. They are harmless to humans and all other life forms.

Phage therapy was pushed out of the way when **antibiotics** were introduced.[1]

As the threat of **antibiotic-resistant infections** grows,[2] the medical establishment has begun to refocus on the potential of **phage therapy**.[3]

Mainstream media is paying attention too: The benefits and history of **phages** were recently explored in a feature in ***The New Yorker*** magazine.[4]

Scientists have found, in a laboratory study, that **phages** can help beneficial **probiotic bacteria** thrive and grow. This happens even in the presence of competitive bacteria that would otherwise suppress them.[5]

This may be related to the ability of specific **phages** to "seek and destroy." This means they can be selected to help protect against undesirable or disease-causing bacteria.[6]

A combination of **phages** with **probiotics** holds great promise to promote the health of the gut microbiome and to improve **intestinal function**.

What are Phages?

The word **bacteriophage** means "**bacteria eater**."

Phages are submicroscopic packages of DNA or RNA enclosed in a protein envelope that target and kill specific bacteria—and ***only*** these bacteria. Different phage strains target different bacteria. They pose no harm to *any* other life form, including humans.

Phages were first identified about a century ago and were used at the time to treat and prevent bacterial infections. But when **antibiotics** were discovered, focus shifted away from phages.[4]

Over time, **antibiotic-resistant bacteria**, also known as "super-bugs," have developed.

Today, about **700,000** people die every year from drug-resistant infections. That number is expected to reach ***10 million*** annually by 2050.[2]

This frightening reality has sparked renewed interest in **phage therapy**.

Phages Promote Microbiome Health

Scientists have identified a **blend of four phages** that may help decrease intestinal populations of undesirable bacteria while supporting probiotics.

Antibiotics employ a mass-killing technique, destroying both good *and* bad bacteria. But phages target ***only specific bacteria***.

This means the right **phages** can target undesired or **unhealthful bacteria** in the gut, helping to make room for the organisms we want to flourish. The end result is that the **gut microbiome** can be restored to a more healthy, balanced state.[6]

Promoting Growth of Beneficial Probiotics

E. coli (***Escherichia coli***) is a normal part of our gut microbiome. Usually it is harmless, though some strains can cause diarrhea, urinary tract infections, pneumonia, and other illnesses, and also crowd out beneficial organisms.[7]

To determine whether **the four-phage blend** could promote the growth of beneficial bacteria, researchers conducted a laboratory study.

E. coli was combined with various individual **probiotic bacteria** in test flasks that served as the control. In separate flasks, the **four-phage blend** was combined with *E. coli* and the probiotic bacteria.[5]

The growth of the beneficial bacteria was measured.

In the control flasks that contained *E. coli* but no phage blend, the probiotic bacteria grew very poorly. It appears that *E. coli* inhibited their growth—in other words, it outcompeted them.

In the flasks that also contained the **phage blend**, the probiotic bacteria **thrived**.

For instance, when the healthy probiotic bacteria ***Bifidobacterium longum*** was combined with ***E. coli***, there was little growth of the probiotic.

But in the flasks that contained the **phage** blend, beneficial ***B. longum*** colonies multiplied over **20 times** more than in the control flasks. The phages successfully promoted the growth of the beneficial probiotic.[5]

When this study was repeated using the probiotic ***Lactobacillus acidophilus***, similar results were obtained.

L. acidophilus growth was more than **10-fold *higher*** in the flasks containing **phage** plus probiotic and *E. coli*.

The scientists tested the **phage blend** again with another probiotic, this time ***Bifidobacterium bifidum***. The result in this case was **more than 30-fold higher growth**, in the presence of the phages.

Phages in Mice

Researchers next studied the effectiveness and safety of this **phage cocktail** in live animals.

Two groups of mice were given the beneficial probiotic ***B. longum***, along with a disease-causing ***E. coli*** strain. One group also received a **phage** blend specifically designed to target *E. coli*.[8]

After ***just 24 hours***, phage treatment decreased dangerous ***E. coli*** levels by about:[8]

- **10-fold** in the small intestine,
- **100-fold** in the large intestine, and
- **100-fold** in fecal matter.

WHAT YOU NEED TO KNOW

A Probiotic-Phage Blend for Digestive Health

- **Bacteriophages**, or **phages**, target *only* specific bacteria. They are harmless to all other life forms, including humans.
- As antibiotic-resistant bacteria have become a growing threat, scientists are focusing on using phages to treat deadly **infections**.
- Scientists have now identified **four phages** that promote the growth of beneficial bacteria.
- This probiotic blend can help improve a wide range of digestive issues, including **irritable bowel syndrome**, diarrhea, bloating, and gas.

At the same time, phage treatment increased beneficial ***B. longum*** levels by about:[8]

- **100-fold** in the small intestine,
- **100-fold** in the large intestine, and
- **40-fold** in fecal matter.

These results translated into clear benefits. The phage-treated mice had **healthy digestive function**, compared to mice infected with ***E. coli***, and the phage was not associated with any harmful side effects.[8]

The mice given only *E. coli* and *B. longum*—without added **phages**—became constipated, and their intestines showed swelling, redness, and leaks.[8]

Given these results, scientists have now added this same **bacteriophage** blend to **probiotics** for humans, to boost their effectiveness.

Super-Charging Probiotics

Two qualities to look for when selecting the **type** of **probiotic bacteria** is to ensure:

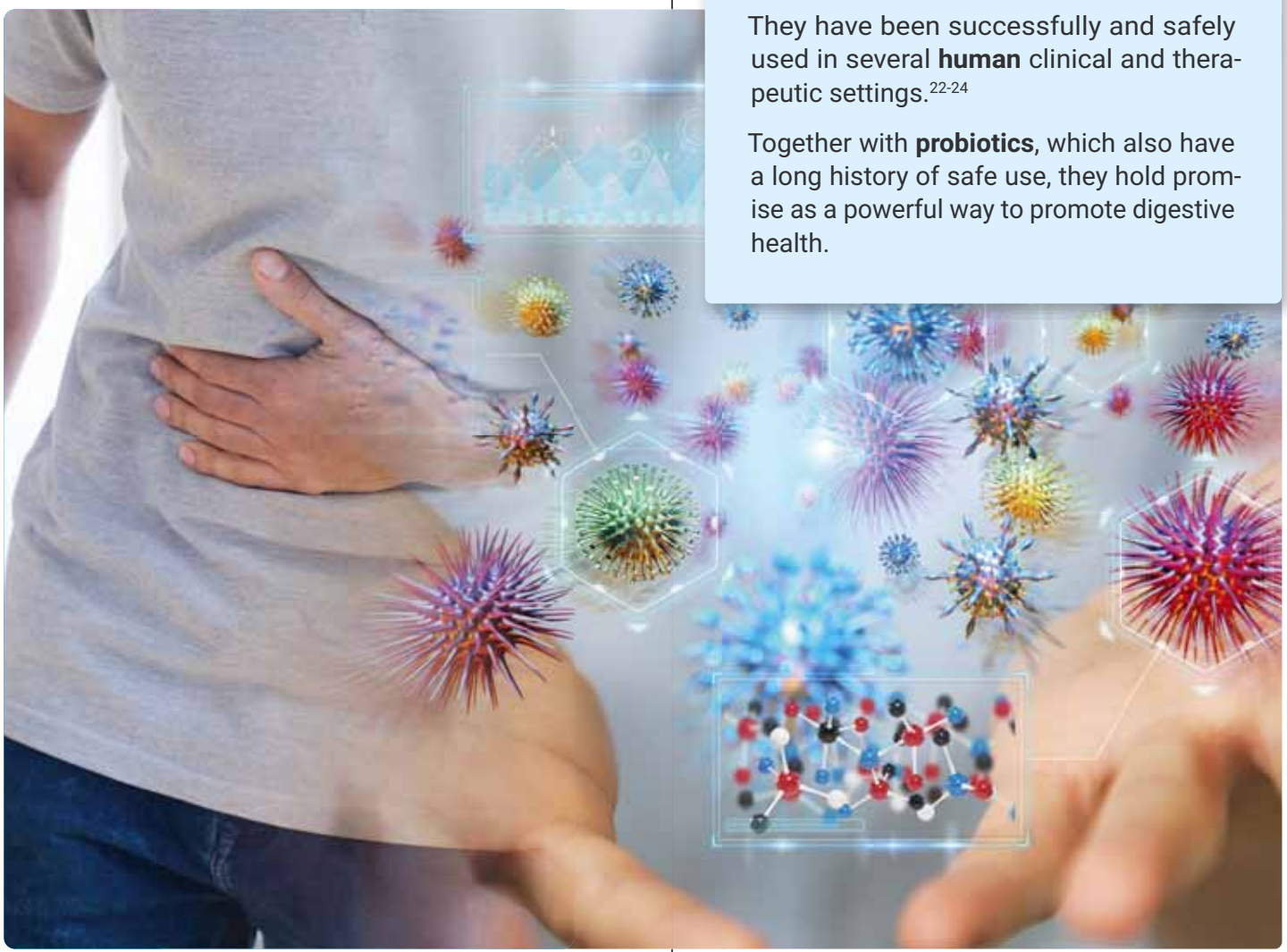
1. They have been studied in different combinations and shown to help improve a variety of **digestive symptoms**,[9-19] and
2. Some of the **probiotic** species multiplied to a much greater extent when cultured along with a specific **bacteriophage blend**.[5]

Deadly for Bacteria, Safe for You

Bacteriophages are found almost everywhere—from soil, hot springs, and the ocean depths, to the animal and human body.[21]

They have been successfully and safely used in several **human** clinical and therapeutic settings.[22-24]

Together with **probiotics**, which also have a long history of safe use, they hold promise as a powerful way to promote digestive health.



Specific **probiotics** have demonstrated the following benefits:

- ***B. longum SP54***, ***L. paracasei IMC502***, and ***L. rhamnosus IMC501*** provide antimicrobial effects against **Candida** (a fungus that can cause problems when it overgrows), ***H. pylori*** (a bacteria that can cause ulcers), and ***E. coli***.[16,18,20]
- ***B. lactis BLC1*** and ***L. acidophilus LA1*** relieve symptoms of **ulcerative colitis** (a disease that causes inflammation and ulcers in the colon)[12] and ease **lactose intolerance**.[19]
- ***B. breve Bbr8*** and ***L. plantarum 14D*** reduce symptoms of **celiac disease**, which can include diarrhea, bloating, and gas.[9,11]

In addition, these **probiotic strains** have been shown to improve **irritable bowel syndrome**.[9,10,12-15]

Scientists have combined seven **probiotic strains** with a **four-phage blend**.

This combination holds promise for those with gastrointestinal issues and anyone searching for a way to improve digestive health.

Summary

Bacteriophages, or **phages**, destroy only *specific bacteria*. They are harmless to humans and all other life forms.

Phages were once used as a powerful weapon against deadly infections, but they were pushed aside when **antibiotics** were discovered.

As bacteria have developed a resistance to antibiotics, scientists have begun focusing on **phage** therapies again.

A **four-phage blend** has been shown to promote the growth of *beneficial* probiotic bacteria.

By combining these **phages** with seven specific **probiotics**, scientists have developed a potent way to target and improve an array of digestive issues. •

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PLANT PIGMENTS PROTECT AGAINST **VISION LOSS**

BY MICHAEL DOWNEY

A major cause of **blindness** in the United States is **macular degeneration**.[1]

Up to **11 million** Americans are afflicted with it.[2]

Scientists have identified **plant pigments** that accumulate in the eyes and protect macular density.[3-5]

Lutein, **zeaxanthin**, ***meso*-zeaxanthin** and **astaxanthin** can help protect against age-related macular degeneration.

People with the *highest* intake of **lutein** and **zeaxanthin** have a ***41% lower risk*** of advanced macular degeneration.[6]

For people *already* afflicted, extracts of the spice **saffron** have been shown to improve **visual function**.[7]

One study in patients with early macular degeneration showed that **80%** of those taking saffron daily for three months improved **visual acuity** on the Snellen eye chart (by one line) compared to baseline.[8]

An improvement by one line on the Snellen chart means someone whose visual acuity at a distance was **20/40** would be able to see with **20/30** vision after just **three months** of daily **saffron** use.

Several other compounds have been shown to help *prevent* and even partially *restore* the **vision loss** that occurs with age-related macular degeneration.

