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LifeExtension.com

June 2020

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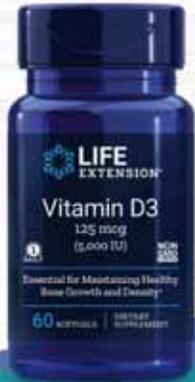
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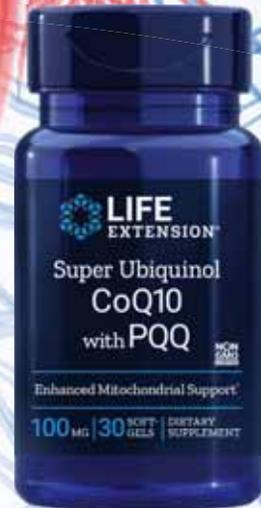
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My Approach to Healthy Immunity

The Wall Street Journal recently published an article titled, "Who Are You Calling Elderly?"¹



WILLIAM FALOON

The article described people over **age 60** who are appalled at being branded "**elderly**" as it relates to their **immunity**.

These individuals go to great lengths to prevent degenerative disease by making the right dietary choices, exercising, and even competing in triathlons. They also do not outwardly appear "**elderly**."

What they don't realize is that despite healthy lifestyles, **aging** is often accompanied by marked declines in **immune function**.

An example of these **immune deficits** is **reactivation** of the **chickenpox virus** that causes painful **shingles** outbreaks as people age past **45 years**.

A more insidious impact of age-related **immune impairment** is a *higher* rate of **cancer**, severe **influenza**, and **pneumonia**.

In the elderly, **vaccinations** can fail because of inability to generate a robust **antibody** response.

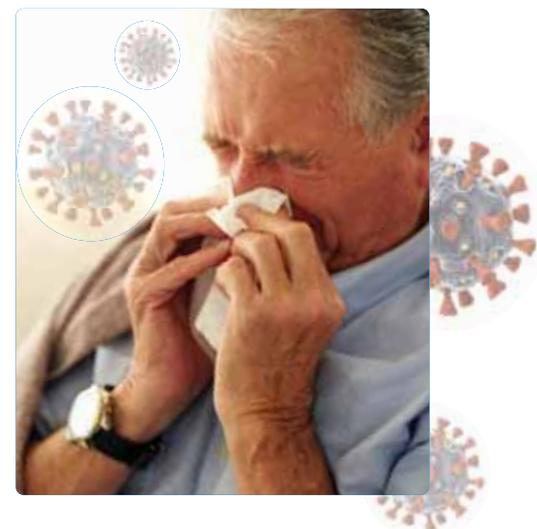
The realization about **immune senescence** has been brought to the forefront by the current viral pandemic.

More serious complications and deaths occur in **older** persons compared to younger people with healthier **immune function**.

While antiviral treatments are being investigated, **immune senescence** remains a major impediment.

Most of you already take steps to help protect **immune function** by supplementing with **vitamin D**, **vitamin C**, **zinc**, **melatonin** and **DHEA**.

I describe in this editorial what I have personally done to maintain healthier **immunity**.



Don't Wait for Full-Blown Illness to Manifest

People often wait until they are very sick before seeking treatment for a flu or common cold virus. In some cases, treatment delay can be lethal.

I have found enormous personal benefit by taking aggressive action at the onset of the very first cold-flu symptom.

I take strong proactive measures when I have mild symptoms the way some people do after they have suffered days of agonizing flu virus miseries.

My strategy is to not let the virus gain a foothold inside my cells.

Up until now, my approach has succeeded: I have not suffered more than a day of significant cold or flu symptoms since **January 1983**.

I am going to explain my personal program, but the key point is that you should immediately address the very first symptom of a cold-flu viral infection like it is the most lethal agent you have ever encountered.

This approach may be analogized to dropping a nuclear bomb when conventional weapons might be adequate.

While some people wait until full-blown viral symptoms manifest, I don't have that option.

Life Extension® is a 24-hour-a-day operation with no room for down time. I can't call in sick just because a **virus** has invaded my body.

The box on this page describes **antiviral drugs** that are effective when administered soon after onset of cold/flu symptoms.

This same strategy may hold true for certain **nutrients** that must be initiated upon the very first symptom of a common flu or cold virus.

My immediate-attack strategy may also be important before *any* virus infects too many cells, though the culprit behind the current pandemic is too new to know this yet.

Unleashing the Nuclear Bomb

I maintain an intense schedule with exposure to many people, yet I have gone **37 years** without



suffering a serious cold-flu viral infection.

On top of that, I have genetically defective **bone marrow** that killed my brother at age 22 and has caused chronic illnesses in another family member.

While it would be convenient to credit the many supplements I take, it seems more likely that my success avoiding acute illness is a result of the aggressive protocol I initiate as soon as I feel that a **viral** infection may be taking hold.

Published scientific studies substantiate the benefit of the components of my immune-boosting regimen but there have been no clinical trials to support the efficacy of my entire protocol.



One-Pill Protection Against Common Flu Viruses

If you contract the flu this year, you might want to initiate a **drug** called **XOFLUZA®**.

This new antiviral drug is approved to treat Influenza A and Influenza B with just a single pill that costs around **\$150**.

Some preclinical studies show XOFLUZA® is effective against certain **avian viral** strains like H7N9 and H5N1.²

XOFLUZA® functions via a different mechanism than **Tamiflu®**, which is important because some flu viruses have developed resistance to Tamiflu®.^{3,4}

XOFLUZA® is not effective against **coronavirus**.

Antiviral drugs like XOFLUZA® are effective against common flu virus strains, but only when they are initiated within **24-48 hours** of the manifestation of symptoms.⁵

I'll discuss some of the research that supports my rationale, but here are the *drugs, nutrients, and hormones* I take as soon as the first symptom of common cold or flu manifests:

- **Cimetidine** (Tagamet®) – **800 mg-1,200 mg** each day. This drug is sold over the counter in pharmacies to combat heartburn. It has a beneficial side effect of boosting immune function by activating natural killer cells and reducing T-suppressor cells.⁶ This helps the **immune system** function more efficiently.

Cimetidine is sold over the counter, but it is wise to read the package insert in case this drug is contraindicated for you—for instance, if you have kidney problems.

For most people, cimetidine provides a powerful immune stimulation that is particularly effective against certain viruses. The brand name of **cimetidine** is **Tagamet®**, but the generic (cimetidine) costs less.

- **High-allycin garlic extract** – **6,000 mg-9,000 mg** once or twice a day. This potent form of garlic will cause painful stomach-esophageal burning if you don't eat food right afterward. The high intake of this kind of garlic will cause you to reek of a strong sulfur odor but saturating the body with this pungent garlic is the objective. Garlic has shown direct viral-killing effects in several published studies.^{7,8}

- **DHEA** – **50 mg-200 mg** early in the day. Doses over **25 mg** a day are much higher than normal, but DHEA has shown some benefits in boosting one's ability to mount a stronger immune response and also protecting against over-active inflammatory cytokine responses that can occur when your immune system hyper-reacts to viral infections.⁹

- **Lactoferrin** – **300 mg-1,200 mg** a day. This natural constituent of mother's milk boosts natural killer cell activity and can prevent certain viruses from binding to cell membranes and entering the cell, where they replicate.¹⁰

- **Zinc acetate lozenges** – one to two **18.5 mg** lozenges every two waking hours. Please be aware that this is a very **high dose** of zinc and is considered toxic if taken over the long term.^{11,12} You should **only** do this for a few days. Zinc lozenges have shown a direct effect of inhibiting the ability of certain cold viruses to latch on to the cells in the back of your throat where they multiply and can descend into your lungs to potentially cause pneumonia.¹⁰

- **Melatonin** – high dose of **10 mg-50 mg** at bedtime. Melatonin induces a potent immune response and this high dose can facilitate the deep sleep one often needs to fend off an infection. This dose of melatonin may make you extremely tired, so please only take this before bedtime

and do not operate any machinery or vehicles after ingestion.¹³

- **Aged garlic extract** – **3,600 mg** a day. There are unique immune-boosting compounds in **aged garlic** that work differently than those found in the high-allycin garlic.¹⁴ So I take both aged garlic extract and high-allycin garlic extract when I am concerned about viral infections.
- **Whey protein concentrate** – **2-4 scoops** a day to provide a glutathione boost and can ramp up vital **antibody** responses.

I take the above doses when I develop *any* symptom that may signal the beginning of a flu or cold in addition to the supplements I use every day.

My daily personal program probably closely resembles what most of you do, such as taking over **5,000 IU** of **vitamin D3** to maintain optimal blood levels.

As you might expect, I also take high-potency multi-vitamins, CoQ10, curcumin and other plant extracts, along with several grams of vitamin C, and more.





Garlic's Unsung Benefits

With all the high-tech medical advances occurring, **garlic** would appear to be a relic of the past. Yet the scientific literature documents that garlic has powerful effects against certain viruses.

For instance, a study tested one capsule daily, from November through February, of an allicin-containing **garlic** supplement on a group of 146 people.⁸ Half the group received the **garlic** while the unfortunate other half got a **placebo**. The placebo group suffered **63% more** common cold infections compared to the garlic group.

Even more significant, those in the **garlic** group who did catch a cold only suffered symptoms for an average of **1.52 days** compared to **5.01 days** for the **placebo** group. This placebo-controlled study corroborates the benefits I have personally derived by taking much **higher** doses of high-allicin garlic as soon as cold or flu symptoms present.

The conclusion of the doctors who conducted this garlic study was,

“An allicin-containing supplement can prevent attack by the common cold virus.”

Considering the number of people afflicted with a **common cold** each year, you would think this would have been the lead news story of the day. Instead, this study

has remained buried in a scientific journal while the medical establishment still says,

“there is no cure for the common cold.”

Ribavirin is a prescription drug that has broad-spectrum antiviral effects.¹⁵⁻²¹

Yet a Chinese study showed that at least in the test tube, **garlic** is more effective than **ribavirin** in inhibiting viruses that attack the intestinal tract.²² **Life Extension** has recommended **ribavirin** to treat various viral infections since the early 1980s. In this study **garlic** was shown to be superior.

Aged Garlic Extract

Garlic contains compounds that enhance beneficial proliferation of immune T-cells and function of natural killer (NK) cells.²³⁻²⁶

Aged garlic extract contains little **allicin**, which is one of the reasons it is sold as “odorless”. An impressive volume of data supports the **antiviral** and **immune-enhancing** properties of **aged garlic extract**.

A randomized, double-blind, placebo-controlled intervention study recruited 120 healthy subjects (60 per group) to determine the effect of **2,560 mg** a day of **aged garlic extract** supplementation on immune cell proliferation and cold and flu symptoms.²³

In individuals who consumed an encapsulated **aged garlic extract**, T-cells and NK-cells showed more robust proliferation, compared to individuals who received **placebo**.

After 90 days of supplementation, illness diary entries showed that the incidence of colds and flu, a secondary outcome, were not statistically different. However, the group consuming the **aged garlic extract** was reported to have:

- Reduced severity as noted by a reduction in the number of symptoms reported (**21%** fewer).
- A reduction in the number of days (by **61%**) and incidences (by **58%**) on which the subjects functioned sub-optimally.
- A reduction in the number of work/school days missed due to illness (by **58%**).

The researchers who conducted this study concluded that the results

“suggest that supplementation of the diet with aged garlic extract may enhance immune cell function and that this may be responsible, in part, for reduced severity of colds and flu.”²³

For several years, manufacturers of garlic supplements debated as to which **form** (high-allicin or aged garlic) was most effective.

I have concluded, after reviewing the studies on the immune properties of garlic, that each form has unique antiviral and/or immune-enhancing properties, which is why I supplement with both forms when cold or flu symptoms manifest.^{8,14,27-30}

Low-cost garlic may be an effective weapon against certain viruses.

The Life-Saving Side Effect of a Heartburn Drug

Tagamet® is the brand name of what used to be the most popular drug to treat heartburn. You've likely seen hundreds of commercials on TV for Tagamet®.

Now that it is off patent, we refer to Tagamet® by its generic name "cimetidine."

A little-known side effect of *cimetidine* is that it inhibits the overproduction of T-suppressor cells.⁶ In doing so, it boosts immune function by preventing the immune system from prematurely turning itself down.

Cimetidine has shown other immune-modulating effects such as increasing natural killer cell activity and boosting levels of natural immune stimulants *interleukin-2* and *gamma interferon*.³¹⁻³⁴ Human studies demonstrate cimetidine's efficacy against herpes and viral warts.³⁴⁻³⁸

Cimetidine is safe for most people to take on a limited basis.³⁹ Typical antiviral doses of **800 mg-1,000 mg** at night (or **200 mg** three times a day and then **400 mg** at night) appear to be an effective way to temporarily turn up the immune system.

Cimetidine in **200 mg** tablets can be purchased over the counter at pharmacies. The directions in the over-the-counter package insert say that up to **400 mg** a day is safe, but some published studies where cimetidine is used as an antiviral agent have used over **1,000 mg** a day.⁴⁰

Mother's Milk

It is well known that infants obtain protection against certain infections from components contained in mother's milk. One such component is **lactoferrin**, which has documented immune-potentiating effects.⁴¹⁻⁴³

Lactoferrin may stimulate macrophages, which in turn may help to induce cell-mediated immunity.⁴² Although many of the studies are on animals, **lactoferrin** is naturally present in many **mucous membrane** secretions in humans, suggesting an inborn **human** antimicrobial function.^{10,43}

One study showed that **lactoferrin** inhibits viral infection by interfering with the ability of certain viruses to bind to cell receptor sites.⁴⁴

This is of unique importance because many viral infections are contracted in the **mucous membranes** of our nasal passages and then move into our throats and lungs where they infect cells and initiate rapid proliferation.

Immune-Boosting Hormones

Dehydroepiandrosterone (**DHEA**) and its metabolites have demonstrated immune-enhancing and antiviral effects.⁴⁵⁻⁴⁹

The administration of **50 mg** a day of DHEA to nine elderly men who had baseline DHEA levels well below those of young

adults resulted in the following **immune enhancements** compared to placebo.⁵⁰

- Increase of **29%** in the number of B immune cells
- Increase of **62%** in B-cell activity
- Increase of **40%** in T-cell activity
- Increase of **50%** in interleukin 2
- Increase of **22% to 37%** in natural killer cell number
- Increase of **45%** in natural killer cell activity

One reason that **influenza** can be lethal to aging people is that their immune systems are weakened. A deficiency in **DHEA** may be partially responsible for the age-related decline in immune function.⁵¹

One study showed that a metabolite of DHEA augmented activation of **T-helper** cells and protected mice from a lethal influenza viral infection.⁴⁹



Melatonin's Immune-Boosting Effects

Melatonin has been specifically shown to decrease viral load and prevent death in mice infected with certain viruses. The conclusion of one melatonin study was:

“The immunomodulatory, anti-oxidant, and neuroprotective effects of melatonin suggest that this indole must be considered as an additional therapeutic alternative to fight viral diseases.”⁵²

Another study examined the immune function benefits of melatonin and found that melatonin activated **interleukin 2** and **gamma interferon** which facilitate natural killer cell activity and T-helper cell production.⁵³

Taking higher-dose **DHEA** in the **morning (50 mg-200 mg)** and higher-dose **melatonin (10 mg-50 mg)** before **bedtime** would appear to be a logical approach when battling a viral infection.

Preventing Viruses from Lodging in Points of Entry

Several published studies show that if **zinc lozenges** are taken within **24 hours** of the onset of common cold symptoms, the severity and duration of cold miseries are diminished.⁵⁴⁻⁵⁷

Rhinoviruses is the medical term for viruses that cause the common cold.