A Leading Cause of Blindness

Age-related macular degeneration is the leading cause of severe vision loss and **blindness** in people over age 60.[9]

Risk factors for age-related macular degeneration include:[10]

- Age
- Family history
- Genetics
- Tobacco use
- High blood pressure
- Cardiovascular disease
- Obesity
- Sun exposure
- Diet low in dark green leafy vegetables and omega-3 fatty acids

The *progressive* damage that occurs to the **macula** contributes to the characteristic gradual *loss* of **central vision**. Patients often complain that central vision becomes washed out, with a loss of detail. Straight lines may also appear wavy.[10]

Lutein and Zeaxanthin

Lutein and **zeaxanthin** are dietary carotenoids found in dark green leafy vegetables and colorful fruits.[11]

Within the body, they concentrate in several parts of the eye, including the **macula**.[12-14]

There, they absorb **blue** and **ultraviolet** light, preventing retina damage. They also quench free radicals, inhibiting their destructive impact on the cells of the retina.[13-16]

In one study of adults with age-related macular degeneration, taking **10 mg** of **lutein** daily for **one year** increased macular pigment **density** by almost **40%**, compared to baseline.[17]

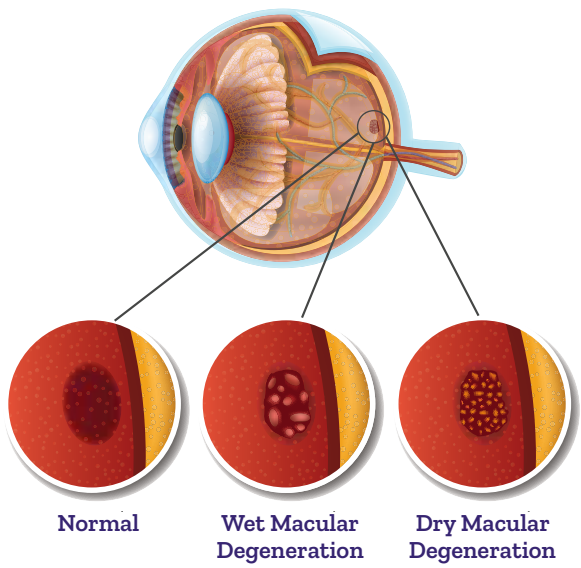
Increased **macular pigment ocular density** means increased protection against ultraviolet and blue light.

Scientists demonstrated that 48 weeks of taking daily **lutein** alone *or* **lutein** combined with **zeaxanthin** produced significant increases in ***electroretinogram signals***.[18] This is a measure of the power of light-sensitive cells to produce electrical impulses after stimulation by light.[19]

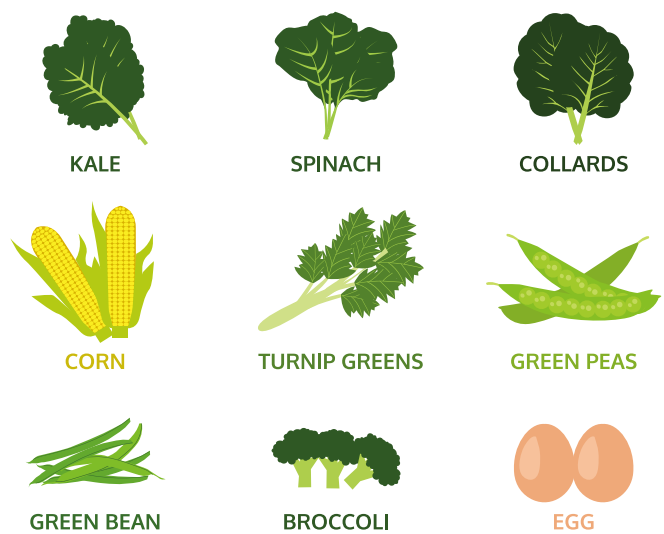
In a series of large clinical studies, researchers documented that oral intake of lutein and/or zeaxanthin can:[6,17,18,20-22]

- Improve **retinal function**,
- Increase the ability to see contrasting **colors** and **shapes**, and
- Improve **visual acuity** (the ability to see sharply at a distance).

Macular Degeneration



Lutein- and Zeaxanthin-rich Foods



One study of over **102,000** people aged 50 and older took more than ***20 years*** to complete.

It found that those with the *highest* intake of **lutein** and **zeaxanthin** had a remarkable **41% lower** risk of advanced macular degeneration.[6]

Meso-Zeaxanthin

***Meso*-zeaxanthin** is a yellow carotenoid derived from lutein. It is known to be produced in the eye itself, and a small amount may occur in certain foods.[23]

Individuals with **macular degeneration** have **30%** less ***meso*-zeaxanthin** in their macula than those with good eye health.[24]

One reason for this deficiency of ***meso*-zeaxanthin** is lack of ingested lutein. Another explanation for the missing ***meso*-zeaxanthin** observed in macular degeneration is inability to adequately convert lutein to *meso*-zeaxanthin.

Meso-zeaxanthin, when taken **orally**, increases protective **macular pigment** levels.[25]

Astaxanthin

Astaxanthin is a reddish carotenoid found in marine algae and some seafood.[26,27]

In preclinical studies, it protects the cells of the retina from being damaged by physical and oxidative **stress**.[26-28]

For example, **astaxanthin** may protect eye cells from UV-induced, free-radical damage by *suppressing* activation of an inflammatory protein, **nuclear factor-kappa B** (**NF-kB**).[29]

In experimental studies, astaxanthin prevented the vision-damaging effects of **wet macular degeneration** that occurs when blood vessels leak fluid into the retina. One rodent study showed it prevented cell damage related to increased pressure in the eye, which is the underlying problem in **glaucoma**.[30]

Astaxanthin's eye-protecting ability may be especially beneficial for people with **diabetes**.

Diabetic retinopathy occurs when high levels of blood sugar damage the retina over time, leading to vision problems. Among those who have had diabetes for over a decade, **80%** suffer from this condition.[26]

In animal studies, astaxanthin targets the retina and *prevents* the early **nerve-cell death** that is caused by excess blood sugar.[26]

Research has found that **6 mg** of astaxanthin daily helped promote visual sharpness and eye health.[31]

WHAT YOU NEED TO KNOW

Powerful Protection for the Eyes

- Age-related **vision loss** is extremely common and may lead to eventual blindness.
- **Lutein**, **zeaxanthin**, ***meso*-zeaxanthin**, **astaxanthin**, **saffron**, and **alpha-carotene** have been identified as key nutrients that can protect the eyes and slow the progression of age-related macular degeneration.
- **Cyanidin-3-glucoside**, found in certain dark berries, enhances night vision.

Saffron

Clinical studies demonstrate that **saffron**, a spice derived from the crocus flower, improves various **visual functions**.[32]

Saffron has been studied for an array of neurodegenerative eye diseases, including:[33,34]

- Age-related macular degeneration, and
- Diabetic retinopathy.

Saffron may provide these benefits thanks to its anti-inflammatory, antioxidant, and neuroprotective properties, along with its ability to help prevent cell death.[35]

In one clinical study, **20 mg** of **saffron** enhanced **visual function** in patients with *mild to moderate* age-related macular degeneration, including those already taking lutein and zeaxanthin.

Compared to those taking a placebo, participants who took **saffron** alone improved on a standard vision-measuring eye chart by **.69** letters. Those already taking **lutein** or **zeaxanthin** improved by **.73 letters**.[7]

In another study, **20 mg** of saffron daily improved the **light-sensing** abilities of retinal cells for patients with *early* age-related macular degeneration. After three months, these subjects were able to read **one entire additional line** on an eye chart, while those taking a **placebo** did not improve.[8]

This means that someone whose **visual acuity** at a distance was **20/40** would be able to see with **20/30** vision after just three months of saffron use.

To test longer-term benefits, scientists gave **20 mg** of saffron daily to patients with *early* macular degeneration for an average of **14 months**. Retinal sensitivity was improved for the entire period, and average **visual acuity** improved by an astounding ***two lines*** on an eye chart.[36]

This showed that *longer* **saffron** use produces *greater* improvement.[36]

Alpha-Carotene

Alpha-carotene, a carotenoid and vitamin A precursor found in pumpkins and carrots, protects retinal cells from light-induced **oxidative damage**.

One study analyzed 63,443 women and 38,603 men, aged 50 and older. It found that those with the *highest* dietary intake of **alpha-carotene** had a **31% reduced risk** of developing **advanced age-related macular degeneration**, compared to those with the lowest consumption.[6]

This yellow-orange carotenoid has even been shown to provide protection for smokers.

In one study of 1,414 men aged 65 and over, smokers with the highest **alpha-carotene** intake were found to have a significantly reduced risk of developing age-related **macular degeneration**.[37]

Saffron

Cyanidin-3-Glucoside

Cyanidin-3-glucoside (C3G) is a flavonoid found in many dark-colored berries.[38,39]

Recent research on human cells suggests that **cyanidin-3-glucoside** may protect epithelial (surface) cells in the **cornea** (the eye's protective outer layer) against damaging effects of **bacterial activity** and **inflammation**.[40]

C3G may also reduce **oxidative damage** from light and free radicals in retinal pigment epithelium cells.[41]

While these investigations are preliminary, **cyanidin-3-glucoside** may offer support to macular degeneration patients.

Many of these afflicted individuals experience difficulties when performing activities at night and under low light, such as driving or reading at night.[42]

The retina's rod cells are the eye's most sensitive cells, allowing us to see in very dim light. *Loss* of rod cells is associated with **night blindness** or **reduced vision** in low light.[43]

Cyanidin-3-glucoside has been shown to enhance the quality and function of **rhodopsin**, a light-sensitive protein found in the rod cells of the retina. It also boosts the ability of rhodopsin to **regenerate**.[39,44-46]

One study of healthy volunteers showed that a berry extract containing **cyanidin-3-glucoside** improved **night vision**, allowing aging individuals to see better in darkness. This improvement was noticeable *after just 30 minutes*.[47]

Taken in combination, C3G and other eye-protecting nutrients may provide the most complete range of benefits for **preventing** age-related **vision loss**.

Summary

Loss of **visual acuity** and **night blindness** are major threats to aging adults.

Extensive evidence demonstrates that the carotenoids **lutein**, **zeaxanthin**, ***meso*-zeaxanthin**, and **astaxanthin** protect the eye and help prevent vision loss as a result of **macular degeneration**, and possibly other conditions as well.

In addition, the spice **saffron** protects against *early* macular degeneration, while **alpha-carotene** helps protect against *advanced* macular degeneration.

The flavonoid **cyanidin-3-glucoside** can enhance **night vision** in as little as **30 minutes**.

In combination, these seven nutrients can provide comprehensive vision protection. •

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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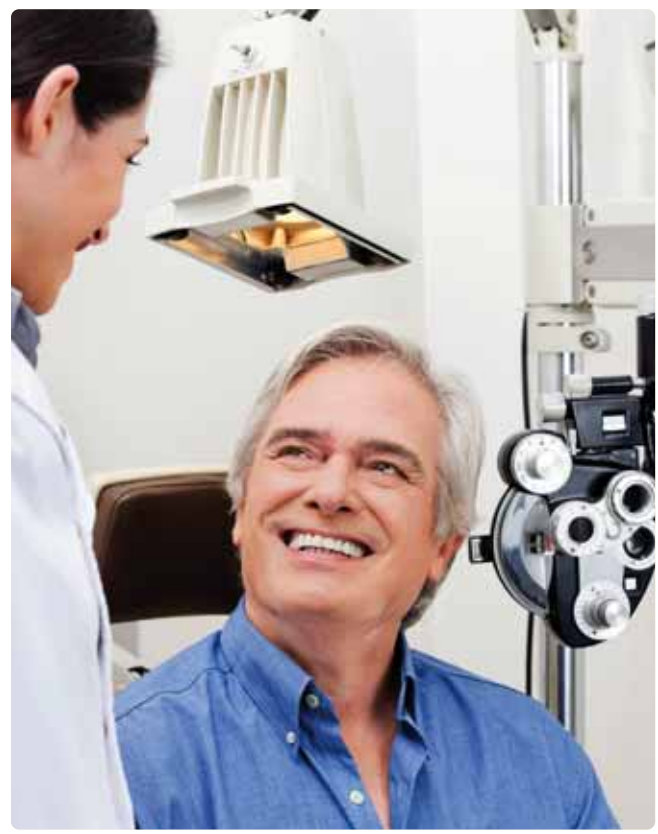

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- **Cyanidin-3-glucoside** assists with night vision.[6-8]
- **Saffron** has been shown to help support **vision** as demonstrated by doctor's eye exams.[1]
- **Alpha-carotene** further helps support **macular density**.[1]

For full product description and to order either of these **MacuGuard®** formulas, call 1-800-544-4440 or visit www.LifeExtension.com

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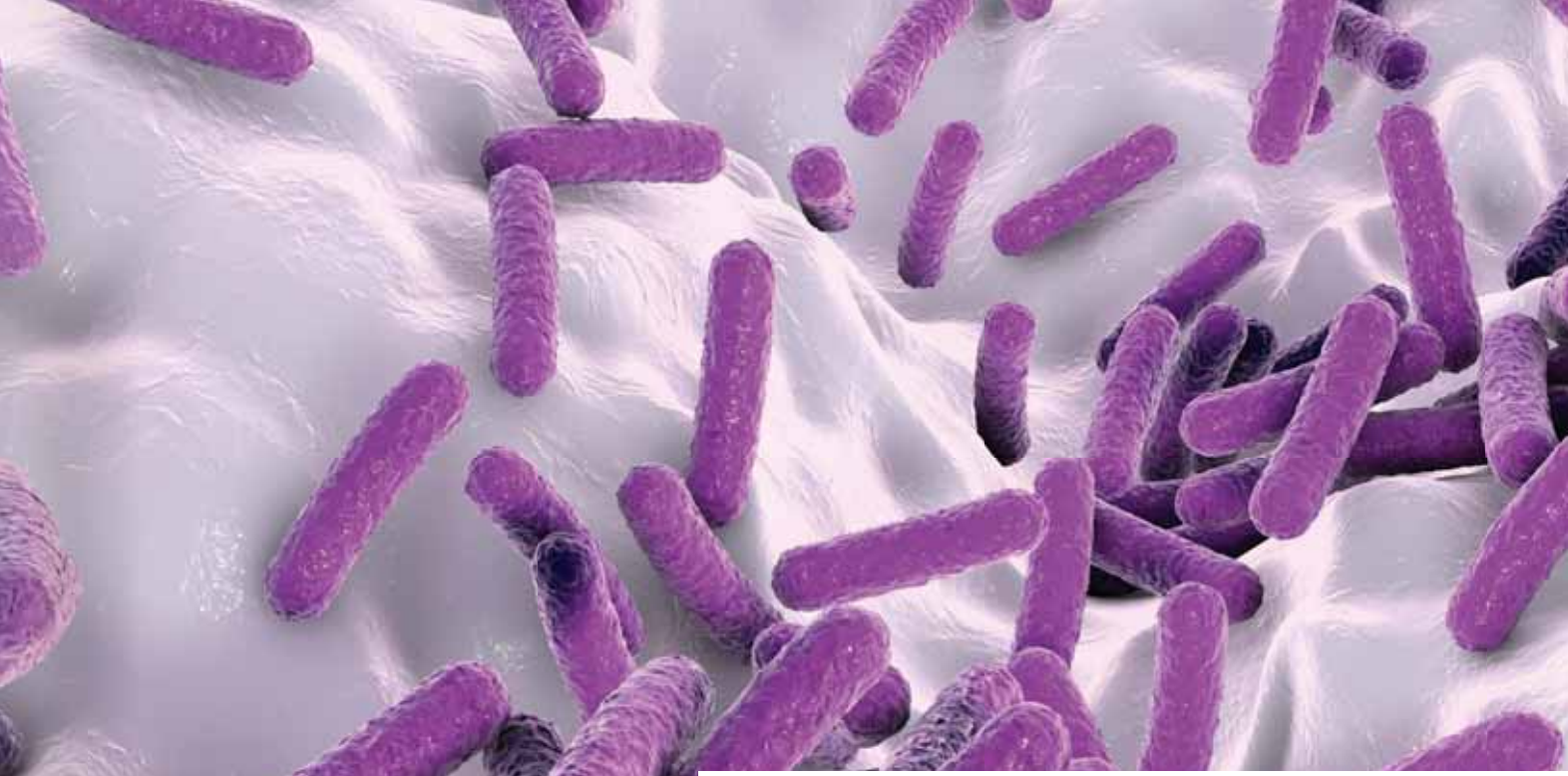
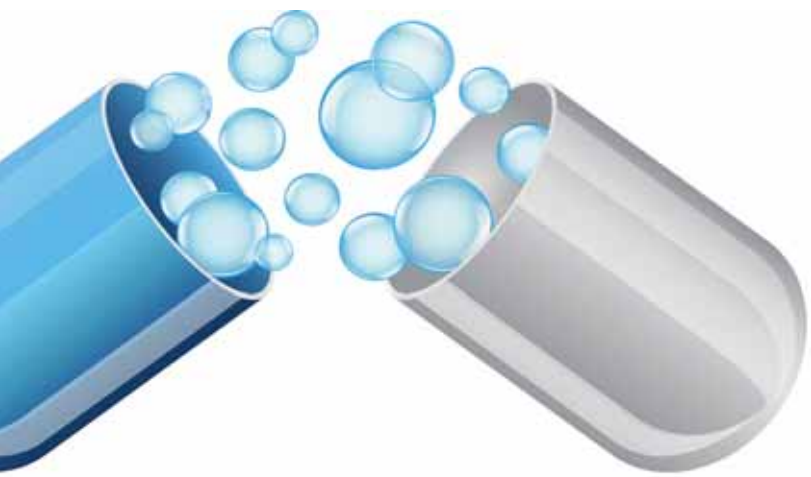
(Each bottle lasts for two months.)

MacuGuard® Ocular Support is available with or without astaxanthin.

REFUEL YOUR IMMUNE SYSTEM

BY MICHAEL DOWNEY





With age, **immune function** markedly declines along with the body's natural defenses.[1]

Until a method to fully reverse this degenerative process is validated, the following nutrients can help support a healthy immune response:

- **Vitamin C**
- **Quercetin**
- **Vitamin D**
- **Zinc**
- **Probiotic *Lactobacillus rhamnosus* CRL1505**
- ***S. cerevisiae* fermentate**

Taking these daily may help defend against infectious agents.

Vitamin C

The activity of many **immune cells** is closely related to their **vitamin C** content.

This is especially true for ***phagocytes***, the cells that engulf and destroy bacteria and other infecting organisms, and ***T-cells***, which regulate and direct other immune cells.[2]

Studies show that some **immune functions** can be improved by taking **vitamin C**.[3,4]

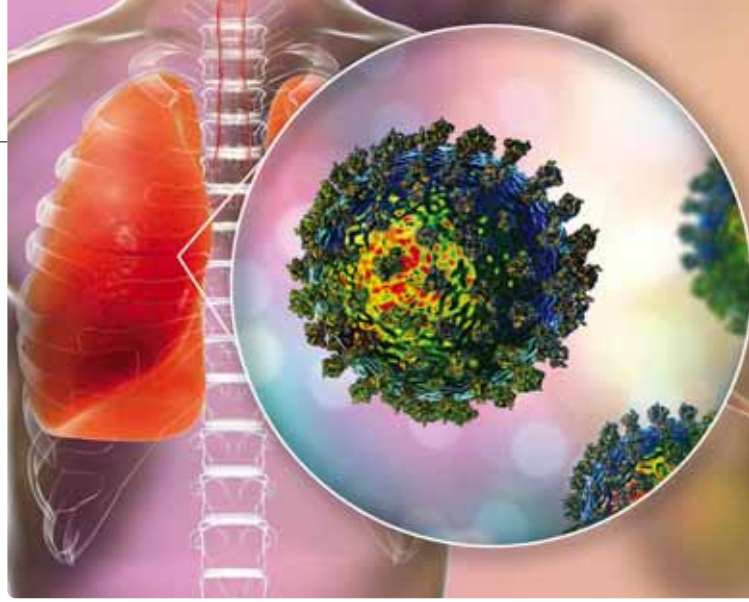
For example, vitamin C *deficiency* is associated in some studies with *increased* frequency and duration of **colds**.[4]

In a human clinical study, oral intake of vitamin C has been shown to *reduce* the duration of colds by an average of **9.4%.** It may also help prevent viral **respiratory tract infections** and reduce their severity.[5]

Evidence from basic research shows that vitamin C promotes a healthy immune system by:

- Enhancing the function and promoting the growth, maturation, and survival of **immune cells** that fight infection,[6,7]
- Increasing levels of **interferons**, the "warning signals" produced by the body that trigger protective immune mechanisms,[8]
- Neutralizing excess **free radicals** caused by infections, limiting oxidative damage and reducing severity of illness,[9]
- Aiding in the production of the structural protein **collagen**, which allows our skin and the linings of our respiratory and digestive tracts to maintain a protective barrier against infection,[10]
- Lowering levels of **histamine**, a pro-inflammatory compound[11] that plays a role in infections,[12] and causes symptoms of allergy,[13,14] and
- As indicated by preclinical studies, vitamin C plays a role in reducing excess levels of other **pro-inflammatory** compounds, countering inflammation caused by infection and injury, and promoting tissue healing.

The human body cannot produce or effectively store vitamin C. What that means is, in order to maintain optimal immunity, it's a great idea to replenish your supply through daily supplementation.



Quercetin

Research has shown that the plant flavonoid **quercetin** can support a prompt immune response to common **colds** and other **upper respiratory tract infections**. These studies found that adults taking quercetin were less likely to develop these illnesses.

One study found that only **5%** of people taking **quercetin** got sick during a two-week period (after three days of intense workouts), while **45%** of those taking a **placebo** developed colds.[19]

In another study of physically fit middle-aged and older adults, daily quercetin intake reduced the number of sick days taken for **colds** by **31%** and reduced the ***severity*** of symptoms by **36%**.[20]

Quercetin may also be effective against **bacterial** infections.

In animal studies, it's been shown to decrease the infection rate and inflammatory response to *Helicobacter pylori*, the cause of many **ulcers** and some potential **cancers** of the stomach.[21,22]

Quercetin also reduced **inflammatory** responses and strengthened host defenses against ***Salmonella*** bacteria in a cell-based model of infection.[23]

Salmonella bacteria cause roughly **26,500 hospitalizations** in the U.S. every year and are especially dangerous in older adults.[24]

Evidence from epidemiological studies shows that people with the *highest* quercetin intake have *reduced risk* for many different deadly cancers, including **lung**, **colon**, and **gastric cancers**.[25-27]

It can be difficult for the body to **absorb** quercetin.[28]

Researchers solved this problem by integrating it into a **phytosome**, a type of fatty substance that serves as a carrier. This makes it up to ***50 times more bioavailable*** (absorbable) than standard quercetin.[29]

Vitamin D

Vitamin D fortifies the **immune system,** helping to protect the body from infections, and lessening their severity. It may do this by:[30-34]

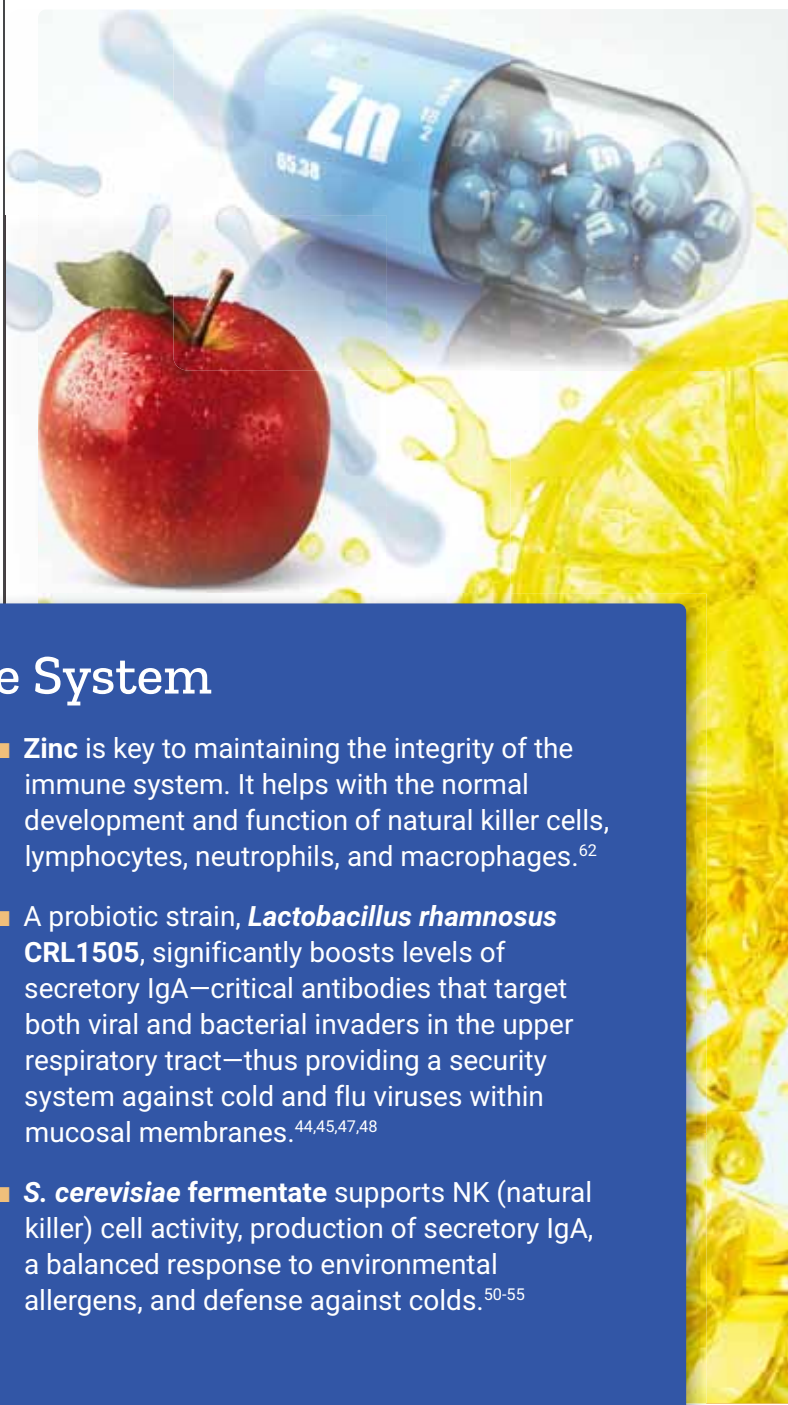
- Interfering with the ability of viruses to **replicate**,
- Supporting and helping to repair cellular linings in the body, including **lung airways**,
- Boosting production of proteins that are protective against **infection**, and
- Helping to prevent the immune system from producing *excess* **pro-inflammatory** compounds in the lungs.