Rhinoviruses attach to cell receptor sites in sinus and throat tissues, become lodged in nose-throat cells, and then replicate out of control.⁵⁸ By binding to the same cell receptor sites as do cold viruses, **zinc** can inhibit the ability of rhinoviruses to take hold in the body.

A meta-analysis of the published literature on **zinc lozenges** was conducted and the conclusion of the report was:

“Clinical trial data support the value of zinc in reducing the duration and severity of symptoms of the common cold when administered within 24 hours of the onset of common cold symptoms. Additional clinical and laboratory evaluations are warranted to further define the role of ionic zinc for the prevention and treatment of the common cold and to elucidate the biochemical mechanisms through which zinc exerts its symptom-relieving effects.”⁵⁴

The key here is to suck on one or two **18.5 mg zinc acetate** (or gluconate) lozenges at the very first symptom of a cold and continue doing so about every two waking hours.

Once rhinoviruses bind to their receptor sites in the nasal tissues and begin replicating, **zinc lozenges** lose their efficacy. Considering how inexpensive **zinc lozenges** are, it makes sense to keep them in the medicine cabinet so that they are immediately available if cold symptoms manifest.

While less than **100 mg/day** of zinc can improve immune function, zinc should not be consumed in amounts greater than **300 mg/day** for more than a day or two, to avoid excessive zinc levels that might suppress immune function.

Lots More to Learn...

Major clinical advances have been made in fields such as cardiology, where sudden **heart attack** deaths plummeted **50%** between the years **1980 to 2014**.

The **Shingrix®** vaccine has been recommended to me by several





respected doctors. So I took this vaccine at age 64 to prevent a **shingles** outbreak that can have immune-damaging effects by exhausting naïve T-cell populations.

Hepatitis C is now largely curable with several different drug options such as **Sovaldi**[®], which was initially priced at \$1,000 per pill. To cure hepatitis C viral infections, 84 **Sovaldi**[®] pills are usually needed plus **ribavirin**.

Effective treatments remain elusive for **common viruses** such as herpes simplex-1, herpes simplex-2, herpes zoster (shingles), Epstein-Barr, cytomegaloviruses, influenza, rhino (common cold) viruses, and the new coronavirus sweeping the world.

As of this writing, several therapies appear promising against coronaviruses, but none has been thoroughly validated.

What we do know is that *younger* people with healthy **immune systems** are less likely to suffer severe effects and death from viral infections.

A “healthy” immune system quickly recognizes a viral invader, mobilizes a coordinated attack, and then “turns off” when its work is done, to avoid damaging healthy tissues.

Failure to “turn off” an over-active immune response is a leading cause of death in elderly persons who suffer bacterial and/or viral infections.

Combat Immune Senescence

In this month’s issue we describe some natural approaches to improve immune function. None of what we publish should be construed as a preventative or treatment for the viral infections plaguing today’s world.

I use these immune-supporting compounds because they have demonstrated varying degrees of efficacy in peer-reviewed published studies.

My hope is to not only ward off flu infections, but also reduce my risk of cancer due to the weakened immune function caused by normal aging and genetic predisposition.

Despite being outwardly healthy, **immune senescence** often begins by **age 50 or 60 years**, making us more vulnerable to infectious diseases, malignancies and chronic inflammatory disorders.

Please know that **Life Extension’s** network of physician-scientists are working around the clock to identify and validate methods to rapidly regenerate immune functionality and we will provide that information to our many supporters.

As I wrote in the opening of this editorial, most of us over **age 40-50 years** have less-than-optimal immunity. Aggressive measures are urgently needed to restore youthful immune responses.

For longer life,

William Faloon, Co-Founder
Life Extension[®]

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In the News



Lactoferrin Helps Fight Infectious Diseases

Lactoferrin is a glycoprotein that plays an important role in the **immune system**.

Research has shown that lactoferrin has **antiviral activity** against viruses such as rotavirus, herpes, and HIV—and against **respiratory viruses** like respiratory syncytial virus (RSV).¹

Now, research published in the *Journal of Microbiology, Immunology, and Infection* has found that lactoferrin can help attenuate **infectious diseases**.²

In this randomized, double-blind, placebo-controlled study, 290 healthy adults took either **200 mg** of lactoferrin, **600 mg** of lactoferrin, or a placebo for 12 weeks.

Both lactoferrin doses reduced the duration of infectious diseases (including cold sores, gastroenteritis, and styes) and the summer cold.

Editor's Note: Lactoferrin is known to have some immunostimulatory effects such as enhancing the production of secretory immunoglobulin A (sIgA), the phagocytic capacity of neutrophils, and the cytotoxicity of natural killer (NK) cells.

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Cancer Patients' Vitamin D Supplementation Associated with Better Survival Rate

Cancer patients who supplemented with vitamin D had improved survival rates, according to a meta-analysis reported in the *Journal of Clinical Oncology*.*

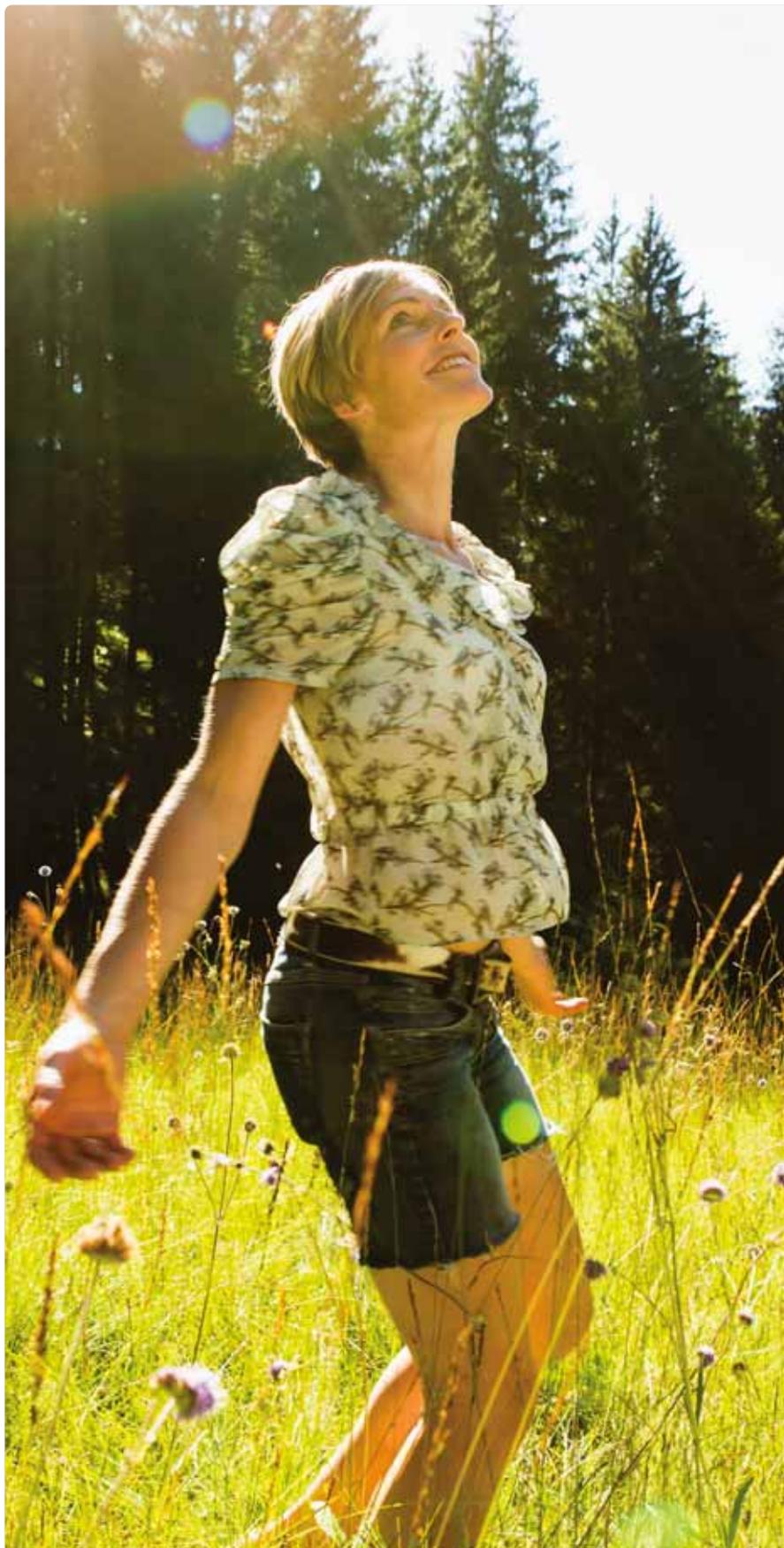
For their analysis, the researchers selected 10 randomized, controlled trials that included a total of 79,055 cancer patients. Trials compared the effects on cancer incidence and mortality of at least three years of vitamin D supplementation, and with a placebo.

The analysis showed that vitamin D supplementation was associated with a **13%** lower risk of dying from cancer compared with taking a placebo.

“Vitamin D had a significant effect on lowering the risk of death among those with cancer,” said coauthor Tarek Haykal, M.D. “The difference in the mortality rate between the vitamin D and placebo groups was statistically significant enough that it showed just how important it might be among the cancer population.”

Editor's Note: Cancer is the second leading cause of mortality in the U.S., the authors noted.

* *J Clin Oncol*. 2019; 37 (15_suppl): 1534.





Meta-Analysis Supports Use of Quercetin for High Blood Pressure

A meta-analysis published in *Nutrition Reviews* concluded that there is a beneficial role for quercetin supplementation in people with high blood pressure.* Quercetin is a flavonoid found in apples, onions, tea and other plant foods.

The meta-analysis included 17 trials that involved a total of 896 participants, many of whom were at risk of cardiovascular disease. Trials compared the effects of quercetin or a quercetin-rich extract to a placebo or no treatment for periods ranging from 2 to 12 weeks. In addition to blood pressure, plasma lipids and glucose and/or insulin were measured at the beginning and end of the studies.

Pooled results of 13 treatment arms revealed an association between quercetin supplementation and reduced blood pressure. Quercetin administration was associated with a **3.09 mmHg** average reduction in systolic blood pressure and a **2.86 mmHg** reduction in diastolic pressure. A decrease in triglycerides and increase in HDL cholesterol levels occurred among participants who consumed quercetin for eight or more weeks.

Editor's Note: The authors concluded that, "Quercetin intake resulted in significantly decreased blood pressure in humans. Moreover, participants who consumed quercetin for eight weeks or more showed significantly changed levels of high-density lipoprotein cholesterol and triglycerides in trials with a parallel design."

* *Nutr Rev.* 2020 Jan 6.

Optimism Reduces Cardiovascular Risk

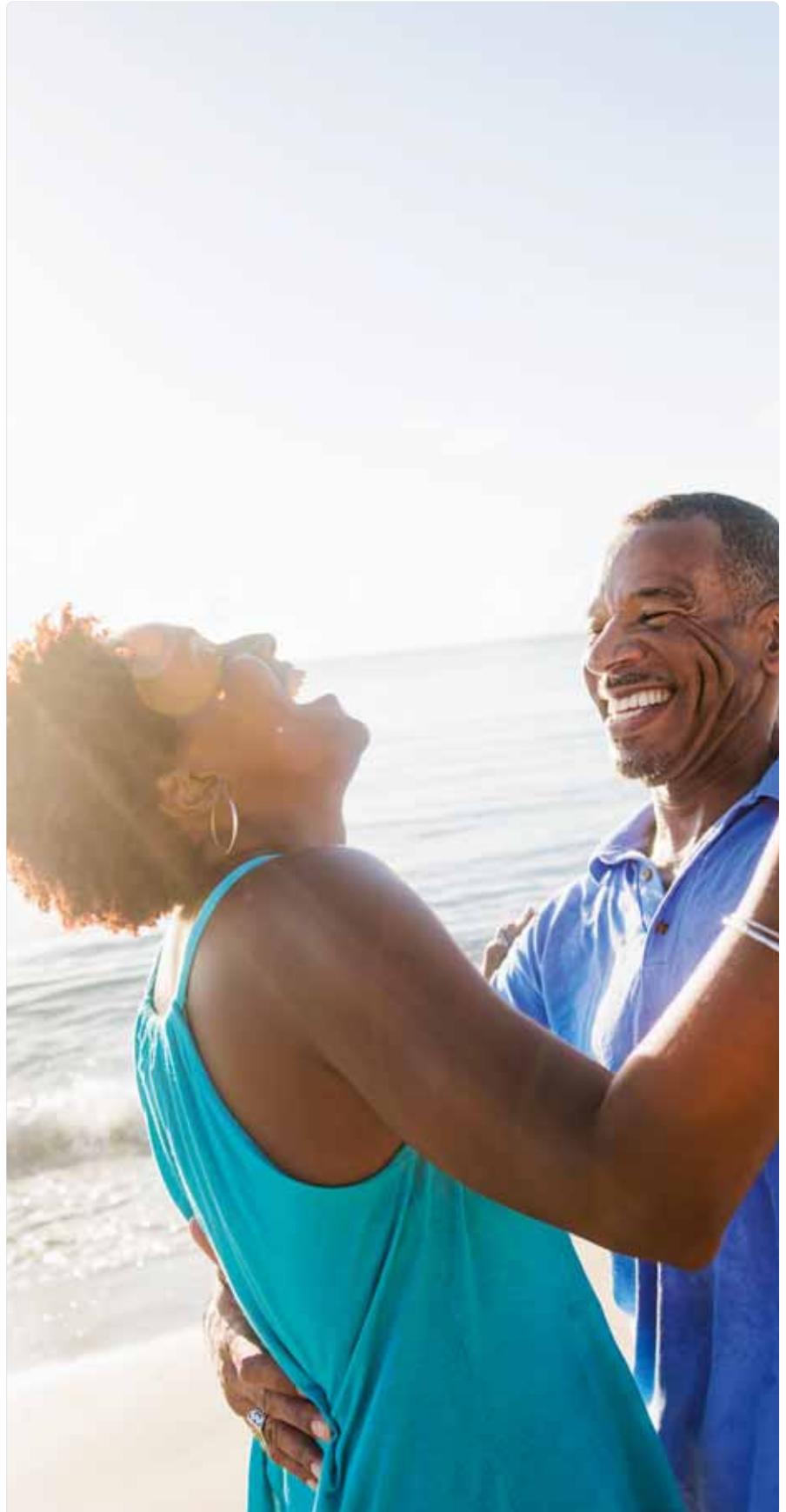
Optimism is associated with a reduced risk of cardiovascular events and all-cause mortality, according to a study published in the journal *JAMA Network Open*.*

Researchers conducted a meta-analysis of 15 studies, including nearly 230,000 people. They found that optimism was associated with a **35% reduced risk of cardiovascular events** and a **14% reduced risk of all-cause mortality**.

Cardiovascular events included fatal cardiovascular mortality, nonfatal myocardial infarction, stroke, and new-onset angina.

Editor's Note: "Future studies should seek to better define the biobehavioral mechanisms underlying this association and evaluate the potential benefit of interventions designed to promote optimism or reduce pessimism," the authors concluded.