Meta-analyses of clinical trials have shown that vitamin D protects against **respiratory tract infections**.[35,36]

In addition, *low* vitamin D levels are associated with *higher* rates of many **chronic diseases**, including cardiovascular disease, cognitive decline, and cancer.[37]

Annual blood tests can let people know whether they are taking the correct dosage to ensure optimal blood levels of vitamin D.

If you do not already maintain an optimal blood level of *25-hydroxyvitamin D* of **50** to **80 ng/mL**, then take between **5,000** to **8,000 IU** of vitamin D daily, with meals.



WHAT YOU NEED TO KNOW

Support a Healthy Immune System

- In order to live long, healthy lives, we need our **immune system** to function at peak form on a daily basis. Several nutrients can help do that.
- **Vitamin C** helps increase levels of antibody-producing cells (lymphocytes), boosts function of infection-engulfing neutrophils, and helps NK (natural killer) cell activity.[56,57]
- **Quercetin** reduces inflammatory immune cells, cuts histamine levels, relaxes airway smooth muscle, inhibits replication and infectivity of cold-causing viruses, and reduces senescent cells and their pro-inflammatory signaling.[58-60]
- **Vitamin D** interferes with virus replication and modulates the immune response via receptors on various immune cell types, thus supporting antimicrobial defenses while limiting inflammatory signaling.[61]
- **Zinc** is key to maintaining the integrity of the immune system. It helps with the normal development and function of natural killer cells, lymphocytes, neutrophils, and macrophages.[62]
- A probiotic strain, ***Lactobacillus rhamnosus* CRL1505**, significantly boosts levels of secretory IgA—critical antibodies that target both viral and bacterial invaders in the upper respiratory tract—thus providing a security system against cold and flu viruses within mucosal membranes.[44,45,47,48]
- ***S. cerevisiae* fermentate** supports NK (natural killer) cell activity, production of secretory IgA, a balanced response to environmental allergens, and defense against colds.[50-55]

Zinc

Zinc deficiency is quite common in the elderly.[38] It is thought to result from reduced zinc consumption and absorption in older individuals.[39]

This may compromise the function of the **immune system** and contribute to atherosclerosis, cancer, neurological disorders, autoimmune diseases, and other age-related conditions.[40,41]

The decline in immune function that happens with aging has been associated with both disease and death.[42]

By restoring zinc levels, aging adults may be able to partially slow immune function decline and protect against **chronic inflammation**.

Oral intake of **zinc** in the elderly has been shown to boost the stress response of **white blood cells**, providing an immune system anti-aging mechanism.[43]

Probiotic *L. rhamnosus* CRL1505

The immune system makes proteins called **antibodies** that fight bacteria, viruses, and toxins.

One of the most common antibodies, called **secretory IgA** (immunoglobulin A), is found in mucosal membranes.

IgA acts as the body's built-in security system within mucosal membranes that line the nose and upper respiratory tract.[44]

Having adequate **IgA** levels is critical because these **antibodies** target both viral and bacterial invaders in the upper respiratory tract. This IgA activity can prevent cold and flu viruses from gaining a foothold and wreaking havoc on the respiratory tract.[44]

Scientists studying the beneficial live microorganisms known as **probiotics** identified a specific bacterial strain that, in a preclinical model, significantly *increased* levels of **secretory IgA**.[45]

Originally isolated from goat's milk in northwestern Argentina,[46] the bacterium ***Lactobacillus rhamnosus* CRL1505** has been shown in preclinical studies to help inhibit viruses and bacteria that can cause:[45,47]

- Common colds,
- Influenza,
- Bronchitis, and
- Pneumonia.

In a clinical trial, one group of healthy male and female children consumed a yogurt drink five days a week that contained **100 million CFU** (colony-forming units) of ***L. rhamnosus* CRL1505**. A second group consumed a drink that did *not* contain the probiotic.

The children ranged in age from two to five years, a population that is particularly susceptible to **respiratory infections**.[48]

Over six months, compared to the placebo group, the children in the **probiotic** group had:[48]

- **61%** fewer cases of **tonsillitis** and **pharyngitis** (a throat infection),
- **55%** fewer cases of **cold** or **flu**,
- **49%** fewer **infections**,
- **46%** fewer cases of **fever**, and
- **33%** less need for **antibiotic** use.

Daily intake of ***L. rhamnosus* CRL1505** can provide protection against viral and bacterial infections.

S. cerevisiae fermentate Fights Allergies and Provides Immune Benefits

The immune effects of ***S. cerevisiae* fermentate** were discovered by accident.

A company in Cedar Rapids, Iowa, had been producing a specialized yeast culture when it became apparent that its factory workers—who were exposed

to the yeast daily, through inhalation—were taking far fewer sick days than its office workers.[49]

***S. cerevisiae* fermentate** helps promote the body's immune response when it encounters environmental allergens, like pollen.

At least six placebo-controlled clinical trials have validated its ability to protect against allergies and colds.[50-55]

In one study, subjects took either **500 mg** of ***S. cerevisiae* fermentate** daily or a **placebo** for five weeks during the beginning of allergy season.[50]

Subjects in the placebo group did not see a change in their seasonal allergies.

The group supplementing with the ***S. cerevisiae* fermentate** saw improvements. **Half** of the treated male volunteers reported a **complete absence of allergy symptoms**, which returned within two weeks once they stopped taking the yeast fermentate.

In two other studies, subjects receiving ***S. cerevisiae* fermentate** reported shorter duration of symptoms and better response to immune challenge, compared to those taking a placebo.[53,54]

***S. cerevisiae* fermentate** appears to work by promoting **natural killer** cell activity as well as the production of **secretory IgA**—two key players in our body's immune defenses.[50,51]

In one study, subjects taking **500 mg** of ***S. cerevisiae* fermentate** daily for eight weeks experienced an increase in **secretory IgA**.[50]

A placebo-controlled, double-blind study found that yeast fermentate increased markers of natural killer cell activity—after just a single **500 mg** dose.[51]

Summary

Aging weakens the **immune system**, leaving us vulnerable to viral and bacterial infections, including colds, flu, and upper respiratory infections—and increases the risk of cancer.

Select nutrients help the immune system function optimally to kill pathogens, and can help prevent the chronic, low-level inflammation that is associated with numerous degenerative diseases linked to aging.

These critical nutrients include **vitamin C**, **quercetin**, **vitamin D**, **zinc**, the probiotic strain ***L. rhamnosus* CRL1505** and ***S. cerevisiae* fermentate**.

They can help support a healthy immune system and may offer protection against viral and bacterial infection, cancers, and other illnesses. •

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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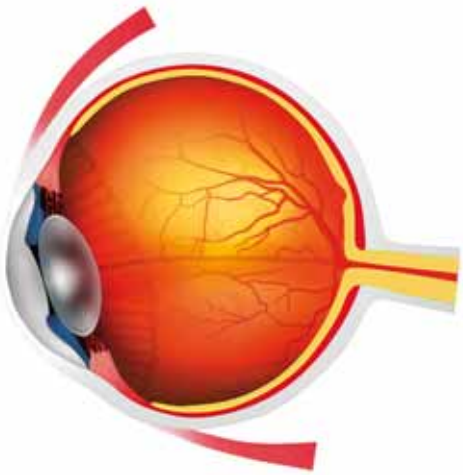

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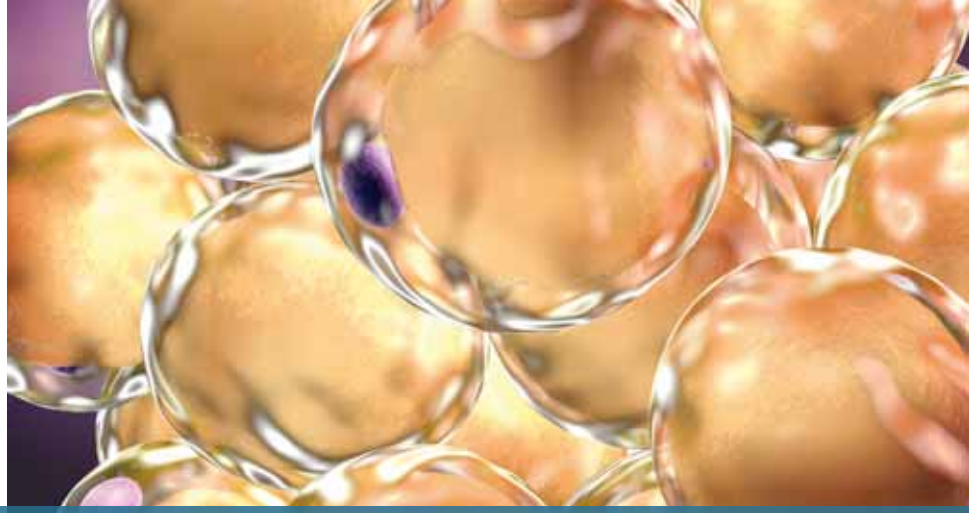


ELEVATED **CORTISOL** AGES SKIN AND HAIR

BY MARSHA MCCULLOCH, RD

With age, levels of most hormones in our body decline. That's not true for **cortisol**.

In several studies, **cortisol** concentrations have been found to increase after midlife.[1,2]

Stress also elevates cortisol levels.[1,3]

Higher **cortisol** in older adults is linked to increased risk of chronic disease and mortality.[1]

Chronically elevated cortisol also damages the **skin** and **hair**.[4,5]

Scientists have identified **plant extracts** that can safely help lower cortisol.[6,7]

This can provide support for the skin and hair.

In one study, **72%** of participants who took a **lychee-green tea extract** blend had a noticeable decrease in **fine lines**, and reported improvements in **hair** growth and thickness.[8]

What is Cortisol?

Cortisol is a hormone that helps regulate numerous bodily functions, including the stress response. It's sometimes called a "**stress hormone**."[3]

Blood levels of cortisol normally ebb and flow. They typically peak in early morning, then gradually decline to their lowest level around midnight.[9]

But chronic stress disrupts this daily rhythm.[10]

In addition, many studies show that average cortisol levels gradually *increase* in older adults as they age.[1,2]

Increased cortisol is associated with higher blood glucose, high blood pressure, weakened immunity, muscle loss, low bone mass, and cognitive decline.[1]

Chronically elevated cortisol also wreaks havoc on the **skin** and **hair**.[4,5]

Cortisol Production

Cortisol is primarily produced by the **adrenal glands**, which are located atop each kidney.

When the brain perceives **stress**, it triggers the release of cortisol from these glands.[9]

Other organs and tissues, including the **skin**, also secrete cortisol.[11,12]

The **epidermis** (outermost skin layer), **dermis** (inner skin layer), **melanocytes** (melanin-producing cells), and **hair follicles** *all* synthesize the **cortisol** hormone.[11]

Both physical and psychological stress can trigger cortisol secretion from the skin.[10]

Enzymes that control cortisol activity are also found in the skin and hair follicles.[11,13]

One key enzyme is **11-beta-hydroxysteroid dehydrogenase-1** (**11-beta-HSD1**). It converts inactive cortisone to *active* cortisol.[14]

Rapid Skin Aging

Higher **cortisol** levels have been found in aging skin.[15]

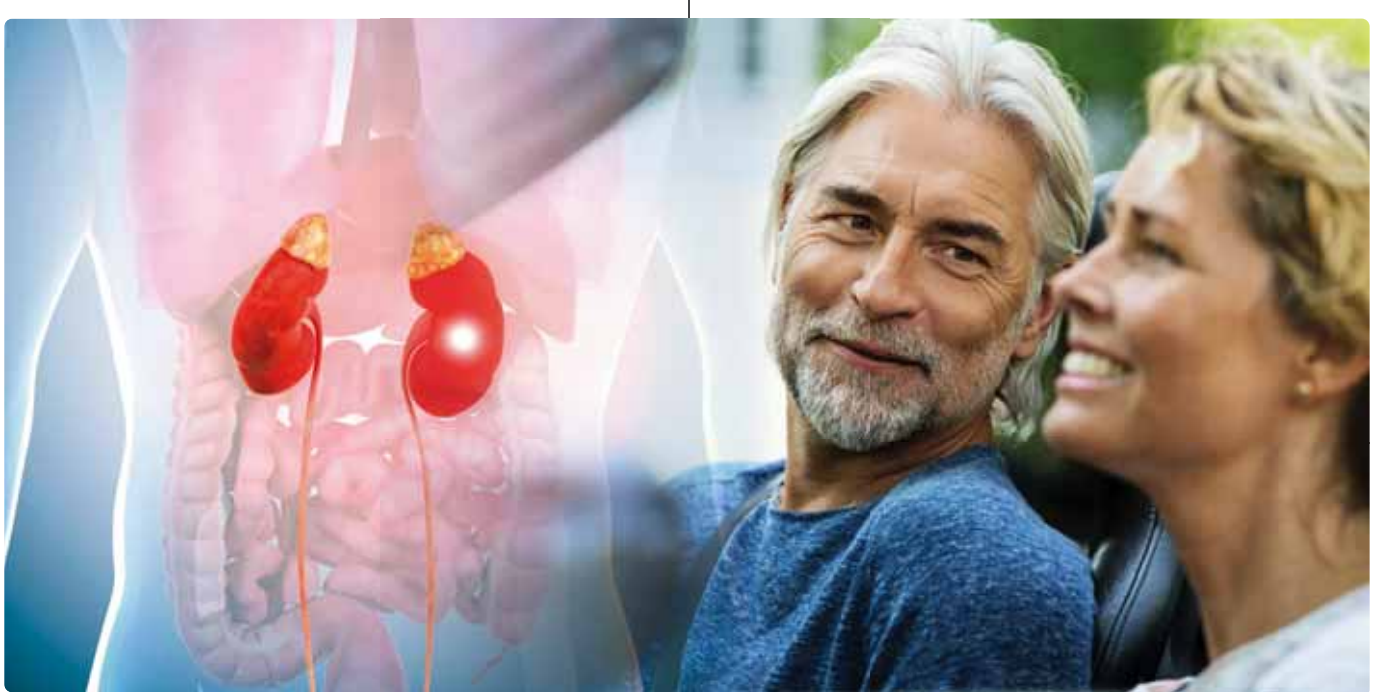
With aging and obesity, the enzyme **11-beta-HSD1** increases.[14] This leads to more activation of cortisol in cells.[15]

In addition, **ultraviolet light** affects cortisol activity in the skin.[9] The sun's **UV** rays increase the *enzyme* 11-beta-HSD1.[14] These actions result in increased skin **cortisol** levels.[13]

Elevated cortisol contributes to **thinning skin**, a decreased ability to make new skin cells, and inhibition of **collagen synthesis**.[13,15] This makes it more difficult to heal cuts and sores.[4,14]

Increased cortisol also promotes **inflammation** and the production of damaging **reactive oxygen species** (ROS).[16]

Higher ROS levels can contribute to an increase in **wrinkles**, dark coloration under the eyes, and **age spots**.[16]



Chronically elevated cortisol also impairs the skin's **barrier function**.[4]

The **skin barrier** helps keep moisture and nutrients in, while guarding against toxins, pathogens, physical damage, and allergens.[17]

A disrupted skin barrier can result in **dry**, **flaky skin**.[9] That may lead to an increased susceptibility to infections and a greater likelihood of becoming sensitized to allergens.[9]

The Skin Microbiome

Every square centimeter of the body's skin harbors **millions** of microbes, primarily bacteria.[18]

This **skin microbiota** plays a key role in maintaining **barrier function** and helps prevent the overgrowth of *harmful* microbes.[18]

Cortisol can disrupt the makeup of the skin microbiome,[19] leading to disease promotion by harmful skin bacteria.[18]

For example, cortisol can increase susceptibility to skin infection by group A *Streptococcus pyogenes*.[19] These bacteria can cause **cellulitis**, a serious infection characterized by swollen, red, and painful skin.[20]

Cortisol can also worsen the inflammation triggered by *Propionibacterium acnes*, one of the main types of bacteria that cause **acne**.[18]

WHAT YOU NEED TO KNOW

Plant Extracts Reduce Cortisol for Skin and Hair Health

- Higher average **cortisol** concentrations, often due to aging or chronic stress, can have damaging effects on skin and hair.
- Increased cortisol levels can contribute to signs of **skin aging**, including wrinkles, thinning skin, age spots, and slower healing of sores.
- Elevated cortisol can also disrupt the skin barrier and the **skin microbiome**, contributing to dry skin, acne, skin infections, and eczema.
- Excessive **hair loss**, thinning hair, and dry scalp are also linked to higher cortisol levels.
- In clinical trials, **lychee-green tea** extracts significantly lower cortisol levels. In one pilot study, taking **100 mg** of this blend twice daily reduced fine lines, wrinkles, and age spots.
- Bark extracts from **magnolia** and **phellodendron** trees also significantly lower cortisol levels in clinical trials. This could help promote youthful skin and hair.
- ***Combining*** a lychee-green tea blend with magnolia-phellodendron extracts may help optimize the benefits for hair and skin health.

Unique Lychee Polyphenols

Lychee is a tropical fruit rich in **polyphenols** that help reduce cortisol levels.[25]

To allow better absorption of the polyphenols in lychee, scientists developed a proprietary blend of low-molecular-size extracts from **lychee fruit** and **green tea**. This enables the beneficial compounds to be absorbed **three** to **four times** more readily than regular lychee polyphenols.[26]

Damaged Hair

When we think of **hair loss**, we think of baldness in men. But in midlife, women may also experience significant changes in the texture and growth of their hair, including **thinning**.[21]

Both short-term and chronic stress, which trigger increased **cortisol** secretion, can promote hair loss.[5,21]

High **cortisol** levels reduce the synthesis and accelerate the breakdown of **hyaluronic acid** and **proteoglycans** in the scalp by about **40%**.This deters the normal activity of hair follicles and can lead to **hair loss**.[5]

Aging makes this even worse. The synthesis of **proteoglycans**, which are vital to hair growth, generally decreases as a person ages.[5]

Research shows that exposing human skin in culture to low **cortisol** levels stimulated the synthesis of hyaluronic acid and proteoglycans and slowed their breakdown by about **25%**.[5] That may support hair growth and health.

Lowering Cortisol with Lychee-Green Tea

Human studies of a **lychee-green tea** extract blend have shown it can reduce cortisol.[22]

Scientists gave **100 mg** of **lychee-green tea** blend or a placebo once daily to 19 sedentary but healthy young men. After a month, the **lychee** group had significantly *lower* blood **cortisol** levels at rest *and* after an exercise challenge, compared to the **placebo** group.[22]

In another study, 13 healthy young men took **100 mg** of **lychee-green tea** blend half an hour before dipping their legs into hot water (a stressor). Their blood **cortisol** afterward was significantly *lower* than in the placebo group.[6]

The men's levels of two inflammatory cytokines, **IL-1beta** and **IL-6**, were also significantly lower after taking the **lychee-green tea** blend, compared to **placebo**. These cytokines increase in response to stress and trigger **cortisol** release.[6]

Healthier Skin and Hair

This **lychee-green tea** blend has been tested directly for skin benefits.

In a pilot study, a group of sedentary men took a **lychee-green tea** extract blend daily.

After three months:[8]

- **72.7%** had a decrease in fine lines,
- **18.2%** had a decrease in deep wrinkles, and
- Participants consistently had a lighter and brighter complexion, including fading of **freckles** and **age spots**, as well as **less skin redness**.

In addition, **54.5%** of those taking the blend had decreased blood levels of **C-reactive protein**, a marker of **inflammation**.

Three participants taking the **lychee-green tea** blend also reported an increase in **hair thickness** and **new hair growth** along their hairline.[8]

Bark Extracts Reduce Cortisol

Extracts from the bark of **magnolia** and **phellodendron** trees have been tested for their ability to lower stress and cortisol.

Both tree barks have been used in traditional herbal Chinese medicine since ancient times.[7,23,24]

In one study, 56 men and women with moderate stress took **250 mg** of the combined bark extracts twice daily for a month. They had an **18%** reduction in daily salivary **cortisol**, compared to a placebo group.[7]

The bark extract group also had an **11%** reduction in **overall stress** and a **13%** decrease in **tension**, based on questionnaires.[7]

By helping lower **cortisol**, **magnolia-phellodendron** bark extracts could support healthy **skin** and **hair**. Taking these extracts in combination with a **lychee-green tea** blend may maximize benefits for skin and hair health.

Summary

Higher levels of **cortisol** can contribute to visible signs of aging skin and hair.

Reducing cortisol levels may help deter **wrinkles**, fine lines, and skin spots, as well as protect the **microbial balance** of the skin.

Lowering cortisol may also help support a healthy scalp and **hair growth**, while inhibiting hair loss.

Lychee-green tea and **magnolia-phellodendron** can help maintain healthy cortisol levels. •

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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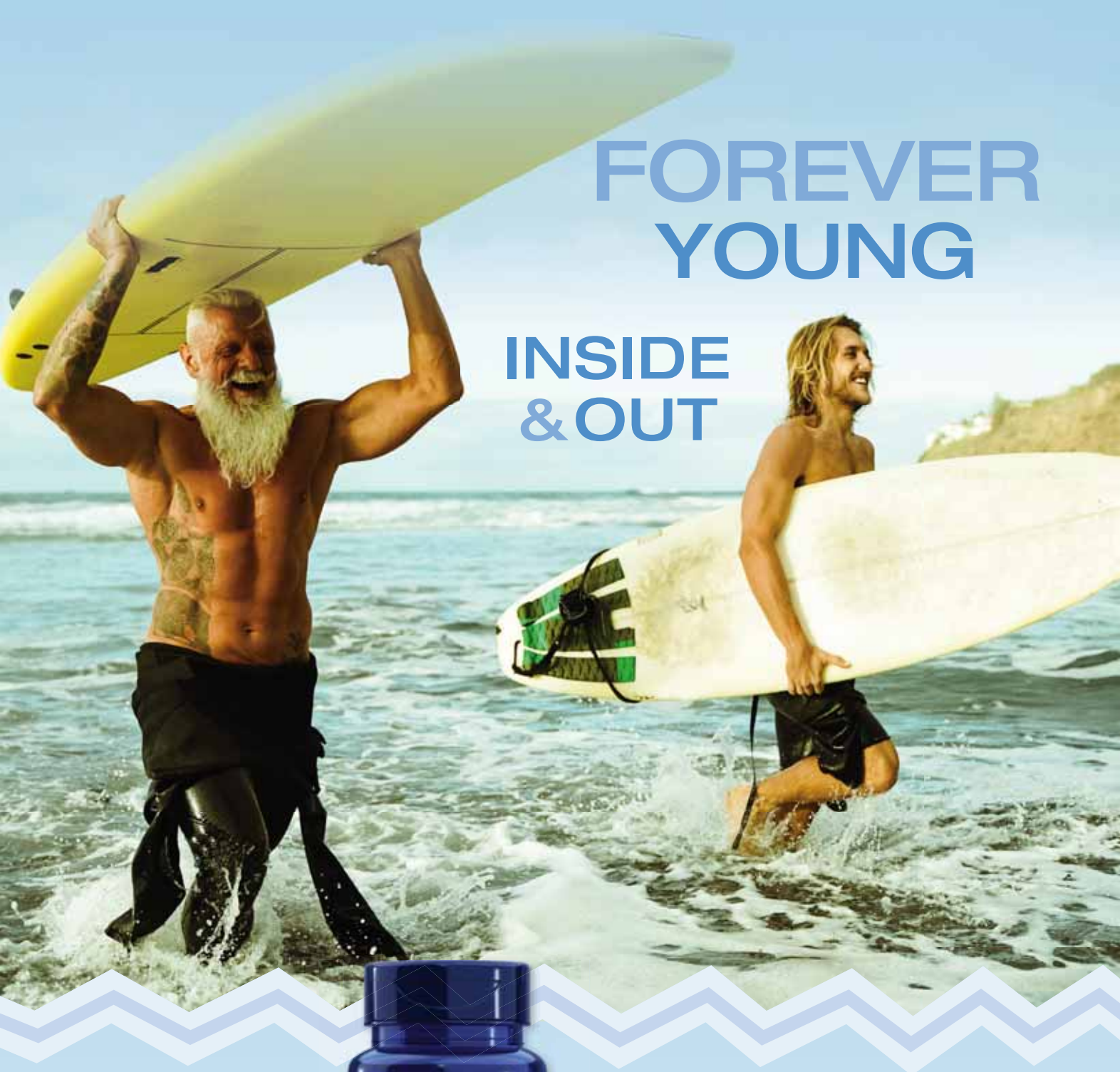