**JAMA Netw Open*. 2019;2(9):e1912200.



Metformin Reduces Acne in Women with Polycystic Ovarian Syndrome

Metformin reduces the severity of acne in women with polycystic ovarian syndrome (PCOS), according to a study published in the *Journal of Clinical and Aesthetic Dermatology*.*

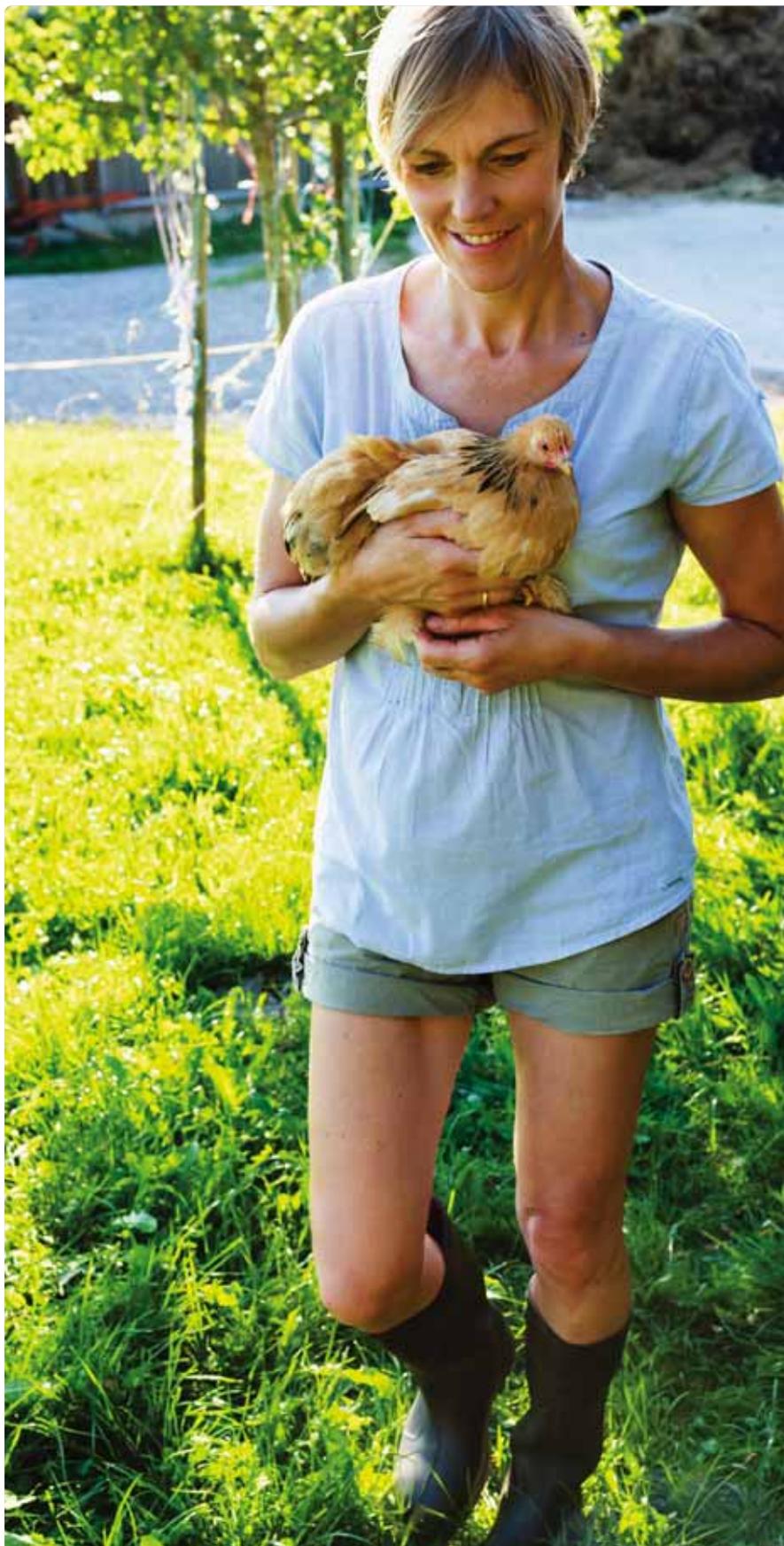
PCOS is a hormonal disorder that can cause hyperandrogenism (high levels of male hormones), which can contribute to acne.

For the study, 40 women with PCOS and acne were given **500 mg** of metformin three times a day for eight weeks.

The results showed that metformin significantly reduced the severity of acne in patients with PCOS by reducing ovarian hyperandrogenism.

Editor's Note: The researchers concluded, "Our results suggest that metformin might serve as an effective therapy for ovarian hyperandrogenism and acne in women with PCOS."

**J Clin Aesthet Dermatol.* 2019;12(5):34-38.



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Increase AMPK to Better Manage Body Weight

Most people today consume too many excess calories.

This results in **mTOR** constantly running at high gear, which is a factor in unwanted **fat storage**.

Studies show that increasing **AMPK** activity turns down excess **mTOR**.¹

Reduce Cell Fat Storage

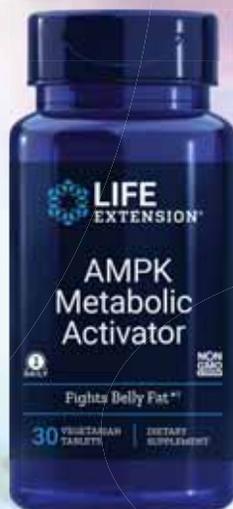
Scientific studies show that increasing **AMPK** activity can encourage cells to store less fat and burn it as energy.^{2,3}

AMPK Metabolic Activator was formulated based on data showing reduced **belly fat** in response to just one of its ingredients (*Gynostemma pentaphyllum*).³

AMPK Metabolic Activator is a dual-nutrient formula designed to support healthy AMPK cellular activation.

References

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2. *Nutr J*. 2016;15:6.
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Natural Methods to Enhance IMMUNE FUNCTION

BY WILLIAM FALON

Immune senescence underlies common diseases of aging.

Most people view weakened **immunity** as a risk factor for **cancer** and **infectious** disease.

A lesser-known impact of an aged immune system is **inflammation** caused by **over-active** cytokines that damage the brain, lungs, arteries and bone.

This dual impairment whereby **protective** immune components like **naïve T-cells** diminish while **pro-inflammatory** cytokines increase, is a hallmark of **immune senescence**.

Not only do we lose the ability to **defend** against cancers and infections, but underlying **inflammation** destroys our neurons, kidneys and joint cartilage.^{1,2}

To reverse this decline, **Life Extension®** has worked with scientists for decades seeking to restore *youthful immune function*.

We reported earlier this year on a landmark study in which the **thymus gland** of older people was **regenerated** after a one-year protocol using **growth hormone**,

metformin, and **DHEA**. The participants were also given **zinc** and **vitamin D3** supplements.

In this study, **immune markers** improved, and the **biological age** of the elderly subjects was reversed by **2.5 years!**

These kinds of medical advances that **Life Extension®** helped support made headline news worldwide.

This **immune-regenerative** protocol using **growth hormone**, **metformin**, and **DHEA** is now moving into expanded clinical trials.

The slides on the next page highlight what I present to live audiences about this **human** study published in December 2019.

As we await widespread availability of better immune-boosting therapies, people are seeking **natural compounds** that have been shown to enhance immune functions in peer-reviewed scientific studies.

The two articles that begin on page 28 will educate readers about some of the approaches currently available that have been shown to help restore immune functionality.

PARTIAL REVERSAL OF IMMUNE SENESCENCE

Study conducted by Dr. Greg Fahy in collaboration with researchers from **Stanford University** and **UCLA** consisted of individualized doses of:

- 1. Human growth hormone (hGH)**
- 2. DHEA**
- 3. Metformin**

Study subjects were also provided with daily **vitamin D3** and **zinc**.



Source: Reversal of epigenetic aging and immunosenescent trends in humans. *Aging Cell*. 2019 Dec;18(6):e13028

As seen in *Forbes*, September 9, 2019.



Cocktail of Drugs Gives First Hope That 'Biological Age' Can Be Reversed

Scientists at Intervene Immune and Stanford Medical Center say they have proven that 'epigenetic aging can be reversed in humans.'

...they are optimistic that a person's biological age can be reversed."

Age markers reversed by 2.5 years!

Source: www.forbes.com/sites/robinseatonjefferson/2019/09/09/cocktail-of-drugs-gives-first-hope-that-biological-age-can-be-reversed

"TURNING BACK TIME!"

Aging is REVERSED in men using a cocktail of growth hormones and diabetes drugs in study that saw test group shed 2.5 biological years."

Source: <https://www.dailymail.co.uk/health/article-7435427/Aging-REVERSED-small-group-men-study-reveals.html>

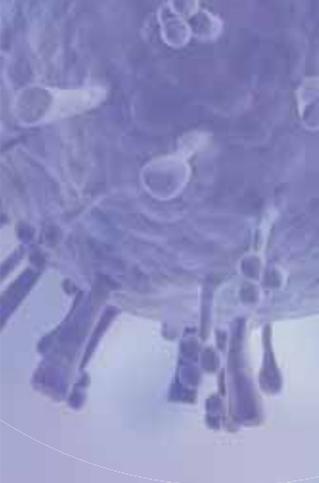
As seen in *Daily Mail*, October 22, 2019.



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LACTOFERRIN Helps Protect Against Viruses

BY TOM MILLER

From the common cold and flu to newer threats, **viral infections** are a major cause of disease and death worldwide.

The protein **lactoferrin** has shown potent **antiviral activity** in preclinical and clinical (human) studies.

It attacks viruses at several points in their lifecycle, through various mechanisms.¹⁻⁴

While some **lactoferrin** is produced in the body, it can also be absorbed from oral intake, bolstering the body's defenses.⁵

The best ways to avoid viral illnesses remain the standard precautions:

- Avoid contact with sick individuals.
- Wash your hands with soap and water frequently, for at least 20 seconds.
- If soap and water aren't available, use a hand sanitizer with at least **60%** alcohol.
- Avoid touching your eyes, nose, and mouth.
- Clean and disinfect frequently touched objects and surfaces.

Lactoferrin should not replace these tried-and-true preventive measures. However, it may provide an *additional layer* of defense to reduce the risk of contracting viral illnesses and to diminish their severity.

How Viruses Invade

Viruses are unlike other infectious agents.

For one thing, they cannot grow and reproduce on their own. They must hijack the controls of a host cell to survive and replicate. Also, they are tiny, far smaller than microscopic bacteria and fungi.⁶

Viruses are made up of miniscule packages of protein that surrounds genetic material. When they find a suitable host cell, they invade, then use that cell to produce new copies of the virus, which can go on to infect other cells.

The first step in this process occurs after the virus enters the body, often through the lining of respiratory airways or the digestive system. Viruses contain surface proteins that are able to recognize specific surface features of cells. This allows them to attach to cells and gain entry.

Once in the cell, the virus takes control of the cellular machinery to make copies of its genetic material and proteins that are then reassembled into new virus particles.

Lactoferrin helps protect by impeding the invasion and growth of viruses at multiple steps in this process.

A Constituent of Mother's Milk

Lactoferrin is a protein found naturally in milk. It's also produced in other bodily secretions, including tears and saliva, and by some immune system cells.⁴

Lactoferrin is found in highest amounts in **colostrum**, the first type of mother's milk produced after a baby is born. It has remarkable powers to shield infants from infection before their own immune systems have fully developed.

In adults, it is an important component of defenses against infections.

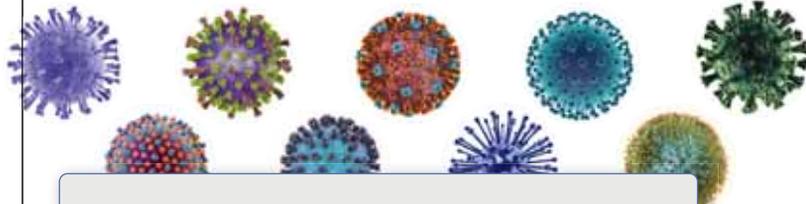
In mucous, saliva, and other secretions, lactoferrin helps prevent pathogens from gaining entry through the linings of the oral cavity, nasal cavity, airways, and digestive system.

One unusual feature of **lactoferrin** is the diversity of viruses it can shield against. It has been shown to possess robust **antiviral** activity against different types of virus, from those that cause the common cold and flu, to HIV and hepatitis B and C viruses.⁴

Inhibiting Viruses from Entering Cells

The most important way lactoferrin defends against viral infections is by **disrupting viruses from binding to cells**.^{1-3,7}

This can **stop the virus in its tracks**, before it has a chance to cause any problems. If the virus cannot attach to and enter cells, it cannot cause illness.



Lactoferrin Defends Against a Wide Range of Viruses

Lactoferrin has been shown in laboratory, animal, and preclinical research to help protect against a huge list of viruses, including:

- Various viruses that cause the common cold,⁴
- Various viruses that cause flu, including several different strains of influenza A (even the H1N1 subtype that caused a global outbreak in 2009),^{4,11}
- Various viruses that cause gastroenteritis (stomach flu) ⁴
- SARS-type coronavirus,⁷
- Herpes simplex virus,^{4,12}
- Human immunodeficiency virus (HIV), which causes AIDS,^{1,2,4}
- Hepatitis B virus,^{1,3,8}
- Hepatitis C virus,^{1,2,8}
- Cytomegalovirus (CMV),^{1,4}
- Poliovirus,^{4,8}
- Respiratory syncytial virus (RSV),^{1,11}
- Hantavirus,^{1,11}
- Dengue virus, the cause of dengue fever,^{7,8}
- Enteroviruses,^{2,8}
- Echovirus,^{1,7,8}
- Coxsackieviruses,¹⁰ and
- Epstein-Barr virus (EBV).¹²

Lactoferrin does this in two different ways:

- It binds to the **virus** directly, blocking the viruses' surface proteins' ability to recognize binding sites on the surface of cell membranes.
- It binds to surface sites on the **cell's** outer membrane that are targeted by viruses.

For example, a compound found on cell surfaces, called **heparan sulfate**, is a common target for various viruses.

Several studies have shown that lactoferrin binds to structures containing **heparan sulfate**, which can prevent viruses from recognizing and entering the cell.^{7,8}

Activating the Immune System

Lactoferrin also has *indirect* antiviral effects. It helps the body fight against a virus by **activating immune** defenses.

Lactoferrin activates **natural killer** cells and increases their number.^{5,9} These immune cells are equipped to recognize abnormal cells, including those infected by viruses, and eliminate them. This can help prevent the spread of a virus in the body.

Lactoferrin also stimulates the production of other antiviral compounds, including the signaling proteins known as **interferons**.^{2,4} One of the important ways that interferons promote immunity is to signal to surrounding cells that viruses are present, and help activate antiviral mechanisms to prevent growth and spread of those viruses.

Lactoferrin may also help block the ability of viruses to **reproduce** even if they're already inside cells.^{1,4}

This helps limit the spread of the virus, potentially reducing the severity of the resulting illness.

Fighting Common Viral Illnesses

Lactoferrin has been shown, in laboratory, animal, and human studies, to have potent activity against a number of viruses.^{1-4,7,8,10-12}

This includes common viruses such as those that cause the **common cold**, the **flu**, and **gastroenteritis** (stomach flu).

There are several different types and strains of virus that cause these illnesses. Although the common cold and viral gastroenteritis are usually mild, influenza can



WHAT YOU NEED TO KNOW

Fighting Viruses with Lactoferrin

- **Lactoferrin** is a protein produced in milk and bodily secretions like saliva. It's also produced by some immune system cells.
- Research shows that lactoferrin is active against a wide assortment of **viruses**.
- Its **antiviral activity** has been shown to aid in the battle against viruses that cause the common cold, flu, stomach flu, and other illnesses.
- **Oral lactoferrin** may reduce both the incidence and severity of disease caused by viruses.

prove deadly in young children, the elderly, and those with other health issues.

Some strains of the viruses that cause influenza are covered by annual flu vaccines, but many others are not. The extra protection afforded by **lactoferrin** could make a difference in helping to lessen the impact of these illnesses.

In one study, healthy women taking **oral lactoferrin** experienced a reduced onset of both common-cold-like and gastroenteritis symptoms.¹³

In other clinical studies, **lactoferrin** was effective for reducing the symptoms of viral gastroenteritis, including those caused by **rotavirus** and **norovirus**. Oral lactoferrin reduced the incidence and severity of the symptoms of these illnesses.⁴

People taking **100 mg** of lactoferrin six or seven days a week had an approximately **4-fold reduction** in the incidence of viral gastroenteritis compared to people who took it only once a week.⁴



Lactoferrin's Other Immunity-Boosting Benefits

Lactoferrin has benefits beyond fighting viruses.

Studies have demonstrated that it can boost healthy immune function, which protects against a variety of pathogen types.

Various disease-causing **bacteria** have been found to be susceptible to the actions of lactoferrin.^{2,3}

The immune system is also important in monitoring for abnormal cells which could develop into cancer. Lactoferrin improves this ability, demonstrating potent **anticancer** effects in many studies.⁵

Emerging Viral Threats

Coronaviruses of differing types have caused **severe acute respiratory syndromes** such as the SARS epidemic in Asia that killed over 700 people in 2003.¹⁴

This same family of SARS viruses emerged this year as the cause of **COVID-19**.

COVID-19 is too new to have been studied in depth, but it shares many features with other **coronaviruses**. These include the **SARS** and **MERS** viruses that caused previous highly serious infectious disease outbreaks.

Lactoferrin shows promise in helping to defend against **SARS-type coronaviruses** in at least two different ways.

In a 2011 study, lactoferrin was effective at blocking a model of a **SARS-type coronavirus** from entering host cells.⁷ It did this by preventing binding of viral elements to the heparan sulfate compounds on the surface of the target cells.

Given the lack of an effective vaccine or drug treatment for so many viral illnesses, **lactoferrin** is a promising new tool in the defense against viral illnesses.

Summary

Lactoferrin is a protein produced in milk, saliva, and other secretions.

Laboratory, animal, and clinical research demonstrates lactoferrin's activity against a wide range of viruses, including those that cause the **common cold** and **flu**.

It works by helping to block viral invasion of cells and by amplifying the immune system's power to eliminate viral infection from the body.

Taken orally, lactoferrin is readily absorbed and can play an important role in bolstering defenses against viral 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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Liver function tests: AST, ALT, LDH, GGT, bilirubin, alkaline phosphatase

Blood minerals: calcium, potassium, phosphorus, sodium, chloride, iron

Blood proteins: albumin, globulin, total protein, albumin/globulin ratio

CARDIAC MARKERS

Apolipoprotein B (ApoB)

Homocysteine

C-Reactive Protein (high sensitivity)

LIPID PROFILE

Total Cholesterol

LDL (low-density lipoprotein)

HDL (high-density lipoprotein)

Triglycerides

COMPLETE BLOOD COUNT (CBC)

Red Blood Cell count including: hemoglobin, hematocrit, MCV, MCH, MCHC, RDW

White Blood Cell count including: lymphocytes, monocytes, eosinophils, neutrophils, basophils

Platelet count

CANCER MARKER

PSA (Prostate Specific Antigen)

HORMONES

Free and Total Testosterone

DHEA-S

Estradiol (an estrogen)

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Vitamin D

FEMALE PANEL

METABOLIC PROFILE

Glucose

Insulin

Hemoglobin A1c

NEW **Serum Magnesium**

Kidney function tests: creatinine, BUN, uric acid, BUN/creatinine ratio

Liver function tests: AST, ALT, LDH, GGT, bilirubin, alkaline phosphatase

Blood minerals: calcium, potassium, phosphorus, sodium, chloride, iron

Blood proteins: albumin, globulin, total protein, albumin/globulin ratio

CARDIAC MARKERS

Apolipoprotein B (ApoB)

Homocysteine

C-Reactive Protein (high sensitivity)

LIPID PROFILE

Total Cholesterol

LDL (low-density lipoprotein)

HDL (high-density lipoprotein)

Triglycerides

COMPLETE BLOOD COUNT (CBC)

Red Blood Cell count including: hemoglobin, hematocrit, MCV, MCH, MCHC, RDW

White Blood Cell count including: lymphocytes, monocytes, eosinophils, neutrophils, basophils

Platelet count

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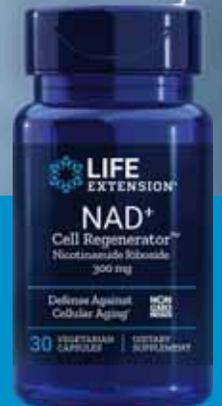
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Reference

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

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References 1. *Int J Gen Med.* 2011 Jan 25;4:105-13. 2. *Br J Nutr.* 2000 Nov;84 Suppl 1:S81-9. 3. *J Dairy Sci.* 2000 Jun;83(6):1187-95.



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Immune-Boosting Effects of MELATONIN

BY RICHARD HARLEY

Melatonin has long been thought of as the “sleep hormone.” It regulates circadian rhythms, the body’s internal biological clock, which can improve sleep patterns.

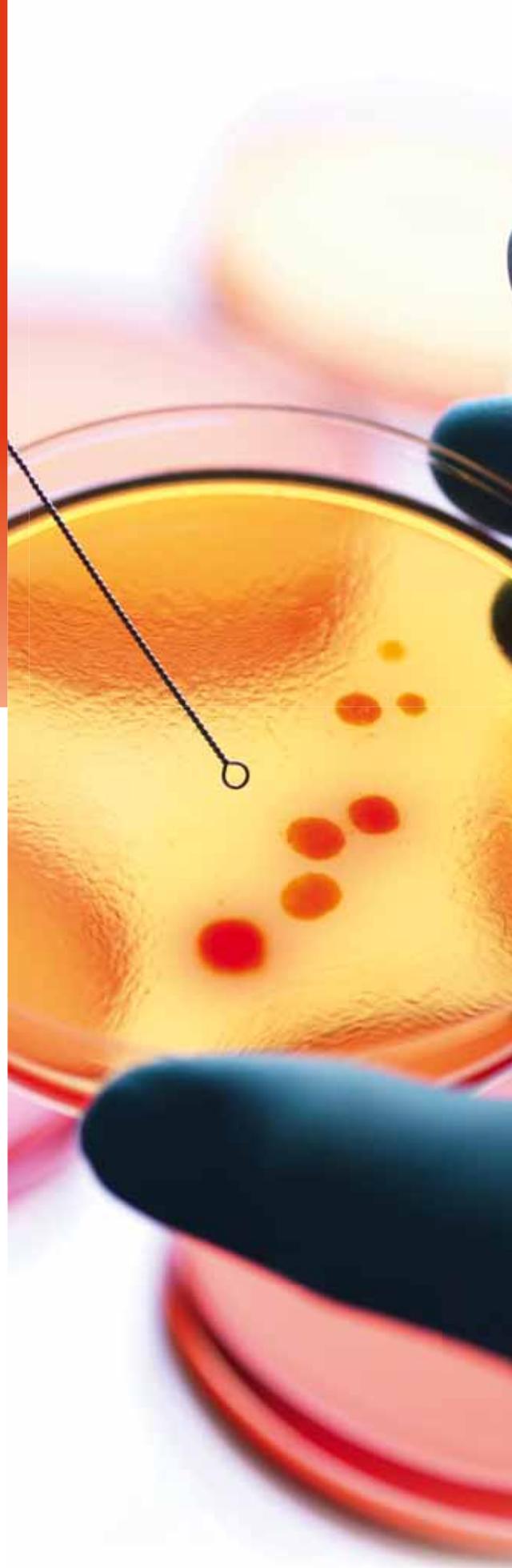
That’s important for optimal health. Inadequate sleep has a well-documented negative impact on **immune** health, increasing susceptibility to *infectious diseases* and *cancer*.¹⁻³

But melatonin does much more.

Melatonin provides vital support to the **immune system**, helping coordinate immune responses to defend against a wide variety of threats, including **viruses**.⁴⁻⁶

Internal production of melatonin drops significantly with age.⁶⁻⁸ This leaves the immune system weakened.

In **1992**, **Life Extension**[®] introduced **melatonin** to the world based on evidence of its **anti-aging** properties, including potential to boost **immune function** and reduce cancer risks.



Melatonin Regulates Immune Function

Melatonin is a hormone produced primarily in the **pineal gland** of the brain.⁶ It is also produced in other tissues, including cells of the immune system.⁹⁻¹²

Its best-known role is in regulating sleep-wake cycles but it has demonstrated other beneficial properties.⁴⁻⁶

Two of melatonin's effects are particularly profound:

- Supporting **immune** health
- Anti-**cancer** activity

Scientists have found that melatonin sends *signals* to the immune system and the immune system “talks” back.

This “cross talk” fine-tunes and coordinates healthy immunity. It bolsters innate defenses that guard against a wide range of pathogens, from viruses to cancer cells.

It also improves immune attacks on specific viruses and disease-causing bacteria and parasites.⁴⁻⁶

The influence of melatonin on immune health was first observed in 1926. Scientists reported that kittens fed pineal gland extracts—now known to be a major source of melatonin—gained significantly improved resistance to infections.⁶

Combatting Immune Senescence

The deterioration of the immune system that comes with age is called **immune senescence**.¹³

It causes a dramatic weakening of immunity. This is a big part of the reason why the elderly are more susceptible to infectious disease from viruses, bacteria, and other pathogens.

A healthy immune system searches out and eliminates abnormalities, including senescent cells, pre-malignant cells and cancer cells.

With immune senescence, this function isn't performed properly, and disease risks rise.^{4,14}

One cause of immune senescence is inadequate production of hormones that control immune function, like **melatonin**.^{4,6} In rodents, boosting melatonin levels can reverse immune senescence, rejuvenating immune function.

The effects can be seen in the **thymus gland**, which produces T cells, the “soldiers” of the immune system. As we age and the immune system declines, the thymus slowly shrinks. Immune function suffers as a result.

But in aged mice, melatonin stimulates *new* growth of the degenerated thymus, producing new T cells that improve immune function.¹⁵

Melatonin counters immune senescence in other ways, including:^{6,13,16-20}

- Enhancing the responses of **antibodies** that “tag” specific viruses, bacteria, and other invaders to be attacked by different components of the immune system,
- Reducing **chronic inflammation**, a cause of nearly all age-related chronic diseases, and
- Enhancing the *activity* of **T cells**, helping to more efficiently destroy pathogens.

Melatonin and Infection

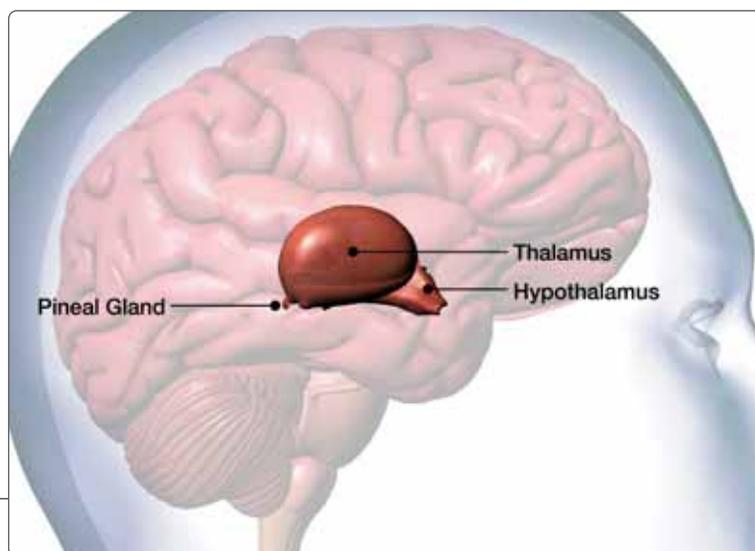
Even with healthy immunity, melatonin can strengthen immune response.

Preclinical studies have investigated the impact that melatonin has on viruses, bacteria, and parasites.⁶ It improves the immune response to infection caused by *all* of these.

It does so by stimulating the production *and* activity of cells that fight infection, including **T cells** and **NK (natural killer) cells** that eliminate virus-infected cells, along with macrophages that engulf and destroy foreign invaders.

Melatonin regulates levels of several key immune system *signaling* factors that are required for an orchestrated immune response.

Together, these effects help rid the body of infectious pathogens *and* keep the immune response to appropriate, safe levels, avoiding a harmful overresponse or excessive inflammation.



In animal models, melatonin protects against infections caused by **viruses** of various types. In severe viral brain infections, it reduces viral levels and prevents paralysis and death.

In one astonishing study, scientists exposed mice to an extremely aggressive virus called **Venezuelan equine encephalomyelitis**, which killed **100%** of infected animals. When treated with melatonin, the mortality rate was reduced to **just 16%**.²¹

Melatonin is protective in **bacterial infections** as well.

Bacterial infections can lead to **sepsis**, a life-threatening condition resulting in shock, organ failure, and death. In patients with sepsis, low nighttime melatonin levels correlate with *more severe* illness.²²

In animal models of sepsis, melatonin prevents multiple organ failure and circulatory failure. And in human newborns born with sepsis, treatment with melatonin **reduces mortality**.²³⁻²⁶

Anticancer Effects

The immune system is one of our body's main defenses against **cancer**.

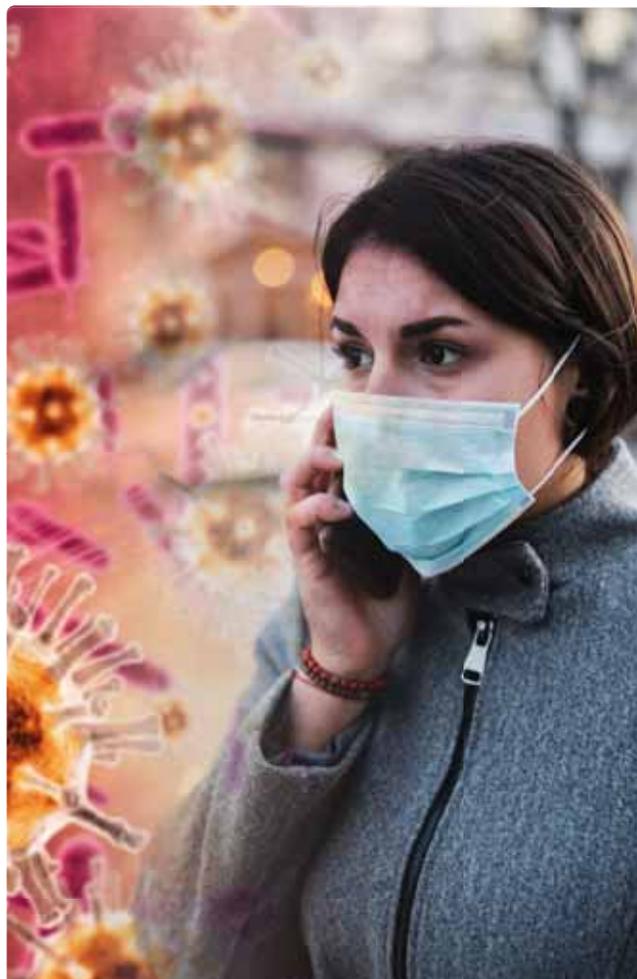
Natural killer (NK) cells are immune cells that identify and eliminate abnormal cells, including tumor cells and cells that are *developing* into cancer cells.

Melatonin augments the activity of natural killer and other immune cells, helping to rid the body of abnormal cells before they can do more damage.

Research has shown that melatonin does even more to prevent cancer, possessing many direct anticancer effects.^{4,27-30} In ways that scientists are still investigating, it fights cancer **at every stage**, working to prevent its initial formation, progression, and spread in the body.²⁹

In preclinical and clinical studies, melatonin has been found to **suppress** many forms of malignancies, including:^{4,31-37}

- Breast cancer,
- Brain cancer,
- Ovarian cancer,
- Endometrial (or uterine) cancer,
- Melanoma,
- Prostate cancer, and
- Colon cancer.