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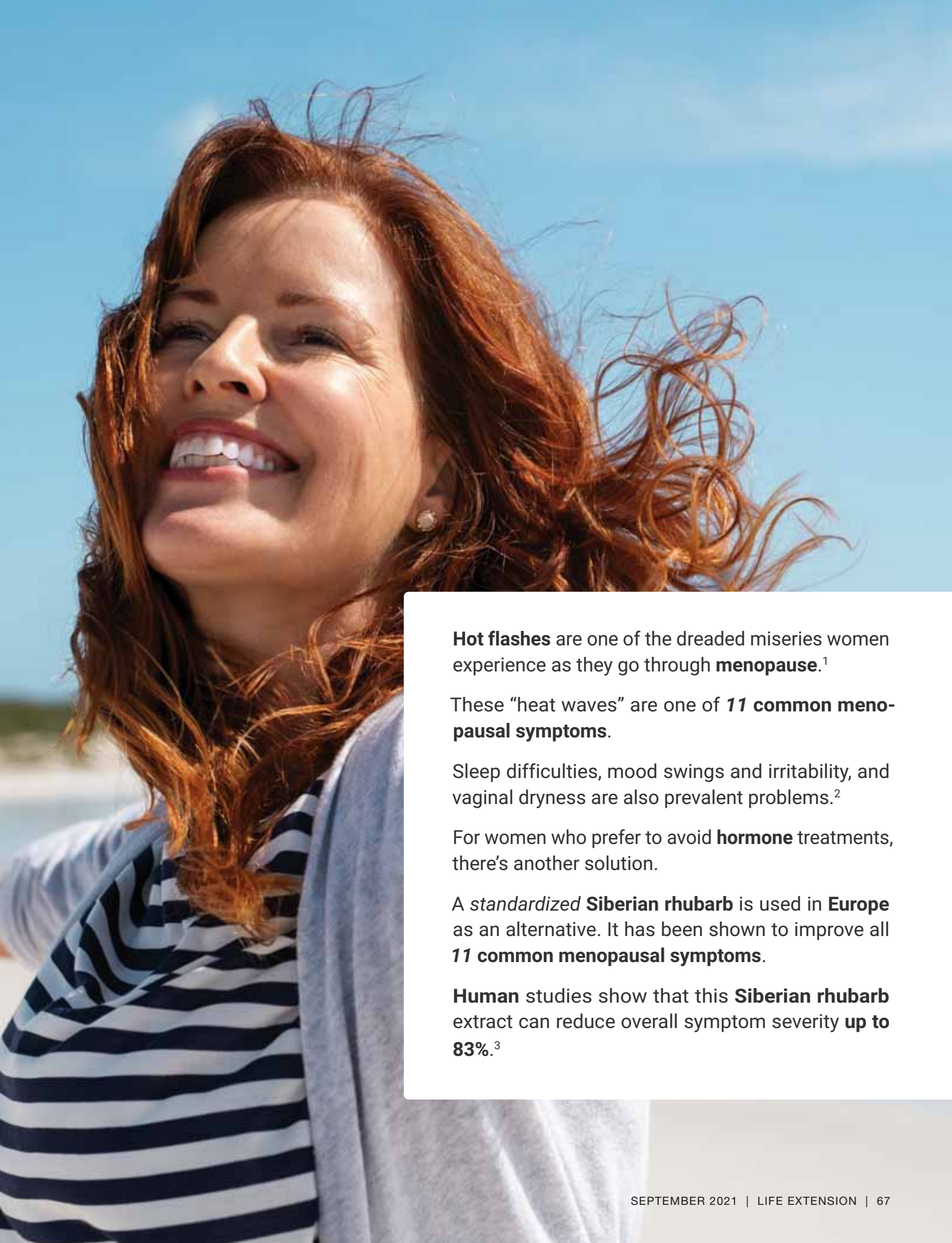
A European Solution for MENOPAUSE SYMPTOMS

BY MARSHA MCCULLOCH, RD



Hot flashes are one of the dreaded miseries women experience as they go through **menopause**.[1]

These "heat waves" are one of ***11*** **common menopausal symptoms**.

Sleep difficulties, mood swings and irritability, and vaginal dryness are also prevalent problems.[2]

For women who prefer to avoid **hormone** treatments, there's another solution.

A *standardized* **Siberian rhubarb** is used in **Europe** as an alternative. It has been shown to improve all ***11*** **common menopausal symptoms**.

Human studies show that this **Siberian rhubarb** extract can reduce overall symptom severity **up to 83%**.[3]

The 11 Common Symptoms of Menopause

Menopause is marked by 12 consecutive months without a menstrual period. It generally occurs at around age **51**, though symptoms can start several years earlier, during **perimenopause**.[4]

As **estrogen** and **progesterone** levels decline during the menopausal transition, women can be affected physically and psychologically.[2]

A frequently used tool to assess menopause symptoms is the **Menopause Rating Scale**.[5]

It includes **11** common concerns:[5]

- Hot flashes/excessive sweating,
- Heart discomfort,
- Sleep problems,
- Joint/muscle discomfort,
- Depressive mood,
- Irritability,
- Anxiety,
- Physical/mental exhaustion,
- Sexual problems,
- Bladder issues, and
- Vaginal dryness.

There is a non-hormonal way to address *all* of these **menopausal** symptoms.[6]

A European Solution

Most of the symptoms of **menopause** are caused by a drop in levels of the hormone **estrogen**.

Estrogen binds to **receptor sites** on cell membranes to activate beneficial and sometimes detrimental cellular processes, including excess proliferation.

Activating the **ER-*beta*** receptor promotes beneficial effects on skin, brain, bone, cardiovascular, and other tissues. This can support menopausal symptom relief.

Activating the **ER-*alpha*** receptor, on the other hand, can produce undesirable growth in some tissues, including initiating and promoting cancer.

Increased activity of the **ER-*alpha*** receptor is believed to cause many of the ill effects of conventional hormone-replacement therapy for menopausal symptoms.[9]

For nearly ***three decades***, German practitioners have been recommending a standardized extract from the roots of the **Siberian rhubarb** plant to safely treat these symptoms.[7]

In preclinical studies, these plant compounds have shown greater affinity for the beneficial **estrogen receptor-*beta*** (ER-*beta*) than for potentially detrimental **estrogen receptor-*alpha*** (ER-*alpha*).[8]

Siberian rhubarb extract didn't activate ***ER-alpha***.[8]

The ability of **Siberian rhubarb** extract to selectively activate **ER-*beta*** but not **ER-*alpha*** is a key reason for its safety.[10]

Proven in Human Studies

In a double-blind clinical trial, 109 symptomatic perimenopausal women took **4 mg** of **Siberian rhubarb extract** or a **placebo** daily for three months.

Within **one month**, the Siberian rhubarb extract group had a significant reduction in the number and severity of **hot flashes**.

By nearly **three months**, they had a **54%** overall improvement in the severity of menopause symptoms, based on the **Menopause Rating Scale**.[11]

These results were confirmed in a similarly designed clinical trial of 112 perimenopausal women, which produced similar results, including an **83%** reduction in the median number and severity of daily **hot flashes**.[12]

After completing the first trial, the scientists continued to follow the women taking Siberian rhubarb extract for up to two years.[3]

WHAT YOU NEED TO KNOW

Natural and Effective Menopause Relief

- **Menopause** is marked by **11** common symptoms, including **hot flashes**, sleep difficulty, joint and muscle pain, mood disturbances, sexual problems, bladder issues, vaginal dryness, and more.
- Multiple human studies show that **Siberian rhubarb root extract** provides relief from ***all 11 symptoms*** on the Menopause Rating Scale and reduces overall symptom severity by up to **83%**.
- Siberian rhubarb extract has been widely used in Germany for **decades** and has an **excellent safety profile**, based on extensive clinical, preclinical, and lab studies.

The women had a remarkable ***83% reduction*** in the severity of menopause symptoms within the first year. This improvement was *maintained* during the second year of follow-up.[3]

In an open-label observational study, 252 symptomatic perimenopausal or postmenopausal women also took **4 mg** of **Siberian rhubarb extract** daily. After six months, **56%** reported *major improvements* and **13%** reported complete recovery from their symptoms.[13]

The *largest improvements* in symptom severity were for hot flashes, sleep problems, and irritability.[13]

In all these studies, Siberian rhubarb extract produced significant improvement in ***every one*** of the **11 symptoms** on the Menopause Rating Scale.[3,11-13]

Ending Hot Flashes

Hot flashes and night sweats affect up to **50%** of perimenopausal and up to **85%** of postmenopausal women.[14,15]

Hot flashes typically continue for **five to seven years**. Some women deal with them for ***15 years or more***.[1]

When 56 perimenopausal women took **4 mg** of **Siberian rhubarb extract** daily for three months, the median number of hot flashes dropped from **12** to just ***two*** per day. That's an astonishing **83% reduction**.[12]

The **placebo** group had a median **8%** *increase* in the number of hot flashes.[12]

That means Siberian rhubarb performed *better* than **conventional hormone replacement therapy**, which decreases the frequency of hot flashes by about **75%**.[16]

Easing Heart Discomfort

Hot flashes are more than just a nuisance. They are linked with an increased risk of **atherosclerosis** (the buildup of plaque in arteries) and **cardiovascular disease**.[17,18]

Hot flashes are also associated with **inflammation** and poor function of **endothelial cells**, which line blood vessels and promote proper expansion and blood flow.[18]

In addition, falling **estrogen** levels appear to be associated with the heart **palpitations** experienced by many during menopause.[19-21]

In vitro research indicates that the **rhaponticin** in Siberian rhubarb extract has **anti-inflammatory** properties. It may inhibit *enzymes* that produce inflammatory cytokines in endothelial cells.[22]

In placebo-controlled studies, **Siberian rhubarb extract** reduced heart complaints by as much as **60%**, on average, in about three months.[3,12]

Improving Sleep

Sleep problems, including difficulty falling asleep or staying asleep, tend to peak around the final transition to menopause.[23,24]

Several menopause-related factors can contribute to sleep issues, including hormonal changes, hot flashes, and night sweats.[24]

Clinical studies have shown that taking **Siberian rhubarb extract** daily decreases the severity of sleep problems by **60%-69%** in perimenopausal women.[3,12]

A review was done of 17 placebo-controlled trials that tested **botanical** products for the relief of menopause symptoms. **Siberian rhubarb extract** was one of the few remedies that improved sleep.[14]

Relief for Mood Disturbances

Shifting hormone levels during perimenopause are associated with a variety of mood disorders, including **depression**, **irritability**, and **anxiety**.[21,25-27]

In a placebo-controlled trial in 109 perimenopausal women,[26] the majority initially reported feelings of **depression**, including being "in low spirits mostly" or "up and down in spirits a lot."

After taking **Siberian rhubarb** daily for three months, **59%** of the women reported being "in good spirits mostly," and **9%** reported being "in very good spirits mostly."[26]

In the same study, the women taking Siberian rhubarb had a **66%** decline in **anxiety** scores on a recognized anxiety scale.