WHAT YOU NEED TO KNOW

Melatonin Benefits the Immune System

- **Melatonin** is a hormone long known to regulate sleep-wake cycles and improve sleep.
- The production of melatonin declines with age.
- **Life Extension®** introduced melatonin in **1992** as an effective anti-aging therapy.
- Science has expanded to look beyond its role in sleep, to investigate its potential in immune function and cancer.

Summary

Melatonin isn't just for improving sleep.

This hormone has been shown to have an impact on the **immune system**, fine-tuning immune responses and protecting against viral and other infections, cancer, and more.

As melatonin levels diminish with older age, immune function wanes, increasing susceptibility to disease. •

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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BOOST Internal ANTIOXIDANT Defenses

BY LESLIE HUNTER

Antioxidants fight **oxidative damage** caused by free radicals, which contributes to degenerative aging.¹⁻³

But not all antioxidants are the same.

The kinds most people know about are found in fruits, vegetables, and other *external* sources.

But our bodies also produce their own *internal* antioxidants.

One of the most important of these antioxidants is an *enzyme* called **superoxide dismutase (SOD)**.

SOD levels in cells drop as we age. This leads to more oxidative tissue damage.⁴

Scientists have discovered that **aronia berry extract** and a **melon concentrate** can stimulate **SOD production**, offering a new way to bolster antioxidant defenses.

Oxidative Stress

Free radicals are unstable molecules with an unpaired electron. This instability leads them to steal electrons from other molecules that inflict damage to delicate cellular structures.

That damage, known as **oxidative stress**, can be outwardly felt when recovering from an alcoholic hang-over. Metabolites of alcohol (such as acetaldehyde) inflict cellular damage that one can outwardly feel.

Internally, oxidative stress contributes to degradation of the body's proteins while body fat is converted to forms that contribute to chronic inflammation.⁵⁻⁸

Over time, this accumulated damage accelerates pathological aging.⁹

Free-Radical Formation

Free radicals are inevitable facts of life.

Various outside factors can contribute to increased free-radical formation in the body—pollutants, toxins, some drugs, cigarette smoke, radiation, and more.¹⁻³

But even if we are careful to avoid unhealthy external factors, free radicals *still* form from within.

Inflammation, infection, and stress contribute to free-radical formation. Even normal, *healthy* processes, such as the metabolism of nutrients to make energy, create free radicals.

With age, defenses against the damaging effects of free radicals sharply decline.^{1,10}



How Antioxidants Help

Nature has provided a way to counter the danger of free radicals—**antioxidants**.⁹

These compounds got their name because they fight *against* oxidative stress. They find free radicals and neutralize them.

When cells have antioxidant defenses in place, they sustain less degenerative damage.

Two Types of Antioxidants

There are two general types of antioxidants.^{11,12}

Endogenous antioxidants are formed *within the body*.

These include **superoxide dismutase (SOD)**, **glutathione peroxidase**, **catalase**, and **glutathione**.

Exogenous antioxidants are formed *outside the body* but can be absorbed and used by our cells if we consume them orally.

Examples include vitamins C and E, carotenoids, flavonoids, polyphenols and other plant extracts.

Although cells make their own endogenous antioxidants, external antioxidants confer additional protection.^{11,12}

What few people understand is that **endogenous antioxidants** (like SOD) are the first line of defense, particularly against the free radicals that are formed within our cells due to everyday, normal metabolic processes.

The Importance of Superoxide Dismutase

One of the strongest **endogenous** antioxidants is the enzyme **SOD**.

A common free radical is produced in each cell's energy-producing **mitochondria**. Known as **superoxide**, this compound is very unstable, meaning it seeks to grab electrons from other molecules, creating pathological havoc.

While normal oxygen is harmless, **superoxide** reacts aggressively with other molecules and can permanently damage them.

Superoxide dismutase is expressly designed to recognize **superoxide** radicals and convert them into water and hydrogen peroxide *before* they can do damage.

Other *enzymes* convert the hydrogen peroxide into water and oxygen.¹³

Superoxide dismutase is found throughout the body. It's in the main compartment of every cell, in the mitochondria, and in the spaces between cells.

When **superoxide dismutase** levels are adequate, they offer remarkably powerful protection against free radicals and oxidative damage.

SOD Declines with Age

Activity of superoxide dismutase dwindles with age. Researchers measured SOD levels in individuals ranging in age from infancy to 69 years old.⁴

They found that after **age 40**, levels of SOD declined.

This study showed that after age 40, **SOD levels** were on average about **20% lower** than those of a 25 to 40-year-old.

Boosting SOD Levels

Scientists have found a way to *reverse* the loss of SOD, thereby *increasing* levels in the body.

This suggests that we can protect against oxidative damage at an early stage, potentially helping to slow degenerative aging processes.

Superoxide dismutase levels in the body can be increased in two ways:

1. Some nutrients help stimulate the body's *own* production of SOD.
2. An external SOD can be consumed orally to further increase bodily levels.

Aronia Berry Stimulates SOD Production

Aronia berries are a potent source of **anthocyanins**, health-promoting pigments.¹⁴

These anthocyanins themselves are antioxidants, helping to neutralize free radicals.¹⁴

Aronia berries also have another important property: They have been shown to activate the protein **Nrf2**, a key regulator of antioxidant response in cells.¹⁵

This ability of **aronia berry** to boost **SOD** has been shown in a human study.

The trial enrolled patients with metabolic syndrome, who had lower SOD levels at the beginning of the study than the healthy controls.¹⁶ Subjects were given **300 mg** of aronia berry extract daily.

After two months, **SOD levels** in the body increased by **29%**.

These subjects also benefited from a **52%** increase in **glutathione peroxidase**, another important "internal" antioxidant.



WHAT YOU NEED TO KNOW

Help Fight Oxidative Stress

- There's no way to stop **free radicals** from being produced. Even our own metabolism leads to the creation of these harmful compounds, which cause **oxidative stress**, a major source of aging and disease.
- **Superoxide dismutase (SOD)** is an antioxidant produced in the body that defends against oxidative stress, particularly against **superoxide**, the dangerous free radical.
- Levels of SOD drop over time, increasing our vulnerability to more rapid aging and risk for disease.
- Taking **aronia berry extract** has been shown to boost the body's production of SOD.
- A unique **melon concentrate** provides SOD directly.
- Together, these two extracts provide powerful protection against free-radical damage.

An Outside Source of SOD

Researchers have identified a **melon extract** high in SOD.

Animal studies have shown that taking this concentrated melon extract orally increases SOD levels in body tissues.^{17,18} In piglets, it led to an almost **37.5%** increase in SOD activity in only 12 days.¹⁸

Two trials tested the effects of the SOD-rich melon extract in people who felt daily **stress** and **fatigue**.^{19,20} These unhappy feelings can be associated with cellular oxidative stress.^{21,22}

In both trials, participants took the **melon extract** or a **placebo** and were put through a battery of tests to assess their quality of life, stress, and fatigue.

In those who took the melon extract, perceived stress scores dropped by **31%** and quality-of-life scores improved by **42%**, compared to baseline.²⁰ Mental fatigue was reduced by **21%** and physical fatigue fell by **9%**, when compared to controls.¹⁹

Together with **aronia berry extract**, this concentrated **melon extract** provides fuel to boost systemic **SOD** levels, protecting against the damage caused by oxidative stress.

Summary

Oxidative stress caused by free radicals is a source of cellular damage. It contributes to degenerative aging processes.

Antioxidants neutralize free radicals, thus mitigating the harm they inflict.

One of the most important **endogenous** antioxidants is the enzyme **superoxide dismutase (SOD)**.

Its levels drop with age. But scientists have found that **aronia berry extract** and a **melon concentrate** extract can boost **SOD levels**.

Aronia berry stimulates the body's *own* production of superoxide dismutase and other antioxidants. **Melon concentrate** increases cellular **SOD** activity directly. •

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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HIGHER POTENCY CARNOSINE



Carnosine is a unique dipeptide that can inhibit *glycation* throughout the body, thereby helping to slow normal aging processes. Suggested dose is one **500 mg** Carnosine cap taken twice daily.

Item #01829 • 60 vegetarian capsules

1 bottle **\$27**

4 bottles \$24 each

Life Extension® was the first to introduce high-dose (**500 mg**) carnosine back in **1999**.



Super Carnosine provides 500 mg of carnosine per capsule along with fat-soluble vitamin B1 (**benfotiamine**) to further impede glycation reactions.

Item #02020 • 60 vegetarian capsules

1 bottle **\$30**

4 bottles \$27 each

Life Extension **carnosine** is available in *three different* formulas to allow you to customize your longevity program.



Mitochondrial Energy Optimizer provides **1,000 mg** of carnosine in each four-capsule dose along with **R-lipoic acid, benfotiamine, taurine,** and **PQQ** to provide broad-spectrum support.

*Item #01868 • 120 capsules

1 bottle **\$51**

4 bottles \$45 each

Each formula provides high doses of **carnosine** to ensure **sustained** benefits.

For full product description and to order **Mitochondrial Energy Optimizer, Carnosine** or **Super Carnosine**, call **1-800-544-4440** or visit www.LifeExtension.com

*Bio-Enhanced® is a registered trademark of Geronova Research, Inc.



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

FEED YOUR BRAIN

FOR OPTIMAL BRAIN HEALTH



Item #02397 • 60 vegetarian tablets

1 bottle **\$43.50**

4 bottles \$40 each



Item #02396 • 60 vegetarian tablets

1 bottle **\$42**

4 bottles \$38 each

For full product description and to order **Cognitex® Elite** or **Cognitex® Elite Pregnenolone**, call 1-800-544-4440 or visit www.LifeExtension.com



Cognitex® Elite contains clinically studied brain-boosting nutrients in one advanced formula.

A new ingredient called **SIBELIUS™**: **Sage Extract** demonstrated improvement in attention and memory performance in healthy, older volunteers.

Cognitex® Elite provides *all* of these ingredients:

SIBELIUS™: Sage extract (leaf)	333 mg
AuroraBlue® Wildcrafted	200 mg
Blueberry Complex	
Sensoril® Ashwagandha extract	125 mg
Phosphatidylserine	100 mg
Uridine-5'-monophosphate	50 mg
Vinpocetine	20 mg

Cognitex® Elite Pregnenolone contains these same powerful ingredients but with **50 mg** of pregnenolone added.

Do not use if you are of childbearing age, pregnant or planning to become pregnant.

SIBELIUS™ is a trademark of Sibelius Limited. CHRONOSCREEN™ is a trademark of Chronos Therapeutics Limited. AuroraBlue® is a registered trademark of Denali BioTechnologies, Inc. Sensoril® is protected under US Patent Nos. 6,153,198 and 6,173,092 and is a registered trademark of Natreon, Inc.

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

BOOST

your
INTERNAL
DEFENSE
against
CELLULAR
STRESS



Young people produce abundant quantities of an internal cell *antioxidant*, called **SOD** (superoxide dismutase).

With age, SOD production declines.

SOD Booster provides unique extracts of **aronia** and **melon** that promote the production of **SOD**.



SOD Booster • Item # 02361

30 vegetarian capsules

1 bottle **\$21**

4 bottles **\$19 each**



Extramel® is a registered trademark of Bionov.

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

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

A Healthy Source of Ketones

Keto Fuel

for Mind & Muscles

Keto Brain and Body Boost is an easy-to-mix, peach-flavor powder that supplies beneficial **ketones** using **beta-hydroxybutyrate**.

It also contains **mangiferin** and **resistant starch** to support the body's natural ability to produce **ketones**.

Keto Brain and Body Boost provides the brain and muscles the benefits of **ketones** without the drawbacks of a ketogenic diet.

Item #02318 • Net Wt. 400 g (14.1 oz.)

1 container **\$37.50** • 4 containers \$34 each



FiberSmart® is a registered trademark of Advanced Ingredients, LLC.



For full product description and to order **Keto Brain and Body Boost**, call 1-800-544-4440 or visit www.LifeExtension.com

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

LITHIUM

The Brain & Body Element

In areas where **lithium** is naturally abundant in the drinking water, people tend to **live longer**, healthier lives.¹⁻³

Lithium is a *low-cost* mineral that supports **cognition, neural function, and healthy aging**.³⁻⁵

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

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5. *JAMA Psychiatry*. 2017 Oct 1;74(10):1005-10.



Lithium
(1,000 mcg of lithium per tiny cap)
Item # 02403 • 100 Vegetarian Capsules

1 bottle \$12

4 bottles \$10.50 each



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



Mg



MAGNESIUM L-THREONATE *Regenerates* Brain Structures

BY HARRY STEIN

For nearly 30 years, scientists have been convinced that increasing **magnesium** levels in the **brain** can potentially prevent or *reverse* some age-related changes that contribute to **cognitive decline** and **dementia**.¹

But it's been difficult to put this knowledge into practice, because taking more **magnesium orally** does not significantly raise **brain** levels.

A unique form of magnesium developed at the **Massachusetts Institute of Technology (MIT)** is changing that.

Magnesium L-threonate has been shown to boost brain **magnesium** levels in animals when taken orally. This effect is due to its unique ability to cross the **blood-brain barrier**.²

Another rodent study showed that oral use of **magnesium L-threonate** raised brain fluid levels of magnesium by **54%**.³

Brain benefits have also been shown in **humans**.

In a clinical study of adults with cognitive impairment, **magnesium L-threonate** *reversed* measures of **brain aging** by **9 years**.⁴

Magnesium's Impact on the Brain

Magnesium is an essential mineral found in varying amounts in a range of plant- and animal-based foods.

Throughout the body, it works as a cofactor, or “helper molecule,” required for the normal function of hundreds of enzyme systems.

In fact, **magnesium** is essential for about **80%** of the body's metabolic functions.⁵

Magnesium plays an especially critical role in the **brain**, where it protects the functioning of **synapses**, the communication connection points between brain cells.

For people to learn and form memories, **synapses** must have a property known as **plasticity**, the ability to adapt and change in response to stimuli.

Declining synaptic plasticity is a major contributor to loss of cognitive function in older age. And magnesium can help stop this decline.

How it Works

As you can see in the graphic below, brain cells release a “messenger” from most **synapses**, known as **neurotransmitters**.

Neurotransmitters bind to a **receptor** for the **neurotransmitter** on the other brain cell, thereby stimulating it.

In areas of the brain where learning and forming memories take place, the most important receptor is **NMDA**.⁶

The **NMDA receptor** requires an *additional* step to become fully activated—one that involves **magnesium**.

Magnesium acts as a **secondary activator** of the **NMDA receptor** and is vital to the **synapses'** plasticity.

Without magnesium, the NMDA receptor and the whole synapse fail to function normally.

In animal studies, researchers have demonstrated that increasing levels of magnesium in the brain **increases synaptic plasticity** and leads to **greater synaptic density**.

That means it helps existing **synapses** work better and *also* increases the overall number of **synapses**.^{2,3,7-10}

These effects translate into improvements in **cognitive** function, including better **learning** and **memory**.

Boosting Magnesium Brain Levels

Scientists at **MIT** developed a form of magnesium called **magnesium L-threonate**.

This form is more easily absorbed, or **bioavailable**, and results in *higher* levels of magnesium in the brain compared to other forms.²

In fact, **oral** intake of **magnesium L-threonate** raises brain fluid levels of magnesium in rodents by **54%**. It also increases **synaptic density** and increases production of **NMDA receptors** in brain cells.³

Most importantly, several studies demonstrate that this boost to brain magnesium directly translates to **improvement** in mental function.

Synapses: The Point of Connection Between Brain Cells

Neurotransmitters stimulate receptors by binding to them.
Information from one neuron flows to another neuron across a synapse.



Making Rodents Smarter!

If you have a pet hamster, you might want to give it a little brain boost.