Research suggests **irritability** is the main mood challenge for women during perimenopause.[25]

In an open-label observational study lasting six months, women who took **4 mg** of Siberian rhubarb extract daily had large reductions in feelings of **irritability**.[13]

Siberian rhubarb may improve mood in several ways.

Both **estrogen** and **progesterone** have mood-improving properties. Their protective effects wane in menopause as hormone levels drop.[26,27]

Animal research suggests that **ER-beta** receptors play a role in mediating anxiety.[26] **Siberian rhubarb extract** may help by activating the **ER-beta** receptors.[26]

In addition, decreasing hot flashes and improving sleep can help improve mood as a side benefit.[24,28]

No More Exhaustion

Roughly **72%-84%** of menopausal women experience **physical** and **mental exhaustion**.[29,30]

These feelings are accompanied by a general decrease in physical and mental performance and concentration, as well as impaired memory, a decrease in concentration, and an increase in forgetfulness.[20]

When perimenopausal women took **Siberian rhubarb extract**, they had an average **57%** improvement in physical and mental exhaustion after *just three months*.[3]

After taking Siberian rhubarb daily for a year, their feelings of exhaustion had improved by an average ***73%***. This level of improvement was maintained for a second year of follow-up.[3]

Siberian rhubarb may achieve these results by interacting with **ER-beta receptors** in the brain, which are involved in memory and cognition.[31]

Countering Urogenital Changes

More than **50%** of postmenopausal women are affected by urogenital symptoms.[32]

These include:[20]

- **Bladder problems** (such as difficulty urinating, increased need to urinate, and incontinence),
- **Vaginal dryness** (which may lead to difficult or painful sex), and
- **Sexual problems** (including a change in sexual desire, activity, or satisfaction).

Perimenopausal women who took **Siberian rhubarb extract** daily for *three months* had a **50%-67%** reduction in severity of urogenital, sexual, and vaginal dryness symptoms, compared to baseline.[3]

Reducing Joint and Muscle Discomfort

Joint pain is more common among postmenopausal women than in men of the same age.[33]

When a group of 427 women aged 40-59 completed the Menopause Rating Scale, joint and muscle discomfort was one of the symptoms *commonly* rated as "**very severe**."[5]

The changes in reproductive hormones that accompany menopause are thought to play a role in the development of **osteoarthritis**, when the cartilage that cushions and protects the ends of the bones wears down.[21]

In placebo-controlled studies of perimenopausal women, taking **4 mg** of **Siberian rhubarb extract** daily for three months resulted in a **46%-50%** improvement in joint and muscle discomfort.[3,12]

Extensive Safety Data

In Germany, **6.7 million doses** of Siberian rhubarb extract are sold *annually*. Scientists have reviewed safety data collected there over two decades and concluded the extract is **safe**.[7]

Four human studies lasting up to two years found **no relevant safety concerns** (such as changes in breast or endometrial tissues) when women took **4 mg** of Siberian rhubarb extract daily.[3,11-13]

In addition, exposing both estrogen-sensitive and estrogen-insensitive breast cancer cell lines to **Siberian rhubarb extract** at a range of concentrations in the lab did *not* promote the proliferation of cancer cells.[34]

Toxicity research in animals found no uterus-stimulating effects or other signs of harm, even when Siberian rhubarb extract was given for three months, in a daily dose approximately ***14,000 times higher*** than the typical human dosage equivalent.[35]

Siberian rhubarb extract has been shown to be a safe, effective way to treat a range of symptoms associated with menopause.

Summary

Most women approaching or going through **menopause** suffer from symptoms like hot flashes, sleep disturbances, and mood changes.

Siberian rhubarb extract has been shown to be a clinically effective, safe, and convenient non-hormonal option for both perimenopausal and postmenopausal women.

Multiple human studies show that **4 mg** of Siberian rhubarb extract taken daily significantly improves all top **11 menopausal symptoms**, including hot flashes, sleep problems, depression and irritability, heart and joint discomfort, sexual problems, and vaginal dryness. •

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

Not All Extracts Are the Same

Based on studies presented, women who decide on a non-hormonal approach to menopausal symptoms should consider extracts of a *clinically studied form of* Siberian Rhubarb standardized to more than **54% rhaponticin** and more than **27% desoxyrhaponticin**.

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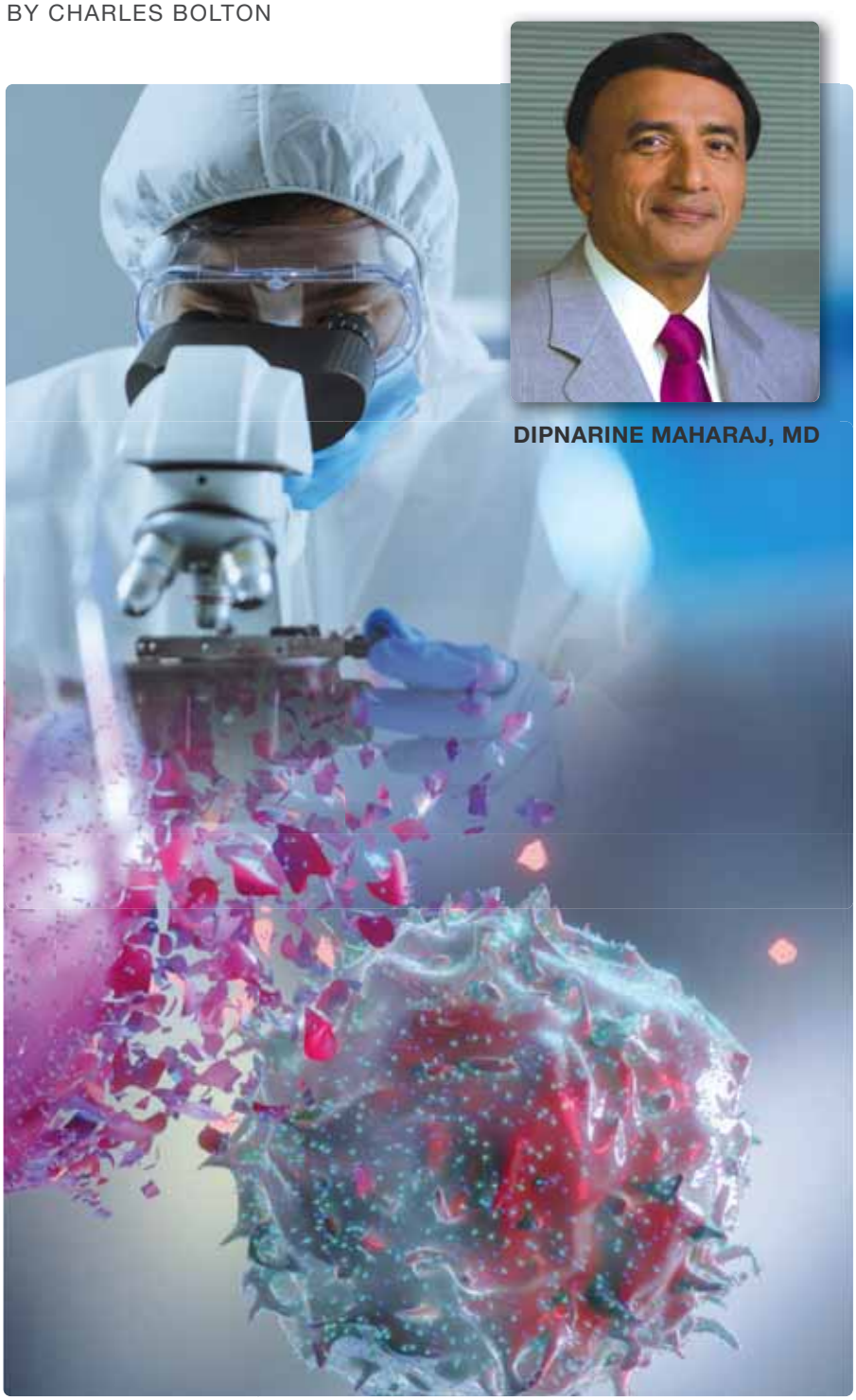
Complete Response in Patient Battling Refractory Leukemia

BY CHARLES BOLTON



DIPNARINE MAHARAJ, MD

The patient was running out of options.

She was suffering from a more aggressive type of **chronic lymphocytic leukemia** (unmutated IGHV gene).[1]

Conventional **chemotherapy** had been unsuccessful. Her prognosis was grim.

Clinician scientists with the **Maharaj Institute of Immune Regenerative Medicine** in Florida turned to one of the most promising new treatments in the war against cancer: **immunotherapy**.

By treating her with an **immune system stimulant** combined with personalized, targeted cancer therapy, these clinicians were able to **halt the patient's cancer** in its tracks.[1]

The ability to achieve **complete remission** with zero evidence of cancer remaining in the blood may represent a new treatment model for **chronic lymphocytic leukemia** and many other cancers.

A Common Killer

Leukemias are a group of related cancers that affect the cells of the blood or bone marrow.

Chronic lymphocytic leukemia (CLL) is the most common form of leukemia in adults.[1] Unlike acute leukemias, it does not progress rapidly–though for many it can still be fatal.[2]

In **2021**, the American Cancer Society estimates that **21,250 new cases** of CLL will be diagnosed, and around **4,320** patients will die from it.[3]

There are different kinds of chronic lymphocytic leukemia. The **unmutated IGHV** type is a more aggressive form. Even with treatment, patients typically have only **one to five years** of progression-free survival.[4]

One of the worst consequences of CLL is that it devastates the **immune system**.

Using Immunotherapy to Fight Leukemia

- **Chronic lymphocytic leukemia (CLL)** is the most common form of leukemia in adults. It has very low rates of remission or cure.
- This cancer causes defects in the patient's **immune system**, helping it evade detection and destruction by immune cells.
- **Immunotherapy** is a treatment that boosts a person's own immune system, helping it to target and attack cancer cells.
- **Clinician scientists** at the **Maharaj Institute of Immune Regenerative Medicine** in Florida successfully used immunotherapy in a female patient with CLL after conventional treatment failed.
- They used a synthetic form of **interleukin-2 (IL-2)**, a signaling protein that regulates immune function, to stimulate the immune system to destroy the cancer.
- They also used a cancer drug, **venetoclax**, at low doses to avoid side effects.
- The combination appeared to boost the effectiveness of treatment, sending the patient's cancer into **complete remission**.

For example, **natural killer (NK) cells** are a vital part of the body's defense against cancer. **NK cells** attack cancer cells directly *and* help to improve function of other immune cells. When working optimally, NK cells are able to control the spread of tumors.[5,6]

In **chronic lymphocytic leukemia**, the cancer weakens the immune system. This causes the loss of NK cell function.[7,8] As a result, NK cells are unable to exert their usual powerful anti-cancer activities.

New Hope from Immunotherapy

Immunotherapy has been at the forefront of recent advances in cancer treatment.

This therapy boosts the body's **own immune system**, improving its natural ability to find and destroy cancer cells.

Immunotherapy treatments are constantly being tested and approved. Physicians at the **Maharaj Institute of Immune Regenerative Medicine**, located in Boynton Beach, Fla., turned to one to treat a leukemia patient who had failed to respond to other therapies.[1]

A Novel Approach to CLL

The patient was a 56-year-old woman with **unmutated IGHV CLL**—a more aggressive type.

She was initially treated with a standard drug that targets leukemia. After suffering a severe adverse reaction, she had to terminate treatment.

The cancer appeared to go into remission. But about a year after stopping treatment, it was back.

The clinicians at the Maharaj Institute decided to use i**mmunotherapy** to ***stimulate the immune system*** to better fight against the cancer.

They opted to use a synthetic form of **interleukin-2 (IL-2)**.

IL-2 is a signaling protein produced in the body which regulates aspects of **immune function**. It is *essential* for the growth and activation of various immune cells, including **natural killer cells**.[9]

Once activated by IL-2, NK cell function gets a boost. These immune cells are more easily able to recognize threats, dramatically improving their ability to **kill tumors** and other abnormal cells.[9-11]

How the Treatment Worked

The patient was started on the **interleukin-2** combined with the cancer drug **lenalidomide**—at a much lower dose than usual, to minimize side effects.

After several cycles of this therapy, the number of cancer cells in the patient's blood *decreased*. But the cancer did not go into complete remission.

After some time, the physicians decided to try a different cancer drug along with the IL-2 treatment. Several cycles of **IL-2** and low-dose **venetoclax** were initiated.