Scientists first tested **magnesium L-threonate** on aged rats. The results showed an enhanced **ability to learn**, with improvements seen in both short-term *and* long-term **memory**.²

Another study pitted **magnesium L-threonate** against other, common forms of magnesium, including **magnesium chloride** and **magnesium sulphate**.¹⁰ **Magnesium L-threonate** led to greater **improvements in memory** than the other forms of magnesium.

Two mouse studies specifically evaluated **magnesium L-threonate** in models of **Alzheimer's disease**, the most common cause of dementia in older adults.^{7,9} In both studies, it prevented the **loss of synapses** associated with Alzheimer's and maintained or *improved* memory.

Magnesium L-threonate was even effective at improving cognition in very-late-stage Alzheimer's disease.

Another study in mice showed that magnesium L-threonate **stimulated growth of new brain cells** in parts of the brain central to memory and learning.⁸ Normally, the growth of these brain cells slows or stops in older animals, but magnesium L-threonate prevented this decline.

A Groundbreaking Human Trial

A group of scientists designed a clinical study to test whether these benefits translate to people.

Adults 50-70 years old, with some level of cognitive impairment, received **1,500 mg-2,000 mg** (depending on body weight) daily of **magnesium L-threonate** or a **placebo** for 12 weeks.⁴

At the end of the study, subjects who were treated with magnesium L-threonate had an **improvement in overall cognitive ability**.

On average, subjects started out with some degree of impairment of **executive functioning**, the ability to think abstractly, plan, and make decisions. By the end of the study, the **executive functioning** of those taking **magnesium L-threonate** was restored to nearly normal for their age.

At the start of the study, the participants averaged 57.8 years of age. However, their **brain age** based on cognitive functioning was **68.3** years old. By the end of the trial, those receiving magnesium L-threonate **improved by 9 years of brain age**, a truly remarkable result.



WHAT YOU NEED TO KNOW

Brain Protection with Magnesium L-Threonate

- The mineral **magnesium** plays a critical role in the brain, protecting the function of **synapses** involved in complex cognitive processes such as learning and memory.
- Inadequate magnesium intake is very common, yet most magnesium isn't absorbed well by the body and can't enter the brain in sufficient amounts.
- Scientists at MIT developed a new form of magnesium called **magnesium L-threonate**, which is highly absorbable and has been shown to **increase brain levels** of magnesium to a much higher degree than other forms.
- Studies in animals and humans show that magnesium L-threonate improves and maintains cognitive function, even in older individuals with prior signs of cognitive decline.
- In one human study, it reversed cognitive measures of brain aging by **9 years**.

Summary

Magnesium is a critically important mineral required for the function of hundreds of *enzymes* in the human body, making it essential for nearly **80%** of our metabolic reactions.

In the **brain**, magnesium is needed for the proper functioning of **synapses** involved in complex tasks such as learning and memory.

A large majority of the population suffers from inadequate magnesium intake. Because most magnesium supplements are poorly absorbed and do not enter the brain in sufficient quantities, fixing this problem has been difficult.

An improved type of magnesium is finally changing that.

Magnesium L-threonate is easily *absorbed* and taken up into the brain, providing cognitive benefits as shown by animal and human studies.

This form of magnesium offers tremendous promise to aging people seeking to maximize their neurological potential. •

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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Getting Enough Magnesium

Most people don't get nearly enough magnesium from their diet.

In the U.S., approximately **65%** of all adults have below optimal intake of magnesium.^{11,12} That number gets even higher in older age, with more than **80%** of people over 71 consuming inadequate amounts of magnesium.

Over time, this leads to **magnesium deficiency**, which contributes to many chronic conditions including cardiovascular disease and age-related loss of cognitive function.^{1,11,12}

Fortunately, supplementation with **magnesium L-threonate** can resolve magnesium deficiency and contribute to improved health and longevity.

Boost “Functional” Natural Killer Cell Activity

Natural killer cell activity declines with normal aging, which can affect immune function.

NK Cell Activator™ supports healthy natural killer cell activity to promote a robust immune response.¹⁻³

Functional NK cells also recognize and eliminate **senescent cells** that accumulate in aged tissues.

The standardized plant extract in **NK Cell Activator™** supports the activity of **natural killer (NK)** cells.

Clinical Studies

In one clinical study, scientists documented a **3-fold** increase of **natural killer** cell activity in healthy individuals within three to four weeks of receiving **500 mg** daily of the rice bran compound found in **NK Cell Activator™**.

In another double-blind, randomized, placebo-controlled study, researchers noted that subjects taking the rice-bran compound found in **NK Cell Activator™** experienced a boost in *myeloid dendritic cells*—cells that act as key messengers between the innate and the adaptive immune systems.⁴

The suggested single serving of one vegetarian tablet of **NK Cell Activator™** provides:

Proprietary Enzymatically Modified Rice Bran	500 mg
---	---------------

Contains wheat.

References

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For full product description
and to order **NK Cell Activator™**,
call 1-800-544-4440 or visit
www.LifeExtension.com



Item #01903 • 30 vegetarian tablets

1 bottle **\$33.75**

4 bottles \$31.50 each



Shield Your Precious Eyesight

**AT FANTASTICALLY
DISCOUNTED PRICES!**

*Shielding your eyes from
destructive ultraviolet
sun rays is one of the most
effective means
of protection against
ocular disease.*

SolarShield® sunglasses • Item #00657

1 pair **\$9.74**

4 pairs \$8.63 each

Consumers often spend hundreds of dollars on just one pair of so-called “designer” sunglasses.

Life Extension® supporters can obtain superior protection against damaging solar radiation at a fraction of the price.

SolarShield® sunglasses are recognized as the **number-one doctor-recommended sunglasses** in the world, with more than 50 million pairs sold to date.

Patented **SolarShield®** sunglasses with **durable polycarbonate lenses** and **100% UV protection** fit comfortably over prescription eyewear.



Compare the **low price** to sunglasses sold in stores and see savings exceeding **90%**!

SolarShield® is a registered trademark of Dioptics, Inc.

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

Restore Connections Between Your Neurons

Neuro-Mag® Magnesium L-Threonate was specifically formulated by MIT scientists to be uniquely absorbable by brain and nerve cells.



The numbers of **synapses** that connect brain cells decline with aging.

Magnesium L-Threonate has been shown to improve **synaptic density** and other structural components of the brain.*



Neuro-Mag® Magnesium L-Threonate

Item #01603

90 vegetarian capsules

1 bottle \$30 • 4 bottles \$27 each

Neuro-Mag® Magnesium L-Threonate Powder

Item #02032

93.35 grams of powder

1 jar \$28.50 • 4 jars \$26 each



For full product description and to order **Neuro-Mag® Magnesium L-Threonate** or **Neuro-Mag® Magnesium L-Threonate Powder**, call 1-800-544-4440 or visit www.LifeExtension.com

Reference: **Gerontology*. 1996;42(3):170-80.

Magtein® is a registered trademark of Magceutics, Inc. and is distributed exclusively by AIDP, Inc. Magtein™ is protected under U.S. patents 8,178,118; 8,142,803; 8,163,301 and other patents pending.



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GAME ON

Clinical trials demonstrate that the plant extracts in once-daily **ArthroMax® Elite** help:

- Support a healthy inflammatory response
- Maintain healthy connective cartilage tissue
- Promote comfortable joint function

Take advantage of the benefits of **Mobile-Ease™ Chinese skullcap, catch tree and white mulberry** TODAY!

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

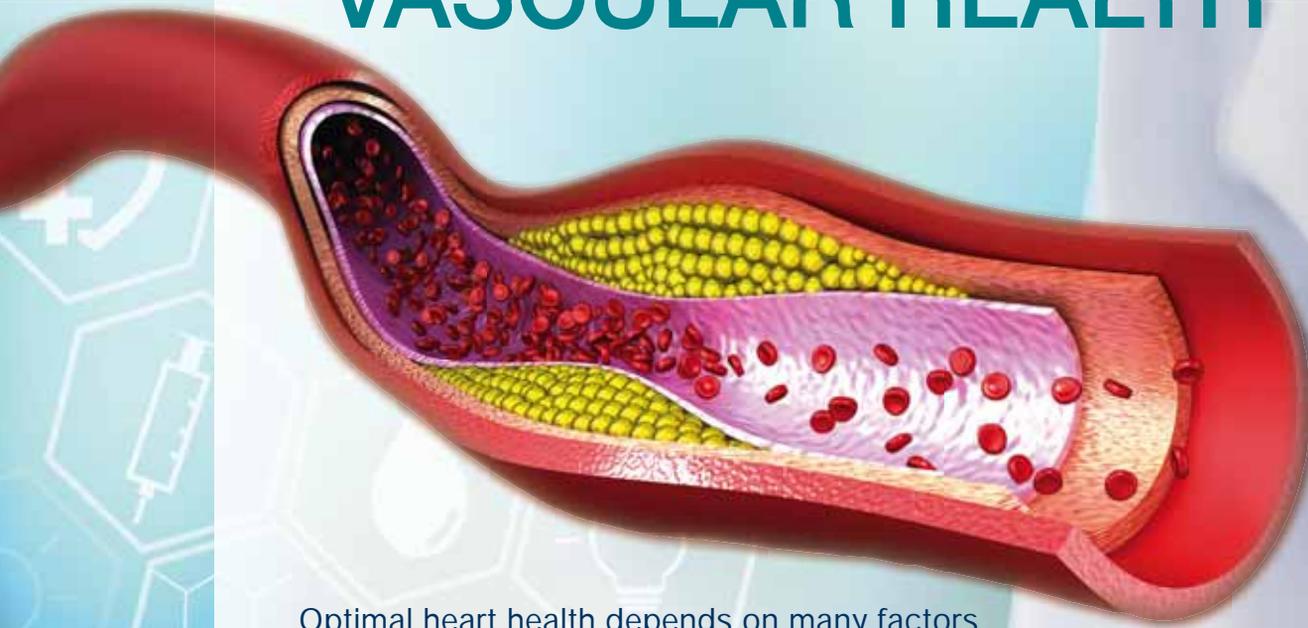


Item #02138 • 30 vegetarian tablets

1 bottle **\$22.50**

4 bottles \$20 each

BOOST AND PROTECT YOUR VASCULAR HEALTH



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

TRIPLE-ACTION PROTECTION

Endothelial Defense™ with Pomegranate Complete

contains three unique ingredients shown to support endothelial health.

1. Pomegranate Complete

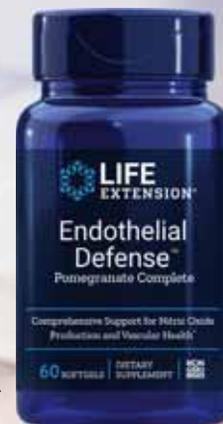
provides potent polyphenols scientifically shown to support healthy blood flow.

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

3. Sweet Orange Peel Extract supports nitric oxide production for healthy circulation.

Item #02097 • 60 softgels

1 bottle \$51 • 4 bottles \$46.50 each



For full product description and to order **Endothelial Defense™ Pomegranate Complete**, call **1-800-544-4440** or visit **www.LifeExtension.com**

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

Cardiose® is a registered trademark of INTERQUIM, S.A. d.b.a. Ferrer HealthTech.
POMELLA® Extract is covered under U.S. Patent 7,638,640 and POMELLA® is a registered trademark of Verdure Sciences, Inc.
Isocell SA, France is the owner of US Patents Nos. 6,045,809 and 6,426,068B1 and trademark of GLISODin®.



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Topical Collagen Helps Restore Youthful Skin



BY ROBERT GOLDFADEN AND GARY GOLDFADEN, MD



Replenishing depleted **collagen** levels is one of the first steps to revitalize aging skin.

Many commercial topical creams target **type I collagen**.

Overlooked is the role of other collagen types in rebuilding the skin's scaffolding.

A topical formula featuring **three peptides** has been shown to synthesize all major **collagen types** in the dermis and dermo-epidermal junction.

By providing total **collagen support**, these **peptides** can visibly improve skin firmness and smoothness, while producing long-lasting anti-wrinkle effects.

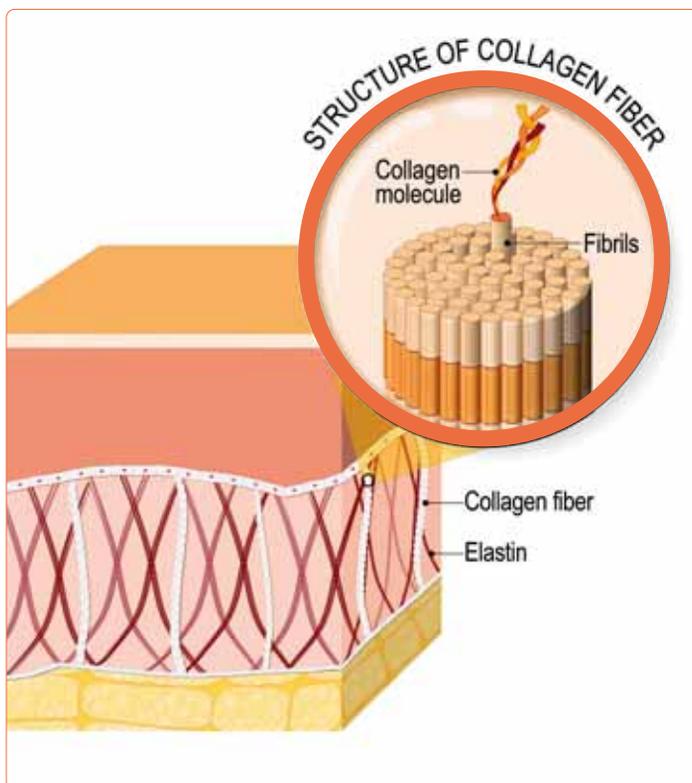
Collagen: The Foundation of Youthful Skin

Collagen is the main protein of connective tissues in humans and accounts for **70%-80%** of the skin's dry weight.¹ It's vital for skin cohesion, firmness, and resilience.^{2,3}

Skin has five major collagen types that can be divided into two classes:

1. **Fibrillar collagens** (type I and III) reside in the dermis where they form well-organized, rope-like fibers that supply robust tensile strength and resistance to stretching and tearing.⁴ In fact, type I collagen is stronger than steel on a gram-for-gram basis.⁵
2. **Non-fibrillar collagens** (type IV, VII, and XVII) reside in the dermo-epidermal junction where they self-assemble a scaffolding network that anchors the dermis to the epidermis above it.⁶⁻⁹ This provides structural integrity and mechanical stability to the skin.

In essence, this collagen team organizes the underlying architecture of the skin to keep it firm, smooth, and youthful.



What Causes Collagen Loss?

Aging decreases the synthesis of **collagen fibers** in the dermis, and causes existing collagen fibers to become disorganized, stiff, and fragmented.^{10,11}

Decreased production of **non-fibrillar collagens** also contributes to skin aging.¹²⁻¹⁵

The unfavorable effects of aging on skin tissue are exacerbated by chronic exposure to sunlight and air pollution.

These environmental factors generate inflammation and oxidative stress that trigger activation of collagen-destroying *enzymes* known as **matrix metalloproteinases** (MMPs).¹⁶⁻¹⁹

The end results are wrinkles, fine lines, dryness, and saggy skin.

Many topical products focus only on **type I collagen** without recognizing the significance of other collagen types in restoring youthful skin integrity and function.

That is why scientists developed three unique **peptides** that renew all major collagen types to rejuvenate aged and damaged skin.

Palmitoyl Tripeptide-5

Peptides are compounds composed of amino acids, which form the building blocks of proteins in our skin, including collagen.²⁰

A group of peptides has been shown to activate **growth factors** that promote youthful **collagen synthesis**.^{20,21}

An in-vitro study found that one of these growth peptides called **palmitoyl tripeptide-5**, along with another peptide:²²

- Increased type I collagen by **110%**
- Increased type III collagen by **40%**
- Increased type IV collagen by **190%**
- Increased type VII collagen by **60%**
- Increased type XVII collagen by **120%**

These findings have translated into impressive real-world benefits.