Although venetoclax can be associated with severe side effects at *standard* doses, at **low doses** it is well tolerated. The patient did not have any significant negative effects during this treatment.

Prior studies have suggested that even at low doses, venetoclax can induce the death of CLL cancer cells.[12,13] In this case, the **IL-2** appeared to boost the effectiveness of the treatment, stimulating the patient's immune system to fight the cancer while also killing cancer cells.

The number of cancer cells in the blood dropped dramatically with this new therapy. Six months after treatment began, tests could find no evidence of cancer in the blood. The patient was in **complete remission**.

The therapy was discontinued, but follow-up testing **three months** and **nine months** later showed that the patient was still in remission, with zero evidence of cancer detected.

Adding a **low-dose** cancer drug like **venetoclax** appears to create a potent combination that kills cancer cells and repairs the immune system defects caused by the cancer.

Summary

Current treatments for **chronic lymphocytic leukemia**, the most common form of leukemia in adults, do not cure the disease and can cause serious side effects.

Cancer experts at the **Maharaj Institute of Immune Regenerative Medicine** used a novel approach that aims to improve the effectiveness of treatment while reducing the risk of serious side effects.

A woman with an aggressive form of CLL was treated with a combination of **immunotherapy** (with a form of the immune-stimulating protein IL-2) and a low dose of the cancer drug **venetoclax**.

The result was **complete remission** of the cancer with no signs of recurrence nine months after stopping treatment.

This preliminary report gives hope that this new treatment protocol can greatly improve the care of patients with chronic lymphocytic **leukemia** as well as other cancers. •

If you have any questions on the scientific content of this article, please call a Life Extension® Wellness Specialist at1-866-864-3027.

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A significant obstacle in patients gaining access to these therapies is that until the therapies receive **FDA approval** for the patient's specific indications, private insurance and Medicare typically do not pay for them.

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DR. THIERRY HERTOGHE

PART TWO

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In this exclusive two-part interview, **Dr. Hertoghe**, president of the International Hormone Society and the World Society of Anti-Aging Medicine, tells ***Life Extension***® how hormone therapy can help fight disease and promote longevity.

There are roughly **50** different **hormones** produced in the human body, controlling a wide range of functions.

In the previous interview, published in our last issue, **Dr. Hertoghe** spoke to ***Life Extension***® about how **hormone replacement therapy** can help prevent disease and promote longevity. In this follow-up, he discusses specific hormones, and the role nutrition plays, as well.

LE: Which hormones do you feel are the most important?

Dr. Hertoghe: **Melatonin** is one of my favorite hormones. It does much more than just improve sleep. High melatonin doses (**10 mg** to **30 mg** a day) can be safely applied in the first days after a **stroke** or **heart attack** and may markedly reduce the damage to the brain and heart and considerably improve recovery. Melatonin can also have profound anti-inflammatory effects and improve resistance against viral and bacterial infections. Melatonin also has a role in protecting against radiation, including electromagnetic and ultraviolet radiation. It reduces blood pressure and can calm excessive anxiety, especially at night, substantially decreasing anxious thoughts and restless legs.

Melatonin has even been shown to have powerful anti-cancer effects and can be used as an important adjuvant treatment (alongside the primary treatment) in various types of cancer. One of the most surprising effects is in rejuvenating the skin when applied topically as a cream. It improves the skin coloring, reduces pigment spots, and thickens the skin.

DHEA is the most abundant hormone in our blood. One often overlooked but important role it plays in the body is to protect us against any side effects of **cortisol**. Cortisol is our most essential hormone—if we stop producing it, we die within 24 hours! But it is so powerful that we need to have equivalent amounts of protective DHEA in our body to block any adverse effects of cortisol. When given alone, DHEA improves mood and quality of life and reduces anxiety. Particularly in women, DHEA may also improve muscle tone—especially in the abdomen—while mildly reducing fat mass and increasing bone mass.

Testosterone is another one of my favorite hormones. I recently wrote a book on testosterone therapy for men called ***Testosterone, the Therapy for Real Gentlemen***. It is, in my experience, an amazing treatment not only for men, but also for women. Testosterone usually increases energy levels all day long. It particularly reduces sports fatigue, making men and women more resistant to exhaustion from physical exercise and activities. It can improve mood and reduce anxiety. Testosterone also improves the bones and is one of my treatments for acute stroke and to protect the heart.

LE: What do you have to be careful about when prescribing hormones?

Dr. Hertoghe: **Balancing hormones** means being careful not to give too much of one hormone, while assuring that enough of *another* hormone is given so that the treatment works safely and efficiently. The right balance is often achieved, in consultation with a physician, after a period of trial and error.

Take, for example, balancing the female hormones. Women need **estrogens** to protect their brain from Alzheimer's disease, their heart and arteries from atherosclerosis, and their bones from osteoporosis. But if the estrogen hormone **estradiol** becomes predominant, women suffer from fluid retention, particularly on the breasts and abdomen. They may develop breast and ovarian cysts and uterine fibroids, and ultimately cancer in these areas. In contrast, the other main female hormone, **progesterone**, protects against estradiol predominance. A woman may safely take estrogens and obtain blood levels that equal those of healthy young women if she also takes sufficient amounts of **natural progesterone**.

Similarly, **testosterone** is one of the best treatments to protect the heart. But it may excessively convert to the potent estrogen **estradiol**, which at high levels has deleterious effects on the heart and arteries by blocking testosterone receptors. High estrogen levels also enlarge the prostate. For this reason, men who receive testosterone should regularly have their estrogen levels checked. Whenever these levels excessively increase, it might be necessary to add a natural or synthetic **aromatase blocker**, which blocks excessive conversion of testosterone to estradiol, to ensure safety for the heart, arteries, and prostate.

LE: What is the most unusual condition you have treated through hormone replacement?

Dr. Hertoghe: We have treated several **eyesight** problems with local hormone injections. Hormone replacement has helped treat autism in children, stabilize Parkinson's disease, reverse some paralysis of one hand three years after a stroke, improve heart condition after three heart attacks, and more. However, the most impressive improvements are usually found in patients with psychiatric disease, such as severe **depression** and **anxiety** disorders.

In fact, the entire body is under the influence of hormones. If a chronic problem appears in any part of the body, the local disorder may not improve without adequate hormone therapy, sometimes administered locally. For example, if you have a wound that does not heal many weeks after surgery, it may be due to a lack of anabolic hormones. One solution is to apply a thin layer of transdermal **testosterone** locally, which substantially accelerates healing, so that after five to seven days the wound may be healed.

LE: You also focus on **nutritional supplements** in your practice in Belgium. How do you use them therapeutically?

Dr. Hertoghe: I prescribe at least as many nutritional supplements as hormone supplements to my patients. Nutritional supplements, such as magnesium, zinc, copper, iron, selenium, fatty acids, vitamins A, B9, B12, D, and E, are given after a blood test shows a low or low-to-normal level. The lab does not test nutrients such as carnitine, which provides energy and improves the body composition, and

the sleep supplements tryptophan and 5-hydroxy-tryptophan, so I may recommend patients take those solely based on their complaints.

In most cases, I start by prescribing the nutritional supplements for six months. If levels are, after this period, normalized in a blood test, the patient may stop the treatment. Some nutritional supplements, such as magnesium, carnitine, and tryptophan, may need to be taken permanently, as the diet or patient may be permanently depleted in these nutrients.

LE: How do you think medicine will change in the next decade?

Dr. Hertoghe: There will be a greater attention to hormonal and nutritional therapies. I also believe that **stem cell** therapy and supplementation with stem cell activators will develop more in the future. They may, for example, be used to regenerate brain areas and regrow teeth. Also, physicians in the future are going to treat more with organ specific peptide therapies (small amino acid chains with restorative properties) such as **follistatin**, which strongly improves muscle tone and volume. I think that **telomerase activators**, which reverse the shortening of our telomeres (the ends of our chromosomes that shorten at each cell division) also have a place in the future. In general, we will see much more focus on prevention of disease and aging, not just treating symptoms. •

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

Dr. Thierry Hertoghe practices medicine at his clinic in Brussels, Belgium, where he specializes in using hormone treatments and nutritional therapies to fight disease, optimize health, and promote longevity. He is president of the International Hormone Society and the World Society of Anti-Aging Medicine.

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References
1. *Front Microbiol.* 2016;7:1204.
2. *Korean J Nutr.* 2007;40(2):154-61.

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SALMON

BY LAURIE MATHENA

References
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Salmon is truly deserving of the term *superfood*. Studies show that eating salmon can help prevent heart disease and age-related memory loss, and key compounds in salmon could also help you *live longer*.

Eating salmon on a regular basis has been shown to improve risk markers of cardiovascular disease.[1]

Consuming more fatty fish, like salmon, has also been associated with a reduced risk of impaired cognitive function in middle-aged adults.[2]

Salmon contains numerous compounds that likely contribute to its health benefits.

For example, it is one of the best food sources of beneficial omega-3 fatty acids (second only to chia seeds). Diets high in omega-3 fatty acids have been linked to a reduced risk of cardiac and sudden death, and a reduced risk of **all-cause mortality**.[3]

Astaxanthin, the carotenoid that gives salmon its signature pink color, helps reduce the risk of heart disease by reducing the oxidation of LDL cholesterol and increasing HDL (good) cholesterol.[4]

Salmon can be pan-seared, baked, or poached. It pairs well with side dishes like asparagus, roasted broccoli, and lemon-herb couscous.

As with other foods, cooking at lower temperatures protects the proteins in the food against damage that injure your body's proteins via a toxic process known as glycation.

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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
00065 MK-7
00373 No Flush Niacin
01939 Optimized Folate (L-Methylfolate)
01217 Pyridoxal 5'-Phosphate Caps
01400 Super Absorbable Tocotrienols
02334 Super K
02335 Super K Elite
01863 Super Vitamin E
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

00658 7-Keto® DHEA Metabolite • 25 mg, 100 capsules
02479 7-Keto® DHEA Metabolite • 100 mg, 60 veg capsules
01509 Advanced Anti-Adipocyte Formula
01807 Advanced Appetite Suppress
02207 AMPK Metabolic Activator
01492 Calorie Control Complex with Phase 3™ and African Mango
02478 DHEA Complete
01738 Garcinia HCA
01292 Integra-Lean®
01908 Mediterranean Trim with Sinetrol™ -XPur
01432 Optimized Saffron
00818 Super CLA Blend with Sesame Lignans
01902 Waist-Line Control™
02151 Wellness Code® Appetite Control

WOMEN'S HEALTH

01942 Breast Health Formula
01626 Enhanced Sex for Women 50+
01894 Estrogen for Women
01064 Femmenessence MacaPause®
02204 Menopause 731™
02319 Prenatal Advantage
01441 Progesta-Care®
01649 Super-Absorbable Soy Isoflavones

Restore Youthful Cellular Energy with PQQ

PQQ (*pyrroloquinoline quinone*) activates genes involved in the production of cellular energy.[1-5]

Studies show **PQQ** supports heart health and cognitive function, complementing CoQ10.[6,7]

In fact, just **20 mg** per day of **PQQ** plus **CoQ10** promotes memory and attention in aging individuals.[8]

This formulation contains **20 mg** of **PQQ** per capsule, which is the recommended daily dose.

For full product description and to order **PQQ** or any other **PQQ-containing formulas**, call 1-800-544-4440 or visit www.LifeExtension.com

Item #01647 • 30 vegetarian capsules

1 bottle **$24** • 4 bottles $18 each

GLUTEN FREE · 1 DAILY · NON GMO LE CERTIFIED

Also available are **10 mg PQQ caps** (Item #01500) and **100 mg Super Ubiquinol CoQ10 with PQQ** (Item #01733).

References

1. *Alt Med Rev*. 2009; 14(3):268-77.
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CoQ10

When Your Energy Matters Most

When every second counts, you need to make sure energy levels are up for any task. **Super Ubiquinol CoQ10 with Enhanced Mitochondrial Support™** can help.

Formulated with a highly absorbable form of CoQ10 and a patented delivery system, our best-selling CoQ10 formula promotes your heart health and your body's youthful cellular energy production, so you can get the job done.

GLUTEN FREE

NON GMO LE CERTIFIED

Item #01426 • 100 mg • 60 softgels

1 bottle **$46.50** | 4 bottles $39 each

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

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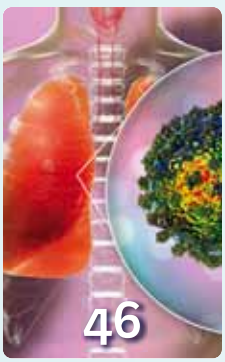

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