In a clinical study, topical application of palmitoyl tripeptide-5, twice daily for two months, increased skin firmness by **10.8%** compared to a placebo.²²

Researchers investigated the efficacy of **palmitoyl tripeptide-5** in diminishing fine lines and wrinkles.



WHAT YOU NEED TO KNOW

Collagen Peptides Restore Youthful Skin

- Collagen is essential for skin firmness, cohesion, and resilience.
- Fibrillar collagens (Type I and III) form rope-like fibers in the dermis that supply high-tensile strength, whereas non-fibrillar collagens (Type IV, VII, and XVII) self-assemble a scaffolding network in the dermo-epidermal junction that tightly connects the dermis to the epidermis above it.
- Aging and chronic exposure to external factors like sunlight and air pollution reduce the synthesis of collagen and increase its degradation to set the foundation for wrinkles, fine lines, and sagging skin.
- Many topical products only target type I collagen and overlook the significant impact of other major collagen types in rebuilding the skin's scaffolding.
- A new topical formula has been developed with a trio of unique peptides—palmitoyl tripeptide-5, palmitoyl tripeptide-1, and palmitoyl tetrapeptide-7—shown to regenerate all major collagen types in the dermis and dermo-epidermal junction.
- Controlled human studies show that these peptides provide total collagen care to reconstruct the dermis and reinforce the dermo-epidermal junction, which improves firmness, smoothness, and erases wrinkles to restore a youthful appearance.

Participants who applied a topical formulation with **palmitoyl tripeptide-5** experienced a reduction in fine lines by **20%** and in deep wrinkles by approximately **28%** *within minutes* of initial application. These parameters further improved to about **38%** and **50%**, respectively, after three months.²¹

Researchers concluded that this topical treatment containing **palmitoyl tripeptide-5** was “*well tolerated and provided both immediate and long-term improvements in the appearance of fine lines and wrinkles.*”²⁰

Palmitoyl Tripeptide-1 and Palmitoyl Tetrapeptide-7

During the aging process, specialized cells known as **fibroblasts** become less active and produce lower levels of collagen than in youth.²³

Two **peptides**—palmitoyl tripeptide-1 and palmitoyl tetrapeptide-7—have been shown to breathe new life into aging **fibroblasts**.

These peptides were shown to increase production of **collagen types I, IV, VII, and XVII**.²⁴

By stimulating dermal regeneration and strengthening the dermo-epidermal junction, these **peptides** can drop years off the outer appearance of skin.

This was demonstrated in a clinical study involving 23 females between the ages of 42 to 67 who topically applied a combination of these **peptides** to one half of the face and a placebo to the opposite side.²⁴

By day 60, researchers observed the following improvements:²⁴

- **39.4%** decrease in area occupied by deep wrinkles
- **32.9%** decrease in wrinkle density
- **19.9%** decrease in main wrinkle depth
- **23.3%** decrease in main wrinkle volume
- **16.0%** decrease in roughness
- **16.2%** decrease in complexity

An assessment of skin tone and elasticity showed improvements of **15.5%** and **5.5%**, respectively, during the same time frame.²⁴

Summary

With advancing age, your skin progressively loses **collagen**, and this is compounded by increased exposure to external damaging factors.

Depletion of collagen weakens the skin's underlying support structure, contributing to wrinkles, sagging, and creping.

A novel, topical formula has been developed with three unique **peptides**—palmitoyl tripeptide-5, palmitoyl tripeptide-1, and palmitoyl tetrapeptide-7—shown to replenish all the major collagen types in the dermis and dermo-epidermal junction.

By providing **total collagen** care, these peptides help correct **structural changes** in aging skin to boost firmness and smoothness, erase wrinkles, and restore a youthful appearance. •

Gary Goldfaden, MD, is a clinical dermatologist and lifetime member of the American Academy of Dermatology. He is the founder of Academy Dermatology in Hollywood, FL, and Cosmesis Skin Care. Dr. Goldfaden is a member of the **Life Extension**® Medical Advisory Board. All Cosmesis products are available online.

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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A report published in Germany showed that SAMe may help maintain healthy neurological function. This impressive report found that SAMe:²

- **Increased** glutathione levels by **50%** and glutathione enzyme activity by **115%**,
- **Decreased** a measurement of free radical activity by **46%**, and
- **Inhibited** lipid peroxidation by **55%** in culture.

In addition to these findings, SAMe also improves brain cell methylation, thereby facilitating youthful **DNA enzymatic actions**, which may help account for SAMe's mood-boosting properties. These enzymatic reactions are required for the healthy conversion of neurotransmitters such as **serotonin** and **dopamine**.

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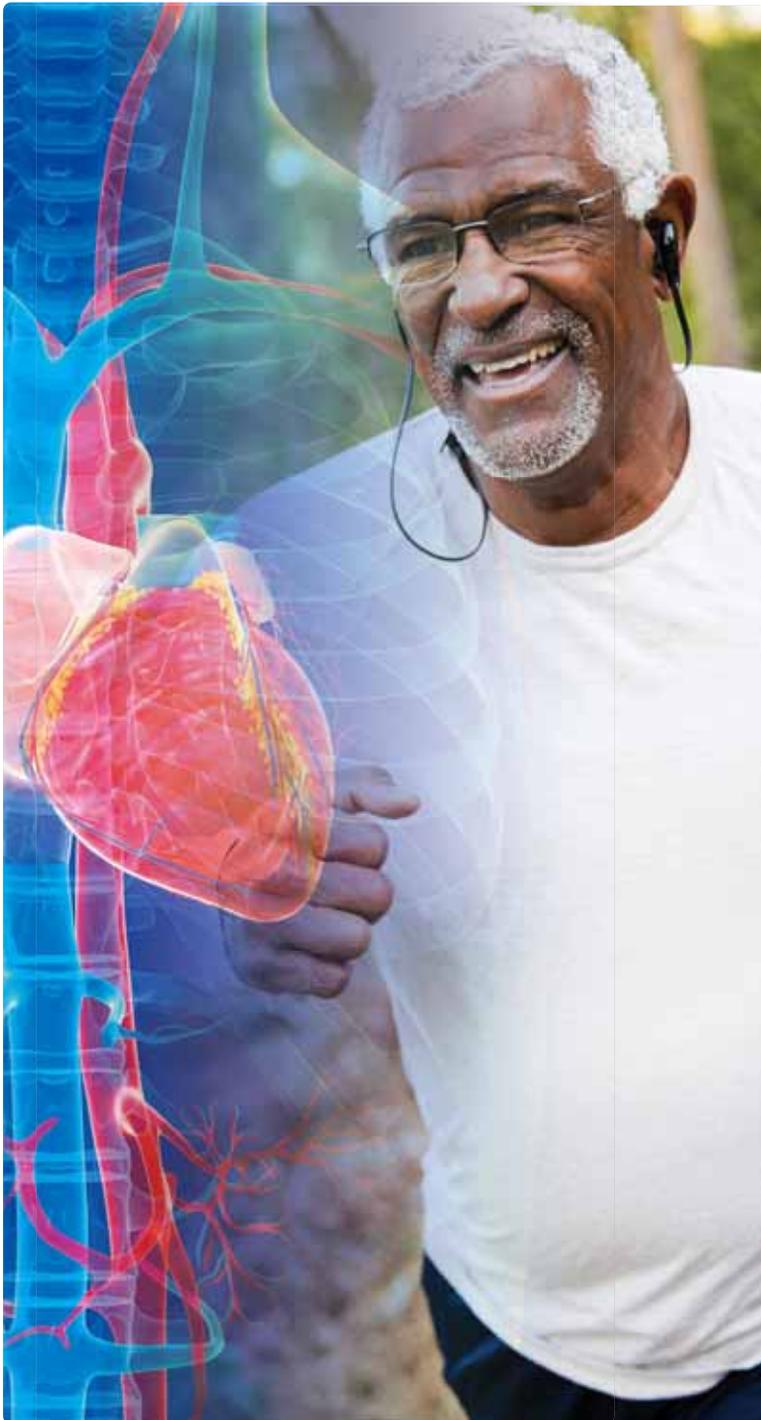
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Fish Oil Prevents Heart Disease by Reducing Adhesion Molecules

BY STEPHANIE CLARK



There is evidence that omega-3 fatty acids can reduce adhesion molecules and the buildup of plaque they cause.

Fish oil has been extensively studied to determine how it may prevent cardiovascular diseases.

That beneficial effect is often attributed to the ability of **omega-3s** to reduce **inflammation**, which drives the formation of artery-clogging plaque.

Other cardioprotective effects of fish oil include lowering of **triglycerides** and reduced **platelet aggregation** that can otherwise block a coronary or cerebral artery.

Heart disease and strokes, however, have another major underlying cause: **adhesion molecules**.

These are tiny Velcro-like barbs present on endothelial cells and on the surface of circulating white blood cells. They are a critical initiator of **atherosclerosis**.^{1,2}

A recent review reports on clinical studies showing that omega-3s (**EPA** and **DHA**) in **fish oil** can *reduce adhesion molecules* by **up to 28%**.

This is another way that fish oil functions to curtail atherosclerosis and lower heart disease and stroke risk.²

How Adhesion Molecules Form Plaque

Endothelial cells line the inside of all blood vessels, including the arteries.

Adhesion molecules on endothelial cells and on white blood cells promote atherosclerosis.^{1,3}

Adhesion molecules are like tiny barbs on the surface of those cells, making white blood cells **stick** to the blood vessel lining.^{1,2,4}

This adhering of **white blood cells** to a **blood vessel** sets in motion the process of arterial plaque formation. The consequences are blood flow blockage and acute rupture of unstable arterial plaques.²

Efforts to reduce adhesion molecule production have become a topic in cardiovascular disease prevention research.



Fish Oil Reduces Adhesion Molecules

There is evidence that **omega-3 fatty acids** can *reduce* adhesion molecules and the buildup of plaque they cause.^{2,3}

A meta-analysis of 18 randomized, controlled, human trials found significant reductions in **adhesion molecules** in subjects who supplemented with omega-3s.⁵

And a recent review found reductions in adhesion molecules of **up to 28%** in people taking fish oil or its omega-3 constituents, **EPA** (eicosapentaenoic acid) and **DHA** (docosahexaenoic acid).²

Doses in this report ranged as high as **4,000 mg EPA** and **3,500 mg DHA** per day.

Multiple Effects of Omega-3s

Lab studies of human endothelial cells in culture show the impact of omega-3 fatty acids on adhesion molecules:

- **Omega-3s**, particularly **EPA**, lower the production of **inflammatory cytokines** and **adhesion molecules**. This can stop white blood cells from sticking to artery walls.^{6,7}
- **DHA**, an omega-3 also found in fish, significantly reduces cell adhesion in response to the inflammation-promoting cytokine **tumor necrosis factor-alpha (TNF-alpha)**.⁸
- **Maresin 1** is formed from **DHA** and has anti-inflammatory properties. It reduces the secretion of inflammatory cytokines and adhesion molecules.

It also reduces stress on the cell that can lead to premature cell death.⁹ **Maresins** have such robust cell-protective, anti-inflammatory, and pro-healing properties that they're being explored as drugs.¹⁰⁻¹²

Animal studies confirm the importance of these findings:

- Hamsters given EPA and DHA-rich fish oil had up to a **six-fold reduction** in white blood cells "sticking" to small artery walls.^{13,14}
- In mouse aortas treated with fish oil, reductions in atherosclerosis were accompanied by significant *decreases* in **adhesion molecules** that lead to the progression of **plaque**.¹⁵
- Hamsters taking fish oil had significantly less vessel damage during **ischemia** and **reperfusion**. These terms (ischemia and reperfusion) refer to the loss of blood flow that occurs during a heart attack or stroke and the impact of sudden restoration of circulation that occurs when a stent is inserted or a blood clot dissolved or mechanically removed from an occluded artery. Fish oil's ability to *suppress* the release of **adhesion molecules** was an important contributor to this beneficial effect.¹⁴
- Mice given fish oil had significantly *reduced* early atherosclerotic plaque, as a result of sharp reductions in molecules that promote the release of inflammatory cytokines and adhesion molecules.¹⁶

Summary

Adhesion molecules are produced on white blood cells and the cells lining our arteries when they are stressed.

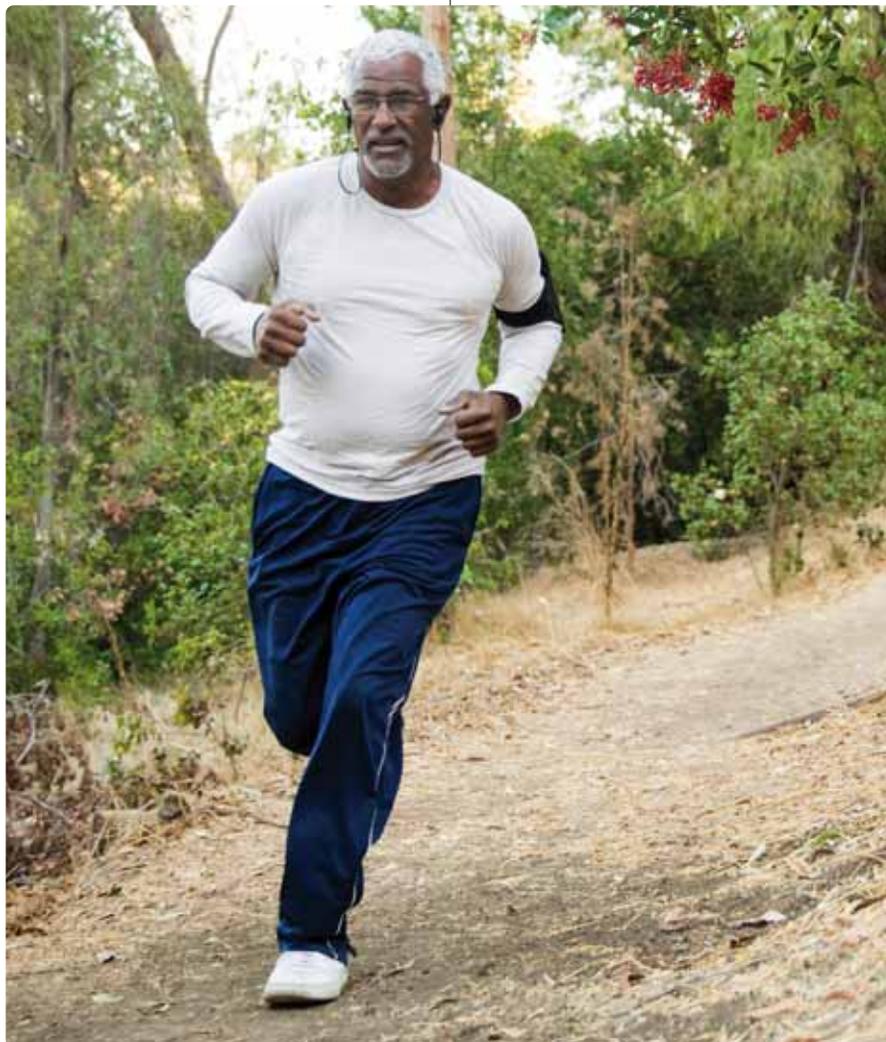
They act like tiny barbs of Velcro that attach to each other and initiate atherosclerotic plaque formation and create further inflammation-driven dysfunction.

Reducing amounts and function of **adhesion molecules** is a major goal of modern cardiovascular medicine.

Studies reveal that daily intake of **omega-3 fatty acids** from fish oil *reduces adhesion molecules*, preventing the sticky, white blood cell/blood vessel interaction, and permitting smoother flow of blood.

This reduced adhesion molecule production is associated with reductions in early atherosclerotic plaque and lower risk of cardiovascular disease. ●

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

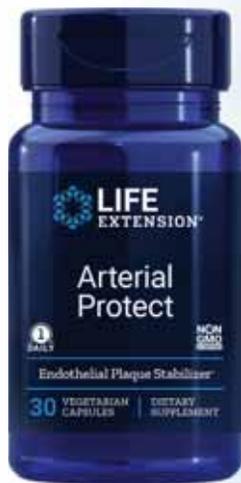


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* *Int Angiol.* 2014 Feb;33(1):20-6.

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Advances in Microbiome and Toxic Chemical Testing

BY DR. SHANTI ALBANI AND DR. SCOTT FOGLE



We're hearing a great deal about the state of our **gut microbiome** and our exposure to **toxic chemicals**.

Life Extension® recently spoke with Dr. Shanti Albani and Dr. Scott Fogle about new tests that help us understand both—and about what steps can be taken to correct any problems.

Check Your Gut Health

Study after study has shown that the makeup of our **gut microbiota**—the bacteria and other microbes living in the large intestine—has tremendous influence on both gastrointestinal issues and overall health.

Life Extension® offers one of the most comprehensive gastrointestinal tests ever developed, which offers insight into a patient's microbiome, and much more.

In this interview, **Dr. Shanti Albani** explains how it works and what it offers.

LE: What can you tell us about this new gastrointestinal (GI) test?

Dr. Albani: The **GI360™ Profile** is named for the 360-degree, detailed picture of gastrointestinal health it provides. The test looks at microbial balance, identifies pathogens, and includes multiple markers of gastrointestinal function, inflammation, and integrity. It provides more quality information than any test I have seen before.

LE: Is this test for people with intestinal issues or a wider range of individuals?

Dr. Albani: This test is for *everyone*. Hippocrates said, “All disease begins in the gut,” and now, more than 2,000 years later, research is proving that to be true. The bacteria in our intestines influence our mood, weight, and cardiovascular and liver health. Our gut



microbiota shape how our immune system behaves in response to toxins, food, and pathogens, which influences our likelihood of an autoimmune disease or allergies. Our gut bacteria make chemicals, including neurotransmitters, which impact us for better or worse. I have seen cases where chronic brain fog only lifted after testing and favorably modulating the gut microbiota.

LE: What exactly does this test reveal?

Dr. Albani: One of the most fascinating components of the GI360™ Profile is the **microbiome abundance and diversity testing**. That tells you which major groupings of bacteria are occupying your intestines. It includes both a high-level view of the balance between the six main groups, or phyla, of bacteria, and detailed identification of individual species of bacteria. Profiling the phyla tells you if your bacterial pattern matches those of healthy

people or is more reflective of the unbalanced bacterial patterns associated with intestinal symptoms, obesity, or other health concerns.

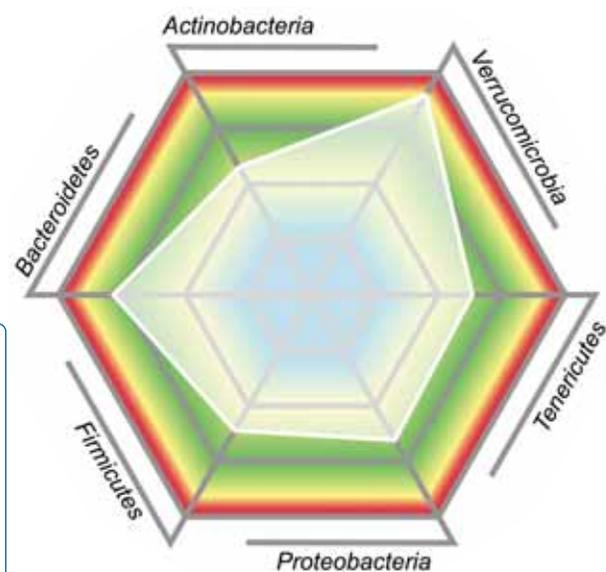
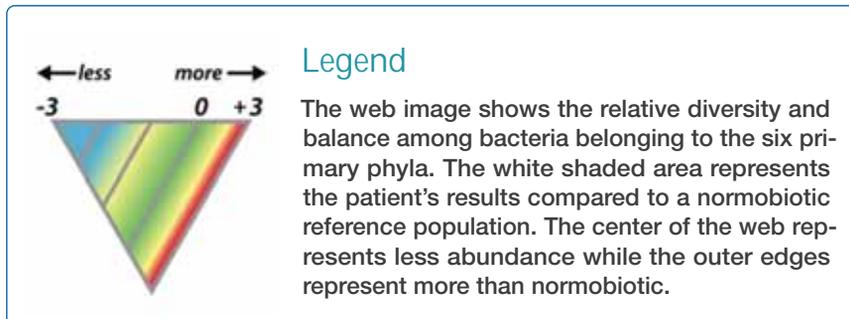
LE: What makes this test different from others on the market?

Dr. Albani: For one, it’s *extremely accurate*. The test uses sophisticated DNA probes to identify intestinal microbes according to their DNA fingerprint. This bacterial profiling has been used in over 20 clinical trials and has been clinically verified to separate individuals with an imbalanced, or *dysbiotic*, gut flora from those with a healthy one.

Also, other gut microbiota tests will often just provide a list of bacteria without any context, leaving the person baffled about what the information means. The GI360™ Profile results include information on the health impact of microbial imbalances *and* potential actions to shift the gut microbiota toward a more balanced state.

Microbiome Abundance and Diversity Summary

The abundance and diversity of gastrointestinal bacteria provide an indication of gastrointestinal health, and gut microbial imbalances can contribute to dysbiosis and other chronic disease states. The GI360™ Profile is a gut microbiota DNA analysis tool that identifies and characterizes more than 45 targeted analytes across six phyla using PCR and compares the patient results to a characterized normobiotic reference population. The web chart illustrates the degree to which an individual’s microbiome profile deviates from normobiosis.



Dysbiosis Index

The Dysbiosis Index (DI) is a calculation with scores from 1 to 5 based on the overall bacterial abundance and profile within the patient's sample as compared to a reference population. Values above 2 indicate a microbiota profile that differs from the defined normobiotic reference population (i.e., dysbiosis). The higher DI above 2, the more the sample is considered to deviate from normobiosis.

DI Score
4



LE: Does the test look for pathogenic bacteria as well?

Dr. Albani: Of course. The next section of the test focuses on **GI pathogens**. It uses microbial DNA probes to detect 14 pathogens, including villains like rotavirus, *Salmonella*, *Shigella*, *Clostridium difficile*, and *Giardia*. Anyone with acute intestinal symptoms or ongoing intestinal distress should be looking to rule these problem-causers out.

LE: Can it detect parasites?

Dr. Albani: Yes. The GI360™ Profile includes a **microscopic stool examination**. This examines the stool for parasite larva, eggs, or adults. The highly experienced lab techs who perform these tests can detect protozoa, tapeworms, flukes, roundworms, and yeast by looking at the stool under the microscope. You would be surprised how many people have unwelcome travelers in their intestines!

LE: Yeast like *Candida* can cause fungal infections. Does the GI360™ Profile screen for that?

Dr. Albani: It does. The test includes a **bacterial and yeast culture**, which is the gold standard for detecting intestinal bacterial and yeast overgrowth. The lab we partner with uses advanced culture techniques, with 10 different

growing conditions instead of the three used by most labs, along with a yeast culture able to detect over 170 species of yeast and 80 species of *Candida*. *Candida* and yeast overgrowth is a common concern associated with bloating, fatigue, and brain fog.

The culture also features a **sensitivity section**. That means if an unwanted microbe is identified, the lab provides information about its sensitivity to various antibiotics and to natural agents. That gives individuals and their healthcare providers treatment flexibility and greater confidence that a treatment will be effective.

LE: Does the test measure anything else?

Dr. Albani: The last section of the GI360™ Profile is **stool chemistries**. This looks at a broad range of markers to evaluate digestive capacity, intestinal immune function, and intestinal inflammation. Our digestive system should efficiently extract nutrients and calories from the food we eat. Stool that tests positive for carbohydrates, fat, or too many muscle and vegetable fibers can indicate a lack of digestive power. In addition, stool should have adequate amounts of the pancreatic enzyme elastase. If elastase is low, it can indicate that your pancreas is not producing adequate enzymes to optimally digest food.

Inflammation is a driver of chronic disease and aging. The GI360™ Profile includes three markers of intestinal inflammation— and one marker of intestinal immune function, secretory immunoglobulin A (sIgA). The inflammatory markers can both identify inflammation and help distinguish its cause. For example, an elevation in all three intestinal inflammation markers would be expected in ulcerative colitis and Crohn's disease, but if only lysozyme is elevated, it is more indicative of an intestinal infection.

LE: That sounds incredibly thorough. Is there anything else the stool chemistries section reveals?

Dr. Albani: It shows levels of a unique marker called β -glucuronidase. High levels of β -glucuronidase may be associated with an imbalanced intestinal microbiota, as well as higher circulating estrogen in premenopausal women and potentially less efficient toxin elimination. Given that we now live in a world saturated with pollutants, this marker can help us determine if our gut microbiota is working well enough when it comes to detoxification.

LE: What steps can someone take if the GI360™ Profile raises concerns?

Dr. Albani: Anything marked as abnormal is commented on at the end of the results report so individuals are not left in the dark about its

meaning. Anyone who has done the test can call to review the results with one of the highly trained **Life Extension® Wellness Specialists** at no additional cost. They can provide a wellness plan that can be discussed with your healthcare provider to assist in making the best decisions related to your results.

Measure Toxic Chemical Levels

As Dr. Albani notes, our **gut microbiota** can help us cope with pollutants, but only to a degree. It's vital to ensure that levels of **toxins** in our body aren't too high.

Life Extension® is also offering a new urine test that can measure levels of toxic chemicals in the body.

In this interview, **Dr. Scott Fogle** discusses what this test can tell us and how we can help our bodies detox.

LE: What does this new test screen for?

Dr. Fogle: Last year, we introduced our **Toxic Metals Panel Fecal Test**, stool testing to look at levels of some of the worst *metal* toxins like mercury. This year, we are introducing the **Environmental Pollutants Profile**, a urine test to look at some of the most problematic *chemicals* like toluene, benzene, xylene, and parabens.

LE: Why is one a stool test and the other a urine test?

Dr. Fogle: It relates to how the body processes, or detoxifies, the different toxins we are exposed to. Heavy metals are naturally detoxified via the liver and then excreted in the stool. Chemical toxins are more often excreted in urine.

LE: How are people exposed to these chemicals in the first place?

Dr. Fogle: They are ubiquitous in the environment nowadays. Here are the most common sources of these toxins:

- **Xylene:** an additive in gasoline which is also used to produce solvents, fragrances, coatings, and paints.
- **Toluene:** an additive used in nylon and plastics that is also found in gasoline, coatings, paints, synthetic fragrance, adhesives, inks, and cleaners.
- **Trimethylbenzene:** a petroleum-based additive that may be found in gasoline, paints, and cleaners, and also in contaminated groundwater.
- **Styrene:** an additive used in plastics, fiberglass, rubber, and latex found in insulation, packing materials, printer ink and toner cartridges, household objects, car exhaust, and cigarette smoke.

- **Phthalates:** plastic additives used in vinyl flooring, raincoats, nail polish, and body-care products.
- **Parabens:** preservatives used in cosmetics, body products, foods, and medications.
- **Methyl tert-butyl ether (MTBE):** a gasoline additive inhaled from gasoline or car exhaust fumes.

LE: Who is at risk from these chemical toxins?

Dr. Fogle: All of us. Even healthy people will become sick if exposed to excessively high amounts of these chemicals. We are, in a sense, filters and air purifiers for the environment around us. We accumulate toxins, and there is a theory that once the body is saturated with chemicals beyond its ability to cope or detoxify them, the toxins start affecting our health. Everyone can benefit from getting their toxin levels checked.



The *most* susceptible people are those who have inherited low-activity forms of detoxification enzymes, those with poor nutrition or poor nutrient absorption due to gastrointestinal issues, or those suffering from existing chronic inflammatory or autoimmune conditions. It may be especially important for these people to monitor and reduce their exposures to toxic chemicals.

LE: What can people do if they have high toxin levels?

Dr. Fogle: There are many approaches that can help with detox. Exercise is often vital. Sweating can help—but make sure to shower right after or you can start absorbing the toxins right back in through the skin. Infrared saunas also helpful. Consume **2-3 liters** of clean water daily. It is also important to consume fresh, organic fruit and veggies. They contain nutrients that support our liver's ability to detox.

LE: Are there nutrients people can take directly that also support detoxification?

Dr. Fogle: Yes. My all-time favorite is **glutathione**. I think of it as a bodyguard that grabs a toxin, binds to it, and escorts it out of the body. **Lipoic acid** is another of my top choices, because it can function as an antioxidant in both a water and fat environment, which means it can work in every cell. The amino acid **glycine** is also needed for detox, as are the minerals **magnesium** and **selenium** and **vitamins E** and **C**. **Sulforaphane**, which is found in broccoli sprouts, also activates detoxification enzymes.



LE: Does gastrointestinal health play a role in healthy detox?

Dr. Fogle: Yes, it is critical for good detoxification. The longer stools stay inside you, the more chance you have of reabsorbing some of the toxins your body works so hard to get rid of. It is best to have two or three bowel movements a day if actively detoxing. Probiotics can be essential to help with this. •

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. Shanti Albani earned her medical degree in Naturopathic Medicine in 2003 from the National University of Natural Medicine in Portland, Oregon.

She practiced medicine for many years in central Mexico specializing in gastrointestinal disorders and hormone balance. During this time she taught courses for physicians in bioidentical hormone replacement therapy. She has worked at **Life Extension®** since 2010 and is currently the Manager of Clinical Information.

Dr. Scott Fogle is the Executive Director of Clinical Information and Laboratory Services at **Life Extension®**, where he oversees scientific and medical information as well as its laboratory division.

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References

1. Available at: <http://lpi.oregonstate.edu/mic/vitamins/thiamin>. Accessed January 4, 2018.
2. *Neurosci Bull.* 2016;32(6):591-6.

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- 01713 Vitamin D3 • 125 mcg (5,000 IU), 60 softgels
- 01718 Vitamin D3 • 175 mcg (7,000 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
- 01823 CalReduce Selective Fat Binder
- 02478 DHEA Complete
- 01738 Garcinia HCA
- 01292 Integra-Lean®
- 01908 Mediterranean Trim with Sinetrol™ -XPur
- 01492 Optimized Irvingia with Phase 3™ Calorie Control Complex
- 01432 Optimized Saffron with Satiereal®
- 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

Maintain Youthful **HOMOCYSTEINE LEVELS**

FOR BRAIN, HEART, AND HEARING HEALTH

Homocysteine Resist supports healthy levels of homocysteine, an unfavorable amino acid that can increase with normal aging.



Item #02121 • 60 vegetarian capsules

1 bottle **\$19.50**

4 bottles \$17.50 each

Just one daily capsule of **Homocysteine Resist** provides:

5-MTHF (activated folate)	5,000 mcg
Methylcobalamin (activated vitamin B12)	1,000 mcg
Pyridoxal 5'-phosphate (activated vitamin B6)	100 mg
Riboflavin (vitamin B2)	25 mg

Suggested dose: If your daily multi-vitamin contains activated B-vitamins, then take one capsule daily of **Homocysteine Resist** at a different time of the day.



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

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

Road Trip!

NON-STOP

*"Thanks,
Ultra Prostate
Formula."*

Ultra Prostate Formula can help:

- Support healthy urination
- Promote healthy prostate size and function
- Encourage healthy inflammatory response
- Help inhibit PSA activity

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

Item #02029 • 60 softgels

1 bottle **\$28.50**

4 bottles \$26.25 each



